

Volume 8 Number 2 April-May 2013

# Respiratory Therapy™

The Journal of Pulmonary Technique

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**STOMAS**  
**NEONATOLOGY**  
**SUCTIONING**  
**ASTHMA**  
**PNEUMONIA**

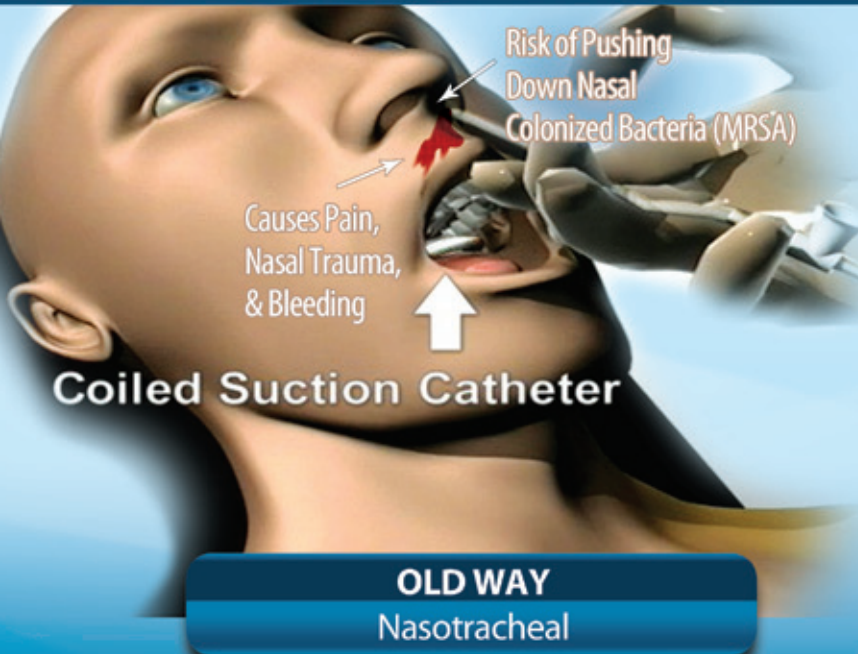


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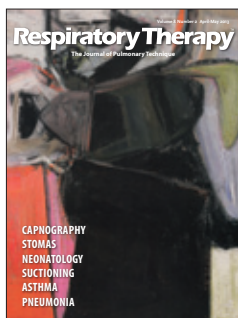
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## Respiratory Therapy™

The Journal of Pulmonary Technique

Vol. 8 No. 2  
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## Guest Editorial

### Bronchodilator Abuse

Albuterol and/or the combination of albuterol and ipratropium bromide is one of the most effective drugs for treating bronchospasm. It is also probably the most abused drug. This abuse is not necessarily by the patient, but by the doctors ordering it, or the nurse calling for the prn. As a registered respiratory therapist, I have been asked to give albuterol for many reasons that have nothing to do with the treatment of a bronchospasm. For instance, oxygen desaturation is one of the most common reasons. My way to combat this is to give the treatment on room air. Otherwise, when the patients' oxygen saturation "magically" rises from the 7-8 liters of oxygen, they believe the treatment worked. Other reasons are tachypnea, hypoventilation, excessive secretions and yes, even snoring. I have been called to give albuterol for croup, upper airway noises, CHF, pneumonia, pulmonary edema and pleural effusions. There is only one indication for giving albuterol and that is to treat bronchospasm. So let's briefly discuss why a prn albuterol will not help with these other conditions.

CHF (congestive heart failure), a condition where the heart is unable to pump sufficient blood flow, can cause fluid to build up in the lungs – pulmonary edema. This will make the patient feel short of breath and even have a cardiac wheeze. However this is not occurring in the bronchioles, so albuterol will have no effect. When this is treated as a bronchospasm, all we are doing is adding more fluid to already fluid-filled lungs. Perhaps the patient would be better treated with a diuretic and even bipap to help keep more fluid from building up on the lungs.

Croup, which is a viral infection of the upper airway, leads to swelling inside the throat. Again, this can interfere with normal breathing but is happening in the throat, not the bronchioles. A bronchodilator will not help here.

Lung cancer can be described as uncontrolled cell growth in the tissue of the lung. If the cancer spreads into the airways it can make it difficult to breathe. But unfortunately, a bronchodilator such as albuterol is defenseless against cancer. It will not absorb the cancer cells, break them up or lessen them in any way.

A pneumothorax is defined as air trapped in the pleural space separating the lung from the chest wall. As with the other conditions, it can also cause difficulty in breathing. However albuterol does not re-inflate collapsed lungs. A chest tube, if inserted properly, can and will help if the situation calls for one.

As respiratory professionals we are well aware of all of these inappropriate treatments. But it seems sometimes that the doctors ordering the bronchodilator and the nurses calling for it do not. I once had a conversation with a critical care doctor on why he orders bronchodilators for every trauma patient on a ventilator, regardless if the patient has a pulmonary history or not. All the while he is charting, "breath sounds clear," and his response was, MDIs (metered dose inhalers) are designed for patients on a ventilator.

I have heard many times from other health care professionals that albuterol doesn't hurt, so why not give it, when in actuality, it can have side effects and interactions, like any other drug when not taken properly. For instance, synchronal use with other adrenergic agents can have increased adrenergic side effects. Patients who use bronchodilators in conjunction with MAO inhibitors may risk a hypertensive crisis; they may also decrease serum digoxin levels. And beta blockers can negate the therapeutic effect of a bronchodilator. Some side effects include restlessness, tremors, headache, insomnia, palpitations, and hyperglycemia, to name a few.

Preventing overuse of bronchodilators is important. Patients should be advised of the potential adverse effects and the risks involved with overuse. In fact, excess use can lead to tolerance of the drug and even paradoxical bronchospasm.

*Continued on page 57...*





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# News

■ April-May 2013

## A MESSAGE FROM THE PUBLISHER

As a respiratory care provider, you should be aware that the Medical Device Tax, a 2.3% excise tax on medical equipment, went into effect on January 1. This tax, which is intended as a funding mechanism for portions of the Affordable Care Act (Obamacare), applies to all medical equipment for human use except those sold directly to the consumer. Pushback against the tax is not merely a political issue. Eighteen Democratic senators, including Harry Reid and Al Franken, had petitioned the President to halt implementation of the MDT, to no avail, with the Administration claiming that the increase in the patient pool as a result of more access to insurance would offset any

losses incurred by medical equipment manufacturers. The claim is specious. There's no actual evidence of an increased pool of insureds, since the majority of devices affected under the law are used in acute care settings, where patient care is already mandated. While the Administration also claimed that manufacturers might pass along the cost of the tax to their institutional customers, it should be noted that raising prices in our current economic climate is a non-starter. Plus, many such medical equipment purchases are fixed contracts. But perhaps the most onerous aspect of the tax is that it is on revenues, not profits. Since most medical equipment manufacturers are in effect small businesses (80% have less than 50 employees), and product manufacturing and innovation is often a long, expensive process, any profit is incremental. This means many companies will have to severely cut back on R&D, staff, and marketing. If fact, as we know from our contacts with manufacturers, this is already happening. In short, the tax is a very bad idea. According to the Medical Device Manufacturers Association, "This tax will stifle innovation, harm patient care and weaken the position of the United States as the global leader in medical device innovation." While the consequences of the tax for RTs and other respiratory caregivers are not immediately quantifiable, it will decidedly hurt innovation in the field. What can be done? We at Respiratory Therapy have contacted our elected representatives to warn them about the fallout from this tax, and are urging its repeal, and I urge you to do the same. (As we went to press, to counter the tax, Senators Orrin Hatch (R-UT) and Amy Klobuchar (D-MN) introduced the "Medical Device Access and Innovation Protection Act" and Reps Erik Paulsen (R-MN) and Ron Kind (D-WI) introduced the "Protect Medical Innovation Act.") – Steve Goldstein, Publisher

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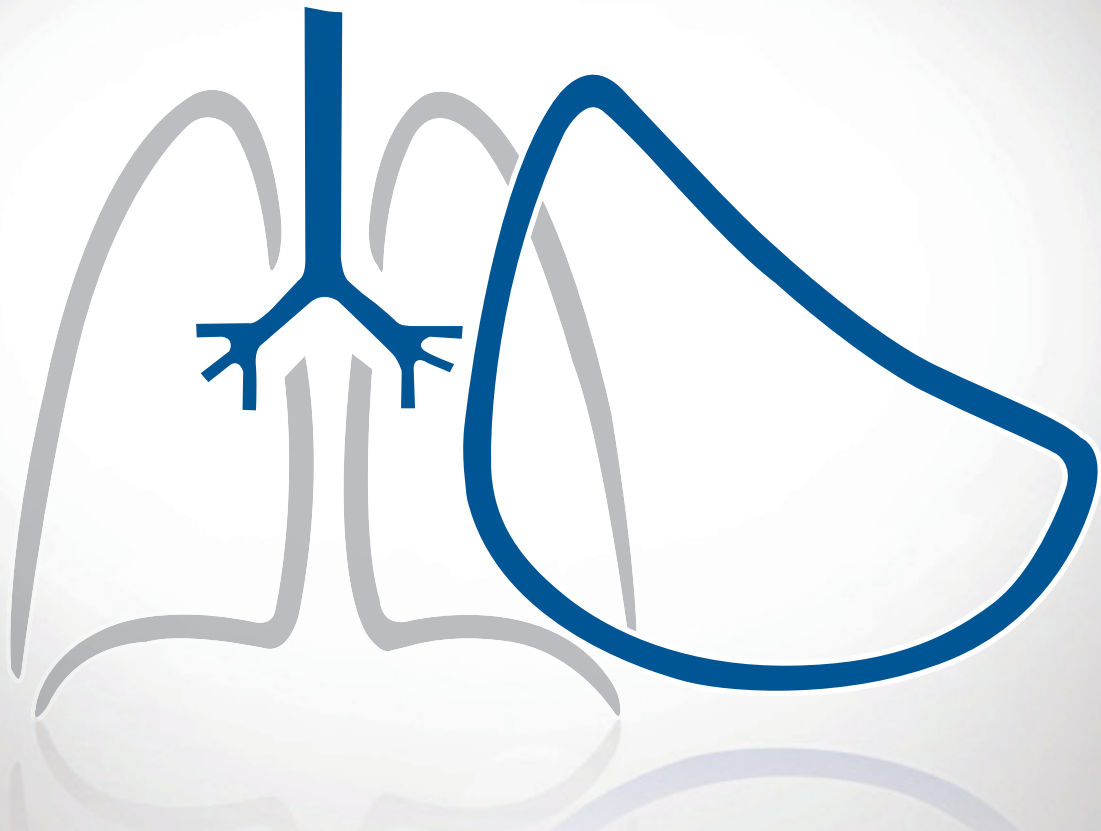
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## COPD

June 14 and 15 are the dates for the COPD8USA conference, hosted by The COPD Foundation. The content for this conference is designed to provide important clinical and scientific knowledge no matter what your role is in the healthcare provider team. The program is designed for primary care physicians, pulmonologists, advanced and registered nurses, physician assistants and respiratory therapists, medical directors, care coordinators and others who are involved and/or interested in the management of individuals with COPD. COPD8USA is dedicated to highlighting the changes in the current healthcare landscape and capitalizing on those changes to positively impact patient care. In order to address the new healthcare environment and educate physicians and healthcare providers about how to best utilize the new system to positively impact patient care, COPD8USA will include 3 tracks: Clinical, Research, and Care Delivery. Visit [www.copdconferencesusa.org](http://www.copdconferencesusa.org).

## BMC NEWS

Cases Database, BioMed Central's valuable new resource for the medical community, has now launched. Cases Database is a freely accessible and continuously updated search interface, developed by BioMed Central, which allows clinicians, researchers, teachers and patients to explore thousands of peer-reviewed medical case reports including content integrated from PubMed Central and publishers such as Springer and BMJ Group. By bringing case reports together, Cases Database adds value to individual reports, allowing comparison of similar cases, helping to highlight trends and patterns which may help researchers to develop hypotheses which can then be tested by systematic research. For more information please read BMC's

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## QUICK BREATH TEST

Researchers at the University of Vermont have identified the chemical fingerprints given off by bacteria in the lungs so diagnosis of TB and related lung infections can potentially be done by a diagnostic noninvasive breath test that shows results in minutes. The researchers infected mice with *Pseudomonas aeruginosa* and *Staphylococcus aureus*, and tested their breath after 24 hours, using secondary electrospray ionization mass spectrometry, which can find traces of compounds to one part per trillion. Such breathprints would be able to identify bacterial, viral and fungal infections of the lung. Information from Medical News Today, written by Catharine Paddock, PhD, copyright Medical News Today.

## DYSFUNCTIONAL

Infants with severe lower respiratory tract infection caused by RSV may have a dysfunctional innate immune response that relates to the severity of their disease, according to researchers at Nationwide Children's Hospital, who sought to determine whether patients with bronchiolitis admitted to the PICU had

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decreased whole blood functional innate immune responses. They also examined the relationships between innate immune dysfunction and disease outcomes. The team evaluated 66 previously healthy children less than two years old who were hospitalized with a first episode of RSV bronchiolitis during the 2010-2011 respiratory season. A nasal wash sample and a blood sample were obtained from each patient within 24 hours of admission to confirm RSV infection, and to measure cytokine concentrations before and after LPS stimulation. The team also enrolled healthy infants for control comparison. It was found that critically ill children with RSV admitted to the PICU had a significantly lower production capacity of innate cytokines compared with healthy controls and infants with less severe RSV bronchiolitis.

### **PERTUSSIS**

A study of 31 infants using medical records from five California PICUs found that taking early and many white blood cell counts is important in finding out whether infants have pertussis. California recently reported its highest pertussis rates in 60 years. The study showed that infants who had more severe pertussis had higher WBC counts and were more likely to show at least a 50% increase in WBC, with a median peak WBC count of 74,100 compared to 24,200 among infants with less severe disease. Thirty of the infants had at least a 50% increase in WBC within 48 hours, while none of those infants with less severe disease had more than a 50% increase. The infants with more severe infections had higher maximum heart and respiratory rates and were more likely to develop pneumonia. This group was more likely to have seizures, hypotension/shock, renal failure, and was more likely to be intubated and receive exchange transfusions.

### **NOTHING TO SNEEZE AT**

A woman's exposure to high pollen levels in late pregnancy increases the risk of early asthma in her child, according to researchers at Sweden's Umea University. In their study, high levels of pollen exposure during the last 12 weeks of pregnancy resulted in a significantly increased risk of hospitalization for asthma symptoms in a child's first years. The researchers posited that pregnant women's pollen exposure may affect the fetal environment, or that severe reactions to pollen might cause women to give birth earlier.

### **BLOWOUT**

People with asthma have an increased risk of pulmonary embolism, according researchers in the Netherlands, who studied 648 people with asthma, finding that those with severe asthma were 9 times more at risk of a pulmonary embolism than the general public. Those with moderate asthma were 3.5 times more at risk, and the study identified oral corticosteroids as a potential risk factor.

### **LEPTIN'S ROLE**

A study at Columbia University Medical Center found that leptin also regulates airway diameter, perhaps explaining why obese people are prone to asthma. Thus, the study suggests that body weight-associated asthma may be relieved with medications that inhibit signaling through the parasympathetic nervous system, which mediates leptin function. Through mouse studies, the researchers showed that abnormally low or high body weight and fat mass results in bronchoconstriction and diminished lung function, and that leptin increases airway diameter independently of its regulation of appetite. The researchers

found that infusing leptin into the brains of obese asthmatic mice had no effect on inflammation but the mice's lung functions were normal. The researchers noted that the therapeutic implication is that asthma could be corrected in people who are obese without affecting inflammation. One drug already available to increase leptin-related brain signaling is methacholine, currently used to diagnose bronchial hyperreactivity.

### **NYC TO THE ER**

Asthmatic children in New York City neighborhoods with high rates of asthma make many more visits to the emergency room than those who live in other parts of the city, according to research at Columbia and Dartmouth. Asthmatic children living in asthma hotspots were twice as likely to experience exercise-induced wheeze than those in neighborhoods with lower asthma rates. Researchers studied 195 middle income kids throughout New York City, finding that 43% had experienced exercise-induced wheeze, with those in hotspots twice as likely to have symptoms and visited an emergency room because of breathing problems. A third of the wheezing kids didn't use an inhaler prior to exercising. A previous report has noted that ER visits for asthma were 20 times more common in poor neighborhoods than elsewhere. This current study found that lung function, airway inflammation, allergy to common asthma triggers and symptom frequency didn't vary based on neighborhood, and it was by a process of elimination they found the link to rapid airway constriction brought on by exercise. But why some areas are asthma-prone, the researchers said, remains a mystery.

### **SLEEP DISORDERED**

About 10% of 6 year olds have sleep-disordered breathing, according to a study by the University of Eastern Finland. The risk was increased among children with enlarged tonsils, crossbite and a convex facial profile. Excess body fat was not associated with sleep-disordered breathing in this group. The study enrolled 512 Finnish 6 to 8 year olds. Since excess weight is a major factor for OSA in adults, the researchers noted that the condition in kids might have a different type of pathogenesis.

### **NO BETTER**

Amoxicillin is no more effective at easing symptoms of bronchitis than doing nothing, according to researchers at the University of Southampton. The researchers noted that using amoxicillin to treat patients with respiratory infections who don't have pneumonia could even harm them. The researchers recruited 2,061 adults from 12 countries with mild chest infections, who were assigned amoxicillin or a placebo. The researchers added the caveat that while most bronchitis sufferers get better on their own, some do benefit from antibiotics; the trick was to find out who. It was also noted that patients taking the antibiotic reported side effects of rash, nausea and diarrhea. Reported by Catharine Paddock, PhD in Medical News Today, copyright Medical News Today.

### **DOCTORS' UNION**

Douglas Farrago, MD writes on his website, Authenticmedicine.com: "As more and more doctors become hospital employees it seems only inevitable that they will eventually unionize. Let's give a quick background. Insurers take over healthcare. Physicians are unable to stand up to them. Docs then get wooed by the hospitals to marry them in order to fight back (the enemy of my enemy is my friend). Docs become the [chattel] of the hospital administrators. The ACA is passed and the rest of the private doctors get employed. Lastly, in frustration,



they unionize which only drives up healthcare even more...” Farrago referenced a Wall Street Journal article which posited that organized labor already views service workers with nonexportable jobs as the last hope of labor unions, and that doctors may come to see themselves as workers, units of labor in a care-delivery system. [Editor’s note: the opinions expressed above are Douglas Farrago’s, not this journal’s.]

### SUPERBUGS

University of Cambridge researchers have discovered how the antibiotic-resistant superbug *P aeruginosa*, exploits oxygen-limited conditions in the lungs of patients with severe respiratory disease to thrive. When the bug encounters low oxygen conditions, a mechanism called the Type III Secretion System (T3SS) is triggered. The T3SS is believed to inject toxins directly from the bacterium into the host cell, where they subvert its function and lead to cell death. A metabolic switch called the glyoxylate shunt is activated when oxygen is sparse.

### LATEST ON SEPSIS

Scientists at Temple University School of Medicine have found that by blocking the activity of the protein STIM1 in cells that line the insides of blood vessels in mice, they’ve halted the cascade of cellular events that ultimately results in sepsis. STIM1 serves as a sensor for the amount of calcium inside a cell and drives calcium signaling, which is used for cellular communication. Researchers created mice lacking STIM1 in endothelial cells and compared these mice to normal mice exposed to the sepsis toxin. They found that without STIM1 in the cells, the calcium fluctuations did not occur, and endothelial cells were protected against the toxin-induced lung injury.

### FOREST FIRES

Pollution from forest fires is bad for people with asthma and other chronic obstructive lung diseases, according to the British Columbia Centre for Disease Control. Researchers studied dispensary records to find out if forest fires caused an increase in use of short acting beta agonist such as salbutamol. They found that pollution due to forest fires increased the need for salbutamol for up to 4 days after a fire, and that even a relatively small increase in smoke (10µg/m<sup>3</sup> increase in PM<sub>2.5</sub>) was associated with a 6% increase in salbutamol dispensations.

### SNORERS BEWARE

Snoring may put you at a greater risk for vascular diseases than being overweight, smoking, or having high cholesterol. Researchers at Henry Ford Hospital in Detroit found changes in the carotid arteries of snorers, and not just in people with sleep apnea. The researchers reviewed data for 913 patients who had been evaluated by the institution’s sleep center. Fifty-four patients completed a snore outcomes survey regarding their snoring habits and underwent a carotid artery duplex ultrasound to measure the intima-media thickness of their carotid arteries. Compared to non-snorers, snorers were found to have a significantly greater intima-media thickness.

### MISSED DIAGNOSIS

Pneumonia can’t be accurately diagnosed solely on a doctor’s analysis of symptoms and patient history, according to a study in the European Respiratory Journal. Researchers analyzed 2,810 patients across 12 European countries. Each patient had an acute cough and their attending doctor was asked whether pneumonia was present after looking at the patient’s signs and symptoms. All patients then received a chest radiograph by a different medical professional. One hundred forty patients were subsequently diagnosed with pneumonia. Out of this group, 29% had been correctly diagnosed by their doctor. Only 31 patients (1%) were incorrectly diagnosed as having pneumonia from an initial assessment that was later disproved by the chest radiograph. In patients without a doctor’s diagnosis of pneumonia, 96% indeed had no pneumonia after chest radiography.

### JOBS WITH RISKS

People with cleaning jobs are at a higher risk for developing asthma, according to researchers at Imperial College of London, who tracked the occurrence of asthma in a group of 9,488 people. Not including those who had asthma as children, 9% developed asthma by age 42. Risks in the workplace were responsible for one in six cases of adult onset asthma, more than the one in nine cases attributed to smoking. Eighteen occupations were linked to asthma risk, four of which were cleaning jobs, and three that involved exposure to cleaning products. Farmers, hairdressers, and printing workers were also found to have increased risk. Farmers were four times more likely to develop asthma as an adult than office workers. Besides cleaning products, flour, enzymes, metals, and textiles were among materials in the workplace identified in the study as being linked to asthma risk.

### ECLS FOR THE FLU

Toronto General Hospital has been using Extra Corporeal Lung Support (ECLS) to support five influenza patients in their recovery from severe respiratory problems. ECLS systems are normally used as a bridge to lung transplantation but recently the hospital was using ECLS on patients when ventilators can’t support patients whose lungs need a chance to rest and heal.

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## OHM

Mindful meditation may help people with chronic inflammatory conditions where stress plays a role, according to a study at the University of Wisconsin-Madison. Mindfulness-based stress reduction consists of continuously focusing attention on the breath, bodily sensations and mental content while seated, walking or practicing yoga. The study compared two methods of reducing stress: a mindfulness meditation-based approach, and a program designed to enhance health in ways unrelated to mindfulness. The comparison group participated in a program of nutritional education, physical activity, such as walking; balance, agility and core strengthening, and music therapy. Immune and endocrine measures were collected before and after training in the two methods. The mindfulness-based stress reduction approach was more effective at reducing stress-induced inflammation.

## EXPECTATION VS REALITY

Researchers at the University of Georgia discovered a large discrepancy in the length of time patients expect acute bronchitis to last, and the reality of the illness, and stated that this mismatch may be a factor in the over-prescription of antibiotics. The researchers found that most patients expect to cough for seven to nine days, but that a bronchial illness takes closer to 18 days to run its course. It was found that when a patient with bronchitis isn't better in four to five days, they see a doctor to get a prescription for an antibiotic, and when this doesn't work, they come back for more.

## PRODUCTS

### HONORED

Norman R. McCombs, Senior Vice President of AirSep Corporation, a wholly-owned subsidiary of Chart Industries, has been awarded The National Medal of Technology and Innovation. The medal is the nation's highest honor for technological achievement, bestowed by the President on America's leading innovators, awarded for outstanding contributions to US economic, environmental and social well-being. McCombs is a pioneer in the field of oxygen separation technology, responsible for 40 patents during his career. He created one of the primary technologies used in today's oxygen concentrators. Products stemming from his inventions include portable oxygen delivery systems for field hospitals in Iraq and Afghanistan, personal portable units greatly improving the quality of life for COPD patients, and the medical clinic at the base camp on Mount Everest, among others. Contact [chartindustries.com](http://chartindustries.com).



Norman R. McCombs receives The National Medal of Technology and Innovation

## AMONG THE BEST

Roche Diagnostics Corporation has been selected to Fortune magazine's annual list of the "100 Best Companies to Work For," joining companies such as Google, Starbucks and Nordstrom. Roche debuted at 89th on the list and is the only Indiana-based company selected. In selecting Roche Diagnostics for the list, Fortune cited the company's on-site medical clinic and fitness center, \$30,000 budget for intramural sports, and health insurance plans tiered to income levels. To see the list visit [fortune.com/bestcompanies](http://fortune.com/bestcompanies). For more about Roche Diagnostics, visit [roche-diagnostics.us](http://roche-diagnostics.us).

## EVIDENCE

Boehringer Ingelheim announced that the FDA Pulmonary-Allergy Drugs Advisory Committee (PADAC) recommended that clinical data included in a new drug application (NDA) provide substantial and convincing evidence to support the approval of olodaterol as a once-daily maintenance bronchodilator treatment for airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema. If approved by the FDA, it is anticipated that olodaterol will be marketed under the brand name Striverdi Respimat in the United States. The Committee also voted affirmatively that data showed the efficacy and safety of olodaterol and supports approval of the 5 microgram dose. The Committee reviewed data from the Phase 3 olodaterol clinical trial program, including data from the 48-week and 6-week duration trials. These data are part of the NDA being reviewed to establish that olodaterol delivered once daily at the 5 microgram dose showed improvements in lung function, as measured by forced expiratory volume in one second (FEV1), in patients with moderate to very severe COPD compared to placebo and also active comparators. In addition to the 48-week and 6-week duration studies, the Committee also reviewed a set of replicate studies evaluating the impact of olodaterol on exercise tolerance in COPD patients. This is the first time a company has sought inclusion of exercise tolerance data in a COPD product's label. Contact [boehringer-ingelheim.com](http://boehringer-ingelheim.com).

## SOLUTIONS

Covidien presented a host of advanced healthcare solutions for enhancing patient care and safety at the New York State Society of Anesthesiologists' 66th annual 2012 Post Graduate Assembly in Anesthesiology. Product demonstrations included the Oridion Capnostream 20 Patient Monitor, the Oridion Microcap Plus Patient Monitor, Nellcor Respiration Rate Software, the Nellcor Bedside Respiratory Monitoring System, the Nellcor Bedside SpO2 Patient Monitoring System, the INVOS Cerebral/Somatic

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Oximetry Monitor, the BIS Brain Monitoring System, the Nellcor SpO2 Single Parameter Module, the Mallinckrodt Tracheal Tube with TaperGuard Cuff, and the McGRATH MAC video laryngoscope. Contact covidien.com.

### GOODBYE AND HELLO

PneumaCare announced the departure of its CEO, Dr Ward Hills. Dr Hills has left the company to pursue other entrepreneurial interests with startups. Subsequently the company announced the appointment of its new CEO, Mark Harwood, who was previously President and CEO of ArjoHuntleigh, President of RF Technologies, and VP of Baxter International Inc. He has wide-ranging experience in medical device technology, and extensive regulatory and quality experience. Contact pneumacare.com.

### ACCELERATED

Janssen Therapeutics, Division of Janssen Products, LP, announced that the FDA has granted accelerated approval to SIRTURO (bedaquiline) Tablets for the treatment of pulmonary multi-drug resistant tuberculosis (MDR-TB) as part of combination therapy in adults. The accelerated approval is based on the surrogate endpoint of time to sputum culture conversion. SIRTURO inhibits mycobacterial ATP (adenosine 5' triphosphate) synthase, an enzyme that is essential for the generation of energy in Mycobacterium tuberculosis. It is a diarylquinoline antimycobacterial drug indicated as part of combination therapy in adults ( $\geq 18$  years) with pulmonary MDR-TB. The FDA accelerated approval of SIRTURO was based on data from two studies. The primary endpoint was time to sputum culture conversion, defined as the interval in days between the first dose of study drug and the date of the first of two

consecutive negative sputum cultures collected at least 25 days apart during treatment. Contact janssentherapeutics.com.

### AT THE ZENITH

Dräger was one of six companies out of a field of nearly 400 selected to receive the esteemed Zenith Award from the AARC. The award, which salutes companies that provide outstanding products and services to the respiratory care profession, was presented during the AARC's 58th International Respiratory Congress. An association of 52,000 respiratory therapists and other clinicians, the AARC established the Zenith Award program in 1989 to honor respiratory care product and service providers who provide the respiratory care community with exemplary service. The AARC members selected award recipients based on five criteria: quality of equipment and/or supplies, accessibility and helpfulness of sales personnel, responsiveness and service record, truth in advertising, and overall support of the respiratory care profession. Contact draeger.us.

### ASSISTANCE

Philips Respironics has received 510(k) clearance to market its latest advancement in airway clearance technology for enhanced patient care in the hospital or in the home. The new CoughAssist T70, provides an alternative to traditional suctioning methods and may minimize the risk of pneumonia and infections that can lead to hospital readmissions. The CoughAssist T70 clears secretions from the lungs by gradually applying positive air pressure to the airway and then rapidly shifting to negative air pressure. The shift in pressure creates a high expiratory flow that simulates a deep, natural cough. Instead of introducing a suction catheter into the airway, air is delivered through a



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facemask, a mouthpiece or through a simple adapter that allows the device to function with an endotracheal or tracheostomy tube, reducing discomfort and risk of infection. In addition, new design and technology updates have been developed to enhance patient and clinician use. The CoughAssist's Cough-Trak feature with automatic sensitivity allows patients to initiate therapy and synchronize treatment with their own breathing pattern. The CoughAssist weighs less than 9 lbs. In addition to AC and DC power options, a detachable lithium ion battery allows up to four treatments on a single charge. New data management software allows patients and caregivers to monitor tidal volume, peak cough flow and oxygen saturation levels to enhance therapy effectiveness. Contact [philips.us/coughassistT70](http://philips.us/coughassistT70).

#### WORLDWIDE DISTRIBUTION

SomnoMed Limited announced that it has entered into a contract with BRAEBON Medical Corporation, a Canadian company based in Ottawa, to become a worldwide distributor for the DentiTrac Base Station and DentiTrac Micro-Recorder, with exclusivity in Europe and parts of Asia Pacific and in SomnoDent's oral appliance design class in North America. The DentiTrac system, developed by BRAEBON, is a micro recorder which will be imbedded in SomnoDent oral appliances and monitors the wearing time of the SomnoDent device, as well as gathering other information (oral temperature, movements and head position) relating to the patient's sleep pattern during the night. Information is transmitted wirelessly to the DentiTrac base station and from there to the BRAEBON cloud. The detailed information about the patient's use of the SomnoDent device, in short one minute intervals during every night of use over a long period of time, can then be downloaded by a medical specialist, SomnoMed network dentists or other authorized entities. DentiTrac will now allow SomnoMed to enter into discussions with professional organizations which insist on nightly treatment of their sleep apnea diagnosed members and that demand proof of compliance. Contact [somnomed.com](http://somnomed.com) or [braebon.com](http://braebon.com).

#### THERE'S AN APP FOR THAT

The iChoice MD50I from Choicemed is an external pulse oximeter for iOS based device, which can measure SpO<sub>2</sub>, HR and display on the iChoice SpO<sub>2</sub>

App from Apple. It's intended for sports, aviation and medical applications on an iOS device. The climbers or pilots (doctors, patients) can use the device to quickly check their oxygen level through the iChoice SpO<sub>2</sub> App installed on an iOS device after connecting the external oximeter with the iPhone. The MD50I provides people a simple and convenient way to know their oxygen saturation and share the measured data with other people very easily using a smart phone. Users can easily review their measurement history and notes on the iChoice SpO<sub>2</sub> app to see if it has changed or improved. For more information, please visit [choicemed.com](http://choicemed.com).

#### NEW SOLUTIONS

Covidien unveiled new research and advanced solutions that enhance patient safety in critical care settings at the Annual Congress of the Society of Critical Care Medicine. The company discussed its latest findings concerning the impact of ventilator use and respiratory complications on hospital operating costs and Medicare reimbursements. Covidien also debuted its new portfolio of Kangaroo feeding tubes, including the first-ever disposable feeding tube that integrates a real-time imaging system to visually aid tube placement, and Covidien experts were available at the conference to discuss the company's new capnography device portfolio. Contact [covidien.com](http://covidien.com).

#### SUPPORT

Covidien announced its support for the Centers of Medicare & Medicaid Services (CMS) proposed quality measure #3040, currently considered for a Medicare program rule. Quality measures help CMS assess the performance of hospitals participating in Medicare and determine reimbursement based on factors that demonstrate compliance with high-care standards and "meaningful use," such as healthcare processes, outcomes and patient perceptions. Proposed quality measure #3040 calls specifically for monitoring respiratory rate, blood oxygenation (through pulse oximetry) and sedation scores in individuals on patient controlled analgesia pumps (PCAs) for longer than 2.5 hours. PCAs, which allow self-administration of pain management drugs, can be associated with dangerous respiratory complications, such as cardiac arrest. Covidien is urging clinicians and other industry leaders to voice their support for quality measure #3040 with guidelines added for continuous

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monitoring through capnography and pulse oximetry. Contact covidien.com.

## GO ON

Philips Respironics offers an advertising aid featuring its SimplyGo portable oxygen concentrator to promote a company's oxygen business on television. Distributors can customize the SimplyGo TV commercial and affordably promote their business to oxygen users. Philips' professionally produced commercial features actual SimplyGo user Mark Junge, who is seen bicycling, sightseeing, and hiking. How it works is: Philips sends a company the SimplyGo TV commercial; and the recipient can customize it with contact information. The company schedules and buys the commercial time; oxygen users and caregivers are directed to contact the company. Contact simplygo.respironics.com.

## UPDATED WEBSITE

Electromed, Inc, maker of the SmartVest Airway Clearance System, is pleased to announce the launch of its updated website: www.smartvest.com (also located at www.electromed.com). The new site is designed to assist patients, clinicians, and payers in making well-informed decisions regarding High Frequency Chest Wall Oscillation (HFCWO) and the SmartVest Airway Clearance System, while reflecting the new look of the company's brand. In addition to a refreshing new design, updated features include: • Improved navigation – will allow visitors to quickly find the information they need to access. • One-click access to prescription forms – immediately directs clinicians to the material they need to order the SmartVest System. Electromed, Inc manufactures, markets, and sells products that provide airway clearance therapy, including the SmartVest Airway Clearance System, to patients with compromised pulmonary function. For further information contact electromed.com or call (800) 462-1045.

## PRODUCT REVIEW

**Abstract:** Evaluation of the Neo-Tee T-piece Infant Resuscitator. Carl R. Hinkson, RRT FAARC, Cynthia White, RRT-NPS FAARC, Thomas A. Barnes, EdD RRT FAARC, Rob DiBlasi, RRT-NPS FAARC. Harborview Medical Center, Seattle, WA, Seattle Children's Hospital, Cincinnati Children's Hospital, Cincinnati, OH, Northeastern University, Boston, MA.

The Neo-Tee is a novel manually-cycled, pressure-limited and flow powered infant resuscitator that allows clinicians to adjust preset pressures and inhalation occurs when the operator occludes a restrictor valve. We hypothesized that there would be no differences between preset pressures on the Neo-Tee and those measured in a test lung following changes in PIP, PEEP, flow, and frequency with the Neo-Tee resuscitator. **METHODS:** An Ingmar ASL-5000 test lung (C:2, R:50) was attached to a Neo-Tee. The operator manually ventilated the lung model for two minutes with: 1) Pressure (PIP/PEEP) 10/5; 20/5, 40/5; 2) flow (L/min) 5, 10, 15; 3) rate (f/min) 20, 40, 60 and 4) different flow/PEEP combinations. Each test was repeated in triplicate using new Neo-Tee resuscitators (n=3). Pressures observed on the NeoTee were recorded in a lab notebook and lung model pressures and other test parameters were stored in the ASL software. Wilcoxin signed-ranks test, Kruskal-Wallis H test and Spearman correlation were used to compare differences between pressures. **RESULTS:** Changing flow from 5, 10, 15 L/min on the Neo-Tee had no effect on the PIP (P = .71) or PEEP (P = .31)

delivered to the test lung. There were significant differences between set PIP and PEEP on the Neo-Tee manometer and PIP and PEEP delivered to the lung model but there was good correlation between the set and delivered pressures (PIP: P = .000, [rs: 0.76 r2 0.58] ; PEEP: P = .01, [rs: 0.74 r2 0.55]). Changing the ventilatory rate from 20, 40, 60 had no effect on the PIP delivered to the lung model (rs -.03. r2 -.09); however, when Neo-Tee was operated at 60/min the lung model PEEP was ~1.81 cm H2O greater than the preset value. **CONCLUSIONS:** Based on these data, the Neo-Tee manual resuscitator operated within a clinically acceptable range for the majority of testing and well within the manufacturer's specifications for all testing conditions. We recommend operating the gas flow >5 L/min and frequently observing airway pressure measurements during resuscitation.

Testing Condition (changes from baseline)	f (rate/min)	I-time (sec)	Insp V <sub>T</sub> (mL)	PIP (cm H <sub>2</sub> O)	PEEP (cm H <sub>2</sub> O)
Baseline*	40.09 (.60)	.65 (.10)	40.54 (3.16)	21.04 (1.50)	5.37 (1.01)
Flow decreased to 5 L/min	40.36 (.38)	.79 (.34)	30.08 (7.32)	17.13 (4.58)	4.54 (1.51)
Flow increased to 15 L/min	39.29 (.26)	.60 (.16)	41.53 (.73)	21.02 (.39)	5.12 (.82)
PIP decreased to 10 cm H <sub>2</sub> O	41.26 (2.5)	.67 (.09)	18.19 (5.85)	11.79 (2.13)	4.8 (.28)
PIP increased to 40 cm H <sub>2</sub> O	39.89 (1.3)	0.9 (.12)	86.88 (7.5)	41.21 (.62)	7.41 (1.86)
f decreased to 20/min	20.33 (.47)	1.01 (.13)	43.74 (1.08)	21.30 (.66)	4.89 (1.02)
f increased to 60/min	60.18 (.46)	.51 (.17)	30.51 (1.72)	20.09 (1.86)	6.81 (1.66)
Flow lowered to 5 L/min PEEP lowered to 2 cm H <sub>2</sub> O	39.69 (.90)	.98 (.12)	36.90 (.53)	18.80 (1.0)	3.59 (.51)
Flow lowered to 8 L/min PEEP increased to 6 cm H <sub>2</sub> O	38.56 (3.36)	.85 (.37)	35.99 (4.76)	20.41 (1.85)	6.31 (.79)
PEEP increased to 9 cm H <sub>2</sub> O	40.09 (.23)	.71 (.19)	34.29 (4.02)	21.68 (1.87)	8.15 (.58)
Flow increased to 15 L/min PEEP increased to 15 cm H <sub>2</sub> O	41.23 (2.38)	.62 (.13)	22.44 (4.14)	22.28 (3.76)	13.65 (2.09)
All values reported as mean (SD) *Baseline: f 40/min, flow 10 L/min, PIP 20 cm H <sub>2</sub> O, PEEP 5 cm H <sub>2</sub> O f, ventilatory rate/min; I-time, inspiratory time; Insp V <sub>T</sub> , inspiratory tidal volume; PIP, peak inspiratory pressure; PEEP, positive end expiratory pressure					

## BRIEF REPORT

### Oximetry and Heart Disease

Recently the e-Journal of Neonatology Research published a paper on the subject of heart disease screening with pulse oximetry [Critical Congenital Heart Disease Screening with Pulse Oximetry in the Neonatal Intensive Care Unit]\* According to the abstract: "A case study of an infant with interrupted aortic arch who was discharged from the newborn nursery is presented for root cause analysis and implementation of a modified pulse oximetry screening program at the parent institution where it was described. A rationale for modification of the American Academy of Pediatrics policy statement supporting universal pulse oximetry screening for congenital heart disease in the newborn is made." The authors highlighted the importance of oximetry screening in the NICU.

The authors presented the case of a 38 week gestation infant delivered by a repeat cesarean section. The neonate had respiratory distress that required intubation. A pulse oximeter probe placed on the right upper limb was 95-98% with 21-25% oxygen requirement. This infant's first chest x-ray demonstrated bilateral hazy lung fields. Within 24 hours, the baby was

extubated and a subsequent chest X-ray showed marked improvement. She was discharged home in room air with pulse oximeter reading in 98-100% in the right upper limb. Two weeks after discharge, an echocardiogram demonstrated interrupted aortic arch with an aberrant left subclavian artery arising from the patent ductus arteriosus. The right common carotid artery, right subclavian and left common carotid artery came off the proximal part of the aortic arch prior to interruption. The infant underwent corrective surgery and was discharged home at four weeks of life.

The authors noted, "it is likely that SpO<sub>2</sub> obtained from the left upper limb or any lower limb would have demonstrated a lower SpO<sub>2</sub> compared to the right hand. During her stay in the NICU, all SpO<sub>2</sub> readings were obtained from the right hand. The detection of co-arcuation of the aorta by pulse oximetry screening is only 53% but the precise detection rate for interrupted aortic arch is not known. The accuracy of this screening is variable with high specificity but low sensitivity. Currently most units do not offer CCHD screenings for all infants admitted to the NICU. There always exists a potential for a positive screen, such as in a patient described above, provided all NICU patients are screened for CCHD. We have developed a modified algorithm, for all patients admitted to the NICU." Some recommendations: "The establishment of a cutoff threshold for an abnormal SpO<sub>2</sub> must be associated with high sensitivity and specificity. Setting a high SpO<sub>2</sub> cutoff value closer to the normal level will decrease the number of false-negative screening results at the cost of increasing the number of false-positive results. Conversely, a lower SpO<sub>2</sub> threshold will lower sensitivity and raise specificity... Neonates requiring oxygen supplementation during their NICU stay [should] be weaned to room air for at least 24 h prior to screening. Infants who are being discharged on home oxygen need to undergo an echocardiogram (if one was not obtained during their neonatal course)." The authors concluded: "We used a root cause analysis to modify the AAP guidelines for pulse oximetry screening in order to improve its specificity and sensitivity for aortic arch abnormality in our NICU. These recommendations are empirical, not evidence-based and need critical evaluation by prospective studies. Collaborative studies among neonatal intensive care units conducting routine

pulse oximetry should analyze pooled data and report detection, false positive rates, false negative rates, and cost-effectiveness of these screening measures for CCHD."

By the way, an excellent up to date primer on oximetry and heart disease is the Hospital Guidelines for Implementing Pulse Oximetry Screening, published by the Alabama Department of Public Health. You can find it by typing the above title into a search engine. Another source to look at is the article "It is Time for Routine Neonatal Screening by Pulse Oximetry," by Julien I.E. Hoffman, published in Neonatology (formerly Biology of the Neonate). You can Google it or find it here: [www.ncbi.nlm.nih.gov/pubmed/20523077](http://www.ncbi.nlm.nih.gov/pubmed/20523077). For nurses, the University of Arkansas for Medical Sciences has published a Nursing Practice Manual, "Congenital Heart Disease Pulse Oximetry Screening of the Newborn." See: [www.archildrens.org/.../heart.../](http://www.archildrens.org/.../heart.../) [\* Critical Congenital Heart Disease Screening with Pulse Oximetry in the Neonatal Intensive Care Unit, Satyan Lakshminrusimha, MD; Stephen Turkovich, MD; Veena Manja, MD; Jayasree Nair, MD and Vasanth H.S. Kumar MD. You can read the entire paper at [http://www.neonatologyresearch.com/?page\\_id=2592](http://www.neonatologyresearch.com/?page_id=2592).]

## OXIMETRY ROUNDTABLE

### Nonin Medical, Inc

**Tell us about your currently available oximetry products.**

Nonin Medical, Inc is the inventor of finger pulse oximetry and a global leader in designing and manufacturing noninvasive physiological monitoring solutions. The Nonin name and Onyx brand are recognized worldwide as the gold standard in pulse oximetry. Our branded and OEM offerings include pulse oximeters, sensors, software and accessories. During the past five years, Nonin has expanded its monitoring solutions to include capnographs and cerebral tissue oximeters, which are used in perioperative procedures. Nonin offers a variety of SpO<sub>2</sub> professional and consumer finger pulse oximeters, tabletops, handhelds and wrist-worn devices. Our newest professional finger oximeter is the Onyx Vantage 9590 Finger Pulse Oximeter. The Onyx has proven accuracy in the most challenging cases, including patients with

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low perfusion or dark skin tones. The proven PureSAT technology provides accuracy in the widest range of patients and settings, and one unit works from pediatric to adult patients. The Onyx Vantage has 6,000 spot checks on two AAA-batteries and a four-year warranty. Visit [www.OnyxVantage.com](http://www.OnyxVantage.com) for more information. For patient home use, the Nonin GO2 finger pulse oximeter (available with a physician prescription) provides highly accurate, quick and easy pulse rate and SpO2 measurements. The GO2 is a helpful tool to use to evaluate vital signs during activities and at rest, helping patients take control and live life to the fullest. Visit [www.go2nonin.com](http://www.go2nonin.com) for more information.

### **Discuss the range of your oximetry products' applications.**

Our quality, cost-effective and highly accurate noninvasive monitoring devices address patients from neonatal to adult, chronic respiratory to acute disorders, continuous monitoring to individualized spot checking and even direct to the patient population and sleep assessments. Nonin has continued to expand its parameter offerings, including exhaled CO2 measurements of respiratory distress and tissue oximetry that can be used in a variety of applications. Our products are used in hospital, physician's offices, long-term acute care, skilled nursing facilities, sleep, emergency medical services, and homecare settings. We continue to develop technologies that can meet the needs and demands for continuum of care – from the hospital to the home. Nonin prides itself on our products' accuracy and ability to work where you need, it when you need it – including patients with low perfusion. Most brands of oximetry devices can take an accurate reading on a healthy patient, but it is when you get a more challenging situation that Nonin's ability to provide reliable readings in the widest range of patients and settings really stands out. In an effort to address rising healthcare costs and promote the use of remote monitoring, Nonin Medical has collaborated with some of the finest healthcare and technology companies worldwide to advance the implementation of telemedicine. Our contribution – the revolutionary Onyx II, Model 9560 fingertip pulse oximeter – is designed for interoperability and is compatible with emerging open standards such as Bluetooth's Health Device Profile (HDP), IEEE11073 and Continua. In addition, as one of the Founding Members of the Continua Alliance, Nonin Medical and its Continua partners are dedicated to the development of cross-industry standards to reduce the cost of healthcare from acute care to the home.

### **What oximetry products do you have in development?**

Nonin Medical is continually leading the advancement and implementation of new physiological monitoring technologies designed to improve patient care. Technologies that are versatile and can work on the broadest base of patients are in highest demand. Nonin has products today that meet these needs, and we continue to design products that simplify the exchange of information, which should ultimately result in lower healthcare costs and improved patient care. We are continuing innovation on our key technologies so they are more sensitive and work on more patients and more parameters. Additionally, we are looking to advance our technologies by combining and integrating technologies and looking towards communication of devices not just among a single manufacturer or platform, but interconnectivity.

### **What type of customer assistance and training do you offer?**

Nonin has been a leader in our proactive approach with educational materials and clinical support. Throughout the years, we have worked with key clinicians in developing or supporting the creation of educational materials. For example, Nonin was the sponsor the WONCA/International COPD Coalition's "Clinical Use of Pulse Oximetry: Pocket Reference" to expand knowledge about the clinical applications and benefits of pulse oximetry. We worked with Dr Thomas L. Petty to create the booklet titled, "Your Personal Oximeter: A Guide for Patients." We supported the efforts of Dr Brian Tjep in the creation of a patient education video on pulse oximetry. All of these resources, along with many others, are available on [www.nonin.com](http://www.nonin.com) to help educate and support clinicians and customers. Finally, we are the only oximetry company to support GOLD (Global Initiative for Chronic Obstructive Lung Disease) and the December 2011 revision "Global Strategy for Diagnosis, Management and Prevention of COPD." Nonin believes in providing clinical support and outstanding products for clinicians and patients.

## **Covidien R&MS**

### **Tell us about your currently available oximetry products.**

Our Nellcor OxiMax line currently features a diverse range of pulse oximetry products with cardiac-based signal processing technology. Specific devices include:

- Bedside monitors, such as the Nellcor Bedside SpO2 Patient Monitoring System and Nellcor Bedside Respiratory Patient Monitoring System. Both systems, featuring user-friendly color interfaces, continuously monitor blood oxygenation in patients across all hospital care settings.
- The Nellcor OxiMax N-600x Pulse Oximeter, which can be used on patients of all ages, including infants.
- The largest line of disposable, reusable and specialty sensors on the market to meet the needs of a wide range of patients. For example, our forehead sensors can be used in poorly perfused patients with reduced blood oxygen to quickly capture accurate pulse oximetry readings when traditional finger sensors can't detect signals.

Note: Our Nellcor pulse oximetry technology is compatible with the monitoring systems of our more than 70 Original Equipment Manufacturing (OEM) partners.

### **Discuss the range of your oximetry products' applications.**

Covidien offers a range of Nellcor pulse oximetry solutions to meet every need in neonate, pediatric and adult patients across all hospital care settings. Many of our pulse-oximetry products are also used in hospital-type facilities, at home and during intra-hospital transport. Because Nellcor devices rely on cardiac-based signals rather than saturation-based signals, they provide a more accurate reading that is closely tied to the patient's physiology, driving consistent performance during various challenging conditions, such as noise and low perfusion, which can impede the assessment of patient respiratory status. Additionally, Covidien offers an extensive portfolio of sensors, including Nellcor specialty sensors, which address individual patient needs. For instance, Nellcor non-adhesive sensors protect delicate skin.

### **What oximetry products do you have in development?**

At Covidien, we're continually building upon our "Sensing Systems" portfolio to provide customers with solutions they need to detect subtle but critical variations in patient status through a combination of pulse oximetry and other monitoring

technologies. Our Sensing Systems provide a holistic view of patient status through interrelated pulse oximetry, respiration rate and capnography technologies. These provide a comprehensive picture of patient's unique respiratory function, hemodynamic response and end-organ perfusion.

#### What type of customer assistance and training do you offer?

We partner with customers to ensure our pulse oximetry and other portfolios best meet the needs of clinicians and patients. Specific support includes in-service programs, in-house continuing education (CE) programs, field-based technical training and web-based tools. We've also recently launched a new Professional Affairs and Clinical Education (PACE) online platform (<http://www.covidien.com/pace/pages.aspx>), which features clinical education content on a variety of topics, including pulse oximetry. The pulse oximetry training module is available by visiting <http://www.covidien.com/pace/pages.aspx?page=ClinicalEducation/Event/260992>.

## FOCUS PREVIEW

### AG Industries Cleaning Products

Booth 210

#### What products will you be showing?

AG Industries has been designing and manufacturing quality respiratory products for 30 years. Now AG is offering a full line of cleaning products to assure that your CPAP products continue operating at their highest capacity. Mask and tube cleaning products provide hassle-free options for patients to clean, dry and store their CPAP supplies and accessories. Products include: Mask cleaning wipes, Tube cleaning wand and replacement pads, and the Tube soaking and drying system. The attractive and convenient retail packaging of these products also means an increased range of offerings for providers.

### Dräger

Booth 413

#### What products will you be showing?

The Dräger ventilation portfolio has been transformed with newly released products to address each area of specialty care. Our newest critical care ventilator is the **Evita Infinity V500**, and our infant-

specific ventilator is the **Babylog VN500**. In addition to the new V-series ventilators, Dräger has introduced its newest turbine-driven ventilator, the **Savina 300** and the newest transport ventilator, the **Oxylog 3000 plus**. The **Carina** will also be showcased demonstrating its latest software designed to better meet the needs of non-invasive and chronic care ventilation. The **Evita Infinity V500** is a comprehensive critical care workstation that can provide for the needs of neonatal, pediatric, and adult populations. Newest features include a "Smart Pulmonary View," standardized nomenclature, PC-APRV with auto-release, and customizable weaning protocols. The **Babylog VN500** is a neonatal-pediatric specific ventilator which offers a wide array of therapies including oxygen therapy, non-invasive ventilation, and invasive modes. Critical to ventilating premature infants is proper monitoring and compensation; the VN500 provides for effective leakage identification and compensation and has the option to volume ventilate small babies to a TV of 2 cc's. The **Savina 300** focuses on the essential elements of ventilation for both standard and advanced modes of ventilation. The **Savina 300** provides for both adult and pediatric patients in settings such as acute, emergency, sub-acute, or post-operative care areas. Both invasive and non-invasive ventilation is available to provide clinicians a greater degree of flexibility for patient care. The **Oxylog 3000 plus** is a compact transport ventilator that can provide for adult and pediatric patients down to 50 cc's tidal volume. In addition to an array of volume, pressure, and spontaneous modes of ventilation, the **Oxylog 3000 plus** can provide AutoFlow as well. Additionally, the **Oxylog 3000 plus** can provide for integrated capnography and data management/export. The **Carina** ventilator for non-invasive and invasive ventilation has focused on the special needs to successfully manage patients requiring non-invasive ventilation. Its convenient and compact design for clinicians is ideal for transporting patients between wards when using non-invasive therapy.

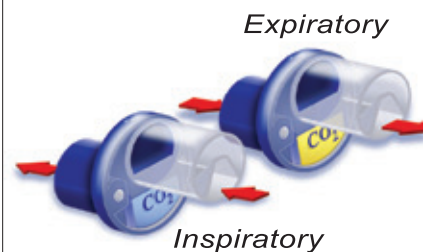
#### Discuss educational/training materials that you'll be distributing or promoting.

Dräger has launched its new website: [www.draeger.com/abreathahead](http://www.draeger.com/abreathahead). The **Breath Ahead** website was designed to provide a venue for respiratory clinicians to speak with key leaders in the field,

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share best practice, and receive complimentary continuing respiratory care education credits. Stop by and listen to current issues in the marketplace. Our 10x20-foot inline booth will showcase our entire portfolio of new products. Whether you are an adult critical care therapist, neonatal therapist, chronic care or focused on transport – there is something new to preview. Stop by and see the latest innovations in respiratory care.

## **Electromed, Inc**

Booth 717 & 719

### **What products will you be showing?**

Electromed, Inc, maker of the SmartVest Airway Clearance System, will be displaying its newly designed 10x20 tradeshow booth at Focus.

### **What new products or upcoming developments will you be highlighting?**

Electromed will be displaying its newest lineup in garment colors, Ginkgo Green.

### **Why should Focus participants visit your display?**

Stop by our booth to find out more about the mechanism of action of HFCWO treatment and receive an educational aid to help inform your patients. Visit us at [www.smartvest.com](http://www.smartvest.com), [www.electromed.com](http://www.electromed.com) or call (800) 462-1045 for information about the SmartVest System.

## **Impact Instrumentation, Inc**

Booth 303

### **What products will you be presenting?**

Impact will be presenting the Eagle II Portable Critical Care Ventilator and the Eagle II MRI Conditional ventilator.

### **What new products or upcoming developments will you be highlighting?**

The latest product introduction from Impact is the Eagle II MRI Conditional ventilator.

### **Discuss educational/training materials you'll be offering.**

Impact has recently launched their product training website available to all customers who purchase a 731 ventilator like the Eagle II. The site features training videos, power point presentations and knowledge exams.

### **Why should Focus participants visit your display?**

Focus attendees should visit our booth because we offer ventilator solutions for transport and bedside applications as well as MRI in full-featured ventilators that only weight 9.5 lbs and require no supplemental oxygen to operate.

## **MGC Diagnostics**

Booth 710

### **What products will you be presenting?**

MGC Diagnostics will feature recent product developments and technology advancements including BreezeSuite WebReview physician review software for test interpretation anywhere, anytime; Platinum Elite body plethysmograph and Ultima Series cardiopulmonary diagnostics systems with RTD real time

diffusion MultiGas technology, delivering clinically significant graphic data and immediate results; together with our latest version of BreezeSuite cardiopulmonary diagnostic software incorporating the latest HIPAA-HITECH Security Safeguards protecting patient identifiable health information.

### **Discuss educational/training materials you'll be distributing or promoting.**

Managing the MGC Diagnostics exhibit will be our Best-in-Class clinical, sales and support staff available to answer not only product questions, but provide expert consultation for clinical application and cardiorespiratory business needs. MGC Diagnostics continues to provide educational opportunities with our annual Cardiorespiratory Diagnostics Seminar held in Las Vegas, NV, October 7-9, 2013. Participants will advance their knowledge of diagnostic techniques, performance standards, quality assurance procedures, and clinical applications. The program format includes lectures, hands-on demonstrations and small group discussions—all conducted by a faculty of experts.

### **Why should Focus participants visit your display?**

MGC Diagnostics delivers diagnostic solutions for detection, classification and management of cardiorespiratory patients worldwide. Our enduring experience and single-minded focus give us unmatched insight into the real needs of our category. These invaluable assets make us uniquely qualified to solve today's challenges, provide unmatched service and support, and anticipate and solve unmet needs.

## **ndd Medical Technologies**

Booth 2014

### **What products will you be presenting?**

ndd Medical Technologies will be exhibiting the EasyOne Plus spirometer, the Easy on-PC and the EasyOne Pro DLCO machine.

### **What new products or upcoming developments will you be highlighting?**

The EasyOne Pro LAB is the newest addition to the EasyOne line of products and has been recently approved by the FDA! The Pro LAB offers complete lung function testing along with multiple-breath nitrogen washout for the measuring of the lung clearance index and moment ratios.

### **Why should Focus participants visit your display?**

ndd Medical Technologies is committed to providing innovative and easy-to-use products. The EasyOne line of products uses TrueFlow ultrasound transit time flow to deliver accurate diagnosis and does not require any calibration! Our EasyOne product family is affordable, reliable and practical.

## **Philips Healthcare**

Booth 403

### **What products will you be showing?**

From our patient interface line, we will be showing our new Respiroics AF531 NIV mask system with interchangeable elbow connectors that allow one mask to be used for specialized procedures, such as bronchoscopy and medication nebulization. The AF531 also allows the connection of the same mask to dual-limb or single-limb circuits. In addition to the AF531, we will be showing our new XL Respiroics PerforMax mask,



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*Introducing the **cobas b 123** POC system.*



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Next-generation technology.  
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designed to better fit larger patients, along with some new pediatric versions. On the ventilator side, we will be showing VentAssist, a new software option for the NM3 respiratory profile monitor that gives real-time ventilation guidance and support for clinical decisions. We have a new triggering mechanism on our V200 ventilator called IntelliTrak, which supports patient-ventilator synchrony even in the presence of leaks and dynamic hyperinflation. We will also be showing our Trilogy 202 ventilator as well as our flagship V60 ventilator. The V60 has an exciting new PPV option that performs proportional pressure ventilation noninvasively.

### **Discuss educational/training materials you'll be distributing or promoting.**

Our Education Manager will have an internet connection showing clinicians how to access the Philips Online Learning Center to take courses for CEU credit. We will also have clinical pocket guides and interactive CD programs for all of our ventilators and monitors.

### **Why should Focus visitors stop by your display?**

Focus visitors know us as the leader in noninvasive ventilation. We always enjoy visiting with our valued customers and friends and hearing how they are using our products to make a difference in patients' lives. We hope they will enjoy seeing how we continue to take NIV further with our new ventilators, patient masks, and educational offerings.

## **Roche Diagnostics**

Booth 209

### **What products will you be presenting?**

Roche Diagnostics will showcase the **cobas b 123** POC system and cobas b 221 blood gas analyzers for the Hospital point-of-care. In addition, Roche Diagnostics will present our **bge link** IT connectivity solution.

### **What new products or upcoming developments will you be highlighting?**

Roche will highlight the cobas b 123 POC system, winner of the 2011 Gold Medical Design Excellence Award (MDEA).

### **Discuss educational/training materials you'll be offering at the convention.**

Roche will feature the computerized "Virtual Simulation Tools" of both the cobas b 123 POC system and the cobas b 221 at our booth during Focus. Customers visiting the Roche booth will be able to visually understand many of the key differentiating elements and benefits of the cobas blood gas analyzers by experiencing these simulation tools designed with feature-rich video animation.

### **What speakers or papers will your company be featuring?**

Roche will have copies of the white paper "Eliminating clot risk with the new cobas b 123 POC system" available for customers at the booth.

### **Why should Focus participants visit your display?**

Customers should visit the Roche booth to learn more about Roche's next-generation technology and total blood gas portfolio solution. The cobas b 123 POC system is the portable, near patient blood gas analyzer that delivers optimal reliability to help

hospital staff provide outstanding patient care. The cobas b 123 POC system features transferrable consumables with smart chip technology, a decoupled sensor, and 1-and-Done maintenance. With 1-and-Done, routine maintenance is complete every time you change the fluid pack. Our customer market research indicates that the reagent pack on many blood gas analyzers fails about 10-14% of the time, often because of blood clots blocking the tubing within the analyzer. The cobas b 123 POC system detects and removes virtually all clots before they ever reach the analyzer system through the use of Roche's innovative clot catcher and 4 levels of clot detection and prevention. The patented sensor technology in the cobas b 123 POC system brings laboratory-class results closer to the bedside. The Roche analyzer also helps customers comply with regulatory requirements in a variety of ways. The onboard AutoQC Pack allows for automated quality control without interrupting workflow. The unique, automatic linearity testing feature with AutoCVC pack provides results that can be graphed, printed, and ready for review and signature. In addition, the cobas b 123 POC system comes with an Electronic Quality Assurance Program (eQAP) that provides linearity and quality control peer performance data to help keep your facility regulatory compliant. With its durable, ergonomically designed mobile cart, the cobas b 123 POC system is easily transported to deliver laboratory-class results wherever you go. Remote management of patient data is available with cobas bge link software which optimizes efficiency by managing all cobas blood gas analyzers and data directly for the manager's office. Remote troubleshooting is available through cobas 3-services.

## **VORTRAN**

Booth 703

### **What products will you be showing?**

- VAR (VORTRAN Automatic Resuscitator)
- VORTRAN PercussiveNEB
- VORTRAN IPPB
- VORTRAN APM Airway Pressure Monitor
- VORTRAN E-Surge Kit

### **What new products or upcoming developments will you be highlighting?**

Highlighting a new study that shows the VAR works perfectly for a 3 Tesla MRI

### **Discuss educational/training materials you'll be distributing or promoting.**

We will have our normal 3 CEUs for FREE to all who visit our booth as well as a take home training CD. The abstract for the VAR in MRI should be published before the show!

### **Why should Focus visitors stop by your display?**

Visitors should visit our booth to see the new improvements we are working on with the VAR. We hope to have new features ready for the show.

# Capnography: An Old Parameter for a New Day

Paul Nuccio, MS, RRT, FAARC

The purpose of this article is to re-introduce a monitoring parameter that has been around for many years and has recently come back into the forefront as an extremely valuable and important piece of a patient's clinical picture. As it is with any topic, correctly defining terminology is important in an effort to reduce confusion and enhance understanding.

To begin, a device called a capnometer is used to monitor capnometry, which can be defined as the numerical measurement of the amount of carbon dioxide (CO<sub>2</sub>) in the exhaled breath. A capnometer simply provides a number that represents the end-tidal CO<sub>2</sub> (etCO<sub>2</sub>) concentration. Next is the term capnogram which refers to the graphical representation of the amount of inhaled and exhaled CO<sub>2</sub>. The CO<sub>2</sub> graph, also known as a waveform, is obtained with a device called a capnograph. In order to have a complete picture of a patient's ventilation status it is important to look at both the numerical value as well as the waveform. The term capnography refers to a device that provides both the numerical value of etCO<sub>2</sub> and the waveform. In addition, a respiratory rate will also be displayed.

Capnography provides a breath-by-breath assessment of the patient's ventilatory status. The etCO<sub>2</sub> represents the concentration of CO<sub>2</sub> in the exhaled breath at the end of expiration or end-tidal. The textbook normal range for end tidal CO<sub>2</sub> is between 35 to 45 millimeters of mercury (mmHg). However, some hospitals may incorporate slightly different normal ranges into their individual protocols.

Although the numeric etCO<sub>2</sub> value is important, the waveform is equally important. The waveform is a graphic tracing of the inhaled and exhaled concentration CO<sub>2</sub> in each respiratory cycle plotted against time. The waveform changes immediately when there is a change in breathing, therefore it is the first sign of a respiratory problem.

Lastly, the respiratory rate provided by capnography is important because it is an airway respiratory rate, measured at the airway.

The respiratory cycle is made up of two separate processes – oxygenation and ventilation. These two processes facilitate the transport of oxygen into and carbon dioxide out of the lungs; this is known as gas exchange. The efficiency of gas exchange is dependent on ventilation, the cyclical breathing movements that

alternately move gas into and out of the lungs. Inspiration fills the lungs with oxygenated air, and expiration removes carbon dioxide.

It is important to remember that pulse oximetry monitors oxygenation. Oxygenation is the process of oxygen being inhaled into the lungs, dispersed by the alveoli to the blood, distributed to and metabolized by the cells of our muscles and organs.

Capnography monitors the adequacy of ventilation. CO<sub>2</sub> is produced as a by-product of metabolism. It is transported by the vascular system from the cellular level to the lungs, where it is removed when we exhale. It is important to note that breathing is the primary method the body uses to regulate CO<sub>2</sub>. This is accomplished by the brain's respiratory centers which send signals to regulate both respiratory rate and depth. If CO<sub>2</sub> is not regulated, a toxic accumulation in the blood can occur, resulting in respiratory failure.

Pulse oximetry and etCO<sub>2</sub> provide **important**, but **different** physiologic measurements.

Capnography monitors "ventilation," providing the etCO<sub>2</sub> which reflects the effectiveness of breathing, and the waveform, a graphical picture of each breath in real time. Capnography provides the earliest indication of hypoventilation, airway obstruction and episodes of apnea, or loss of ventilation as well as perfusion. And, the capnography alarm alerts you of the need for early intervention, before clinical assessment, and more effectively than pulse oximetry. Pulse oximetry monitors "oxygenation," providing the SpO<sub>2</sub> which reflects the percentage of the red blood cells that are saturated with oxygen. Pulse oximetry does not tell you at what rate your patient is breathing, and can be a late indicator with such conditions as hypoventilation, airway obstruction and apnea, or loss of ventilation. In addition, the use of supplemental oxygen can further delay the detection of airway compromise when monitoring with pulse oximetry. This is supported by a recent meta-analysis of eight prospective clinical studies which concluded that cases of respiratory depression were 28 times more likely to be detected if they were monitored by capnography, as those who were not monitored. In addition, the authors note that end-tidal carbon dioxide monitoring is an important addition to oximetry for detecting respiratory depression, but that data in the literature does not support substituting oximetry for capnography when monitoring for respiratory depression. They also note

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Paul Nuccio is the director of pulmonary services at Boston's Brigham and Women's Hospital.

that some investigators have concluded that doing so would actually be dangerous.<sup>1</sup>

Just as etCO<sub>2</sub> monitoring does not measure oxygenation, pulse oximetry does not measure ventilation. Neither should be used as a replacement or surrogate of the other; rather, they should be used in concert with each other.

Capnography can provide information about three physiological functions: metabolism, perfusion and ventilation. Capnography can tell us:

1. **Metabolism:** How effectively the body is producing CO<sub>2</sub>
2. **Perfusion:** How effectively the body is transporting CO<sub>2</sub> via circulation
3. **Ventilation:** How effectively the patient is eliminating CO<sub>2</sub> via exhalation

Capnography displays a signature waveform for each exhaled breath. Below is a representation of a normal waveform. Looking at the diagram of the waveform, let's examine what is happening during each segment of the breath. (See Figure 1)

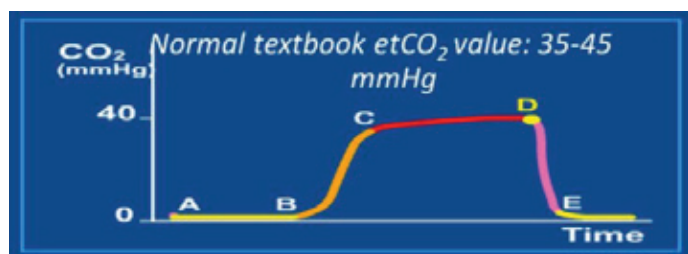


Figure 1. Above image used by permission from Nellcor Puritan Bennett LLC, Boulder, Colorado, doing business as Covidien.

- A to B shows the waveform baseline. This is the start of exhalation and there should be little or no CO<sub>2</sub>.
- B to C shows early exhalation where the rise in CO<sub>2</sub> from the exhaled air in the upper airways mixes with alveolar gas.
- At C to D the waveform levels off representing the concentration of CO<sub>2</sub> in the alveolar gas.
- D is the point at the end of expiration, or “end tidal,” and just before the next inspiration. This is where the etCO<sub>2</sub> is measured.
- The end of the waveform is segment D to E, a rapid, sharp down-stroke indicating a drop in CO<sub>2</sub> back to zero, and the beginning of the next inspiration.

It is important to remember that the absence of a waveform or “flat-line” is the earliest indication of airway obstruction, “no breath,” or absence of ventilation or perfusion.<sup>2</sup>

New guidelines from the American Heart Association and the European Resuscitation Council for CPR emphasize the use of capnography for adults and pediatrics, expressly validating the value and significance of waveform capnography in saving lives. Continuous waveform capnography is an ACLS and PALS Class I recommendation for adults, infants, neonates, and children in terms of airway management for confirmation and monitoring of endotracheal tube placement.

The AHA's 2010 Guidelines state, “Continuous waveform capnography is the most reliable method of confirming and monitoring correct placement of an endotracheal tube. Although other means of confirming endotracheal tube placement

are available, they are not more reliable than waveform capnography. Studies of patients in cardiac arrest demonstrated 100% sensitivity and 100% specificity for waveform capnography in identifying correct endotracheal tube placement in victims of cardiac arrest.” It is also recommended that providers observe a persistent capnographic waveform with ventilation to confirm and monitor endotracheal tube placement in the field, in the transport vehicle, on arrival at the hospital, and after any patient transfer to reduce the risk of unrecognized tube misplacement or displacement.<sup>3</sup> Many hospitals have begun to implement policies requiring the use of portable ventilators with capnography monitoring when transporting intubated patients from the ICU to various testing stations within the hospital.

With continuous waveform capnography, the provider will have continuous, objective confirmation that the ET tube is correctly positioned, as well as immediate notification should the tube become displaced at any point during the peri-arrest period or patient transport process.

Continuous waveform capnography is an ACLS and PALS Class II recommendation for monitoring CPR quality and detecting ROSC based on end-tidal carbon dioxide values. Capnography is an assessment of perfusion, or how well the body is circulating CO<sub>2</sub> through the lungs to be eliminated in the exhaled breath. If there is no circulation, or perfusion, there will be no transport of CO<sub>2</sub>, and therefore no etCO<sub>2</sub> value or capnographic waveform; therefore capnography can also serve as a physiologic monitor of the effectiveness of chest compressions and to detect return of spontaneous circulation.

The AHA Guidelines state, “Monitoring etCO<sub>2</sub> trends during CPR has the potential to guide individual optimization of compression depth and rate and to detect fatigue in the provider performing chest compressions. Ineffective chest compressions (due to either patient characteristics or rescuer performance) are associated with a low etCO<sub>2</sub>.”

In addressing return of spontaneous circulation, the guidelines say that “An abrupt and sustained rise in PetCO<sub>2</sub> may be observed just before clinical identification of return of spontaneous circulation, so use of PetCO<sub>2</sub> monitoring may reduce the need to interrupt chest compressions for a pulse check.” “Falling cardiac output or re-arrest in the patient with ROSC also causes a decrease in etCO<sub>2</sub>.” “Persistently low etCO<sub>2</sub> values, which is <10 mmHg, during CPR in intubated patients suggest that return of spontaneous circulation is unlikely.” An etCO<sub>2</sub> < 10mmHg for over 20 minutes accurately predicts death. In the clinical setting, observations of this ROSC can be quite striking and those who witness this quickly become supportive of the use of this technology.

For an easy way to see how waveform capnography is utilized throughout the resuscitation process, take a look at the ACLS Adult Cardiac Arrest Algorithm available at: [http://circ.ahajournals.org/content/122/18\\_suppl\\_3/S729/F2.expansion.html](http://circ.ahajournals.org/content/122/18_suppl_3/S729/F2.expansion.html). In this new streamlined, circular algorithm, there is an emphasis on high quality continuous CPR, and ACLS actions such as drug therapy and advanced airway placement organized within. Note that in the center of the circular algorithm, quantitative waveform capnography is recommended with placement of an advanced airway. Additional recommendations are found in the highlighted interventions and therapies box to the right of the algorithm.<sup>4</sup>



The new 2010 guidelines from the American Heart Association and European Resuscitation Council for CPR expressly validate the value and significance of waveform capnography in saving lives. The AHA and ERC now recommend capnography to confirm and monitor endotracheal tube placement, assess the quality of CPR, and detect return of spontaneous circulation. Healthcare facilities and providers that resuscitate patients will now require the use of capnography in adhering to AHA and ERC guidelines.

In January of 2011, a man's heart stopped beating normally for 96 minutes and the man survived. The success of the CPR was believed to be due to the fact that he was being monitored with capnography and this monitoring suggested that his vital organs were receiving adequate blood flow.<sup>5</sup> Stories such as this are becoming more and more common as the use of this technology increases.

A common misconception by many clinicians is the belief that if the etCO<sub>2</sub> does not match the PaCO<sub>2</sub>, the etCO<sub>2</sub> should be disregarded and considered inaccurate. Those in a position to monitor patients using capnography should be educated to the fact that the arterial to end-tidal CO<sub>2</sub> gradient is a reflection of alveolar dead space, and in many cases the larger the gradient the sicker the patient. Trending a patient's gradient over time can be useful in determining the progression of illness or the improvement in the patient's clinical condition. Under normal circumstances, the PetCO<sub>2</sub> is lower than the PaCO<sub>2</sub> by approximately 2-5 mmHg in the adult patient. It is also possible, although not common, to have a negative arterial to end-tidal CO<sub>2</sub> gradient. Negative values have been demonstrated following cardiopulmonary bypass, during anesthesia of pregnant patients, and in normal patients during anesthesia while being ventilated with large tidal volumes and low respiratory rates. Negative gradients have also been observed in infants, possibly due to a reduced functional residual capacity (FRC).<sup>6,7</sup>

Clinicians have begun to utilize capnography for monitoring patients receiving noninvasive ventilation (NIV). Given that ventilation is frequently a problem with patients requiring NIV, monitoring with pulse oximetry alone is inadequate. Choosing the correct sampling site is important in order to obtain useful readings.<sup>8</sup> In one study evaluating three different sampling sites the investigators commented that "The data revealed there were significant variations in etCO<sub>2</sub> results at the different sample sites, and the nasal/oral cannula sample site was more consistent throughout all settings and patient leak rates."<sup>9</sup>

There has been a significant increase in the interest and recognized value of capnography over the past several years, particularly outside of the operating room setting.<sup>10</sup> Capnography is quickly becoming a standard of care in the emergency room, intensive care unit, and general patient floor locations where patients may receive pain control analgesia. Many of the latest generation mechanical ventilators have begun to integrate capnography within their ventilator platforms. As healthcare clinicians become more aware of the value of capnography in enhancing patient care and safety, respiratory therapists will be in a prime position to be considered an expert in the use of this exciting and valuable technology.

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# Changing Tracheostomy Tube Material and Utilizing Silicone Dressings Healed This Stoma – A Case Report

Linda K. Dean, RRT

## Abstract

**Introduction:** Tracheostomy tubes are made of a variety of materials such as plastic, silicone or stainless steel. Chronic wound infections and misshapen stomas are a complication of prolonged tracheostomy. Our goal was to see if a change in tracheostomy tube material in conjunction with stabilizing the tube could improve the condition of this stoma.

**History:** 52 year old male with diagnosis of MS who decompensated, requiring tracheostomy and prolonged mechanical ventilation. A number 6 Shiley tracheostomy tube was inserted. Over time, the stoma enlarged and the site was a constant source of infection. There was obvious red, irritated skin at the stoma site, copious foul smelling secretions, and bad breath. In addition, routine 30 day tube change showed a black moldy substance on the shaft of the tube. Furthermore, the weight and constant movement of the ventilator circuit caused the stoma to become enlarged and misshapen. In fact, the cuff could be seen. The decision was made to place a 6 Shiley XLT tube with increased distal length to better seal the airway for mechanical ventilation. This patient weaned from the ventilator, but remained tracheostomized secondary to his weakened neuromuscular state. The stoma site continued to be a challenging wound, so the decision was made to change tube material and stabilize the tube.

**Objective:** Our goal was to see if a change in tracheostomy tube material in conjunction with stabilizing the tube could improve the condition of this stoma.

**Methods:** A #8 Bivona TTS silicone tube was inserted and stabilized with a Sil.Flex TC Pad. This silicone pad was applied under the flange. Nothing else was changed in regards to the patient's routine trach care or oral care.

**Results:** Within 3 days, the foul smell was gone, secretions had cleared, and the mucosa became a normal pink color. There was evidence of new healthy skin growth around the stoma. The patient noted less movement of the tube immediately and greater comfort. Other benefits noted were: increased SaO<sub>2</sub>, skin tone/color and LOC. After one month, routine tube change revealed a remarkably clean shaft of the tube; inside and out.

**Conclusion:** This single patient case study demonstrated significant improvement in the tracheostomy stoma site when the tube material was changed to silicone and stabilized with the Sil.Flex TC Pad.

## Introduction

According to the Agency for Healthcare Research and Quality Data, cost of care associated with the diagnosis of tracheostomy ranks second in the nation – second only to organ transplant patients.

Large, irregular, misshapen tracheostomy stomas increasingly complicate the clinical course of the tracheostomized patient. Stoma erosion can lead to chronic infection, increased secretions, inability to secure the artificial airway, tracheoinnominate artery leak/rupture, formation of tracheoesophageal fistulas, stenosis, and eventually death.

Tracheostomy tubes are made of a variety of materials: plastic, silicone, sterling silver, and stainless steel. Two types of plastics commonly used are (PVC) polyvinyl chloride (Shiley and Portex) and polyurethane (Tracoe). Shiley tubes contain 30% of their weight in DEHP (di-2-ethyl-hexyl phthalate). This plasticizer is toxic to humans, does not chemically bind with plastic, and readily diffuses into its environment. Prolonged exposure to DEHP is associated with male infertility.<sup>1</sup>

There are currently no ATS standards regarding frequency of tube changes in the adult patient. Tube manufacturers recommend tubes be changed every 30 days; a tube used over 30 days would be considered an “implanted” device, and would be regulated very differently by the FDA. More frequent tube changes are associated with less granular tissue formation.<sup>5</sup>

Biofilm formation on tracheostomy tubes is seen as early as 7 days after insertion.<sup>2</sup> Routine 30 day tube change inspection has demonstrated surface degradation changes, and biofilm formation.<sup>1,2,3,4</sup> These biofilms are intricate networks of bacterial microorganisms that are impervious to ultraviolet radiation, unfazed by bacteriophages, and may actively shed to become antibiotic resistant super infections responsible for recurrent pulmonary infections, septicemia, endocarditis, etc.<sup>3</sup>

## Case Report

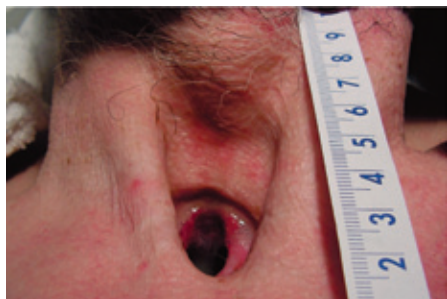
This is a single case report of a 52 year old male with a diagnosis of multiple sclerosis who decompensated, and required prolonged mechanical ventilation and subsequent tracheostomy. A standard size 6 Shiley tracheostomy tube was inserted, but in spite of routine care the stoma deteriorated. The weight and constant movement of the ventilator circuit caused the stoma to become so enlarged and misshapen that the cuff on the tracheostomy tube could be seen when looking down upon the insertion site. At this time the decision was made to change the tube to a size 6 Shiley with increased distal length – XLT. Shortly

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thereafter the patient was sent home, where his 24 hour per day home care nursing staff continued his routine tracheostomy care, and eventually weaned him from mechanical ventilation.

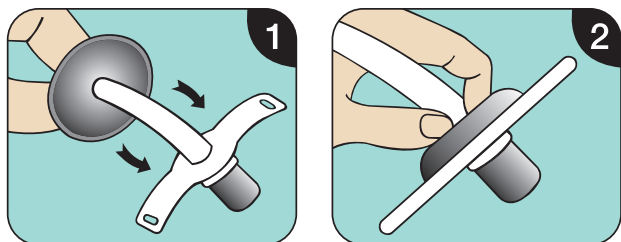
The stoma site remained a constant source of infection; red irritated skin, copious foul smelling secretions, halitosis, and poor condition of the oral mucosa were a constant battle. When a routine 30 day tube change revealed a black, mold-like substance sticking to the shaft of the plastic tube,<sup>1,2,3,4</sup> the decision was made to change tube material to see if the stoma site could begin to heal more normally. Since chronic wound infections and misshapen stomas are a complication of prolonged tracheotomy, our goal was to see if a change in tube material could improve the condition of this stoma.



One goal for this patient was to use a Passy-Muir speaking valve. However, the degree of leak around the stoma made speaking valve use counterproductive to stoma healing, and ineffective in enabling sufficient upper airway airflow for phonation. The decision was made to attempt to seal the stoma with a silicone dressing. We hypothesized that sealing the stoma air leak would allow the patient to utilize his speaking valve.

### Methods and materials

Prior to insertion of the new tracheostomy tube, a “donut shaped” silicone dressing was applied over the shaft of the tube using standard sterile procedure.



Placement of the Sil.Flex TC Pad on to the tracheostomy tube

Unfortunately, the stoma was so large and irregularly shaped that the silicone pad could not completely cover it. Since this particular silicone pad is applied to the tube prior to insertion, we decided to leave it in place and not put the patient through another tube change. Even though it did not meet our original goal to seal the stoma, an immediate side benefit of using the silicone pad became greater stabilization of the tracheostomy tube, noted by greater comfort from the patient. The following was hypothesized: Could the silicone pad stabilize the tube to promote wound healing in conjunction with changing tube composition?

The new tube selected was a size 8 Bivona TTS. This tube is made of silicone, and had a comparable outer diameter and length to the previous plastic tube. (Since the patient occasionally required nocturnal ventilation, a tube with a cuff

was required.) We changed to silicone to see if tube composition would make a difference in stoma healing by decreasing or eliminating the biofilm buildup we were finding upon routine monthly tube changes. There were no other changes in regards to his routine tracheostomy or oral care.



### Results

After only 3 days it was noted the foul smell from the stoma site was eliminated, tracheal and oral secretions had cleared, halitosis was gone, and the oral mucosa had become a normal pink color. There was also evidence of new healthy skin growth around the stoma. The patient noted less movement of the tube and continued greater comfort. Other benefits noted were increased SaO<sub>2</sub>, skin tone/color, and LOC.

After 30 days, routine tube change revealed a healed stoma site, with reduction in stoma size. A remarkably clean shaft of the tube, inside and out, was noted by the nursing staff and attending physician upon tube change. The decrease in air leak around the stoma allowed the patient to use, and benefit from, his speaking valve.



### Conclusion

This single patient case study demonstrated significant improvement in the tracheostomy stoma site when the tracheostomy tube material was changed to silicone, and the tube was stabilized with a silicone pad. It remains unclear if the change in tube material, addition of the silicon pad, or the combination of both can be accredited for this clinical improvement.

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# The Chronically Critically Ill Patient

Ray Braxton, RRT

I read with interest the June issue of my *Respiratory Care Journal*<sup>1</sup> as it covered the topic of the Chronically Critically Ill (CCI) patient. We in the profession of respiratory care know this patient well. He or she has been on our service for an extended period of time, usually requiring prolonged mechanical ventilator support and sometimes placement of a tracheostomy tube. They typically have made it out of the intensive care setting to a step-down intermediate unit and are reported to be “difficult to wean.”

As I read Doctor Carson’s article<sup>2</sup> outlining the definition and epidemiology of the CCI patients, the following bullet-points were noted: • Consensus definition of CCI is a patient requiring > 21 consecutive days of mechanical ventilation for > 6 hours/day; • The overall 1- year survival for CCI is between 40% to 50% depending on the cohort studied; • CCI patients constitute 5 to 10% of patients with acute respiratory failure; • The number of long term acute care (LTAC) admissions to care for CCI patients have increased over the past years and projected to be even higher in the coming years.

The take away message here is that we will be seeing a greater number of patients advance to the chronically critically ill state which will further stretch our resources to care for them.

The next article by Doctor Cox<sup>3</sup> outlining the presence and effects of systemic inflammation in CCI patients also provided me with insight into how difficult it is to prevent and treat this condition in our patients. It is suggested that the following interventions seem to have some effect in mediating the course of this condition such as: • Low tidal volume ventilation; • Daily awakenings from sedation followed by a spontaneous breathing trial when appropriate; • Glucose control strategies; • Targeted use of corticosteroids; • Early goal directed therapy for sepsis; • Early mobilization of critically ill patients.

All of these strategies have demonstrated some favorable effect on both mortality and morbidity of the CCI patient. The development and utilization of protocols by respiratory care departments that incorporate several of these strategies plays a big part in the role and responsibilities of the respiratory therapist.

In Doctor White’s article,<sup>4</sup> he outlines management strategies for patients requiring prolonged mechanical ventilation (PMV). These patients are described as requiring extended ventilator support for either isolated failure of the respiratory system or respiratory failure occurring as a component of CCI. Generally

these patients have failed multiple attempts at weaning and have received a tracheostomy tube to facilitate extended mechanical support.

The following are listed as barriers to weaning: • Aging process resulting in increased muscle breakdown and reduced muscle strength of the CCI patient contributing to impaired diaphragm function; • Cardiopulmonary disease whereby there is a reduction in lung mechanics, increased work of breathing through air-flow obstruction, and/or impaired oxygen loading capacity; • Elevated body mass index; • Comorbid conditions such as: - Impaired central drive; - Congestive heart failure; - Critical illness neuromyopathy; - Ventilator-induced diaphragm dysfunction.

Dr White also outlined the importance of a correctly sized and positioned tracheostomy tube. Its placement is usually required to facilitate transfer of the PMV patient from the ICU to a lower level of care, such as a weaning unit. He also provides us with insight to some guidelines into when to change or downsize a tracheostomy tube in adults with CCI.

The respiratory therapist has a large impact in the quality of care that the PMV receives each day. It can be as simple as being alert to improvement in lung mechanics and/or oxygen loading capacity. Or it could be to ensure patient-ventilator synchrony by setting appropriate cycle time to avoid the effects of air-trapping. Assessment and interpretation of ventilator graphics is an important skill set for the respiratory therapist.

In conclusion, I encourage us all to take the time to pull out and read the June 2012 issue of *Respiratory Care* as it provides the clinician with further insight on how to care for this growing population of CCI patients that we will be faced with in the future.

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Ray Braxton is Clinical Support Specialist, Hamilton Medical, Inc. This article appeared in Hamilton Medical’s Newsletter, Intelligent Ventilation.

# Evaluation of the Vortran Automatic Resuscitator and the Vortran Airway Pressure Monitor in the MRI Environment

A. Berthiaume, Dave Swift RRT

**Introduction:** The magnetic resonance imaging (MRI, 3 Tesla strength) scanner creates a unique electromagnetic environment that allows high fidelity images of patients. With critically ill patients requiring mechanical ventilation, this environment produces some unique challenges in management of ventilation and monitoring of ventilation. Currently, there are a limited number of ventilatory devices that can provide mechanical ventilation in the MRI environment.

**Methods:** To determine if the Vortran Automatic Resuscitator (VAR Plus model) can be safely utilized in the MRI environment. To evaluate, if the Vortran Airway Pressure Monitor (VAPM) can deliver accurate monitoring capability within the MRI environment. The VAR-Plus performance was verified in a bench top setting, within the MRI core (with and without extension lines) and outside of the MRI core (with and without extension lines). The VAPM was used in parallel to verify the VAR-plus performance.

**Results:** The VAR-plus consistently delivered the RATE (within one bpm) and pressure set using a static lung compliance & resistance model. The VAPM unit consistently monitored the set rate. However the unit's ability to monitor the inspiratory time was limited by its design characteristics of only displaying the inspiratory time by rounding up at the 0.05 mark (ex. Ti of 0.56 displays as 0.6 and 0.45 displays as 0.4). The VAPM (Vortran Airway Pressure Monitor) is not designed to be used within the immediate magnetic field of the MRI machine. The magnetic field interferes with its operation and the authors recommend that it not be used within that magnetic field – it does provide effective remote monitoring capability for the VAR-plus.

**Conclusion:** The VAR-plus can effectively function, according to established performance characteristics, within the MRI environment. The unit is not impacted by the electromagnetic field of the MRI scanner. The VAPM provides an effective remote monitor for ventilation within the MRI environment (outside of the magnetic field) for adult and pediatric populations not requiring very low inspiratory times.

**Proposal:** Verify the VAR (Vortran Automatic Resuscitator) performance under the following conditions:

- reaction to MRI while in the core (no extension line)
- reaction to MRI while in core (with extension line)
- reaction to MRI while just outside of core (with extension)
- reaction to MRI while just outside of core (without extension)

Verify the AMP (airway pressure monitor) performance, used with the VAR, under the following conditions:

- pressure accuracy before and after MRI exposure
- reaction to MRI while VAR in the core (no extension line)
- reaction to MRI while VAR in core (with extension line)
- reaction to MRI while VAR just outside of core (with extension)
- reaction to MRI while VAR just outside of core (without extension)

**Evaluators:** Alain Berthiaume, MRI Charge Technologist, Ottawa Hospital; Dave Swift RRT, Campus Coordinator & Charge Respiratory Therapist Ottawa Hospital.

**Equipment:** VAR-plus (VAR plus extension kit) product PCE 5012 & PTE 5002; VORTRAN TEST LUNG model VTL-3600; Vortran Airway Pressure Monitor -3800/pediatric model IP31; MRI: Siemens TIM TRIO, software version V17.3 tesla magnet, TQ-engine (45mT/m@200T/m/s); Draeger C500 Infinity

**Manometer:** Baumanometer BP Manometer with noncompliant tubing (W.A. Baum Co Inc, Coplague, NY, USA).

**Verification of the Vortran Airway Pressure Monitor 3800/pediatric model IP31**

Bench Top Test: Using an in-line manometer & the C500 ventilator as the controller the displayed data was compared (ventilator, manometer vs VAPM)

Parameter	C500 ventilator	Manometer	VAPM (6 inch extension line)
RATE	20	---	19
	24	---	23
	30		29
	40		39
	50		50
	60		59 high rate alarm
PEEP	3 cm H2O	2.1 mmHg (2.85 cm H2O)	3 cm H2O
	5 cm H2O	3.7 mmHg (5.03 cm H2O)	5 cm H2O
	7.5 cm H2O	5.3 mmHg (7.20 cm H2O)	7 cm H2O
	10 cm H2O	7.4mm Hg (10.06 cm H2O)	10 cm H2O
Inspiratory Time (Ti seconds)			
	0.3 sec	--	0.3 sec
	0.35 sec	--	0.3 sec
	0.40 sec	--	0.4 sec
	0.45 sec	--	0.4 sec
	0.50 sec	--	0.5 sec
	0.56 sec	--	0.6 sec

In operator control room of MRI no performance changes noted using var equipped without extension tubing compared to bench top verification.

**Verification of the Vortran Airway Pressure Monitor 3800/pediatric model IP31 in operator control room of MRI with var equipped with extension tubing**

Parameter	C500 ventilator	VAPM
RATE	20	18
	24	23
	30	29
	40	39
	50	49
	60	58 high ratealarm
PEEP	3 cm H2O	3 cm H2O
	5 cm H2O	5 cm H2O
	7.5 cm H2O	7 cm H2O
	10 cm H2O	10 cm H2O
Inspiratory Time (Ti seconds)		
	0.3 sec	0.3 sec
	0.35 sec	0.3 sec
	0.40 sec	0.4 sec
	0.45 sec	0.4 sec
	0.50 sec	0.5 sec
	0.56 sec	0.6 sec

**Conclusion**

The Var-plus functions within its designed/specified parameters within the MRI environment. The VAR-plus is a pneumatically powered, continuous flow, pressure cycled, expiratory time limited automatic resuscitator that can provide effective ventilation to a patient within the MRI. As with all pressure cycled devices, changes in lung compliance and resistance can alter the rate and delivered lung volumes. For patient who may undergo dynamic changes in their resistance and compliance the use of the VAPM is essential.

The VAPM is a small, portable monitoring device that displays the inspiratory time, respiratory rate, inspiratory pressure and intrinsic peep on a continuous basis. It provides a high pressure, high rate, and fail to cycle alarms in either an adult or pediatric configuration. The VAPM is not designed to function within the established gauze field and the authors recommend that the optional extension line be used when used within the MRI environment.

**Vortran Automatic Resuscitator – Performance verification (Outside of MRI core)**

Parameter	Set value*	Bench test		
(non-MRI environment)	MRI with extension line	MRI without extension line		
RATE	10 bpm	10 bpm	9 bpm	10 bpm
	12	12	11	12
	20	20	19	20
	30	30	29	29
	40	40	39	40
	50	50	48	49
	60	60	58	59

**Vortran Automatic Resuscitator – Performance verification (Inside of MRI core)**

Note: the VTL-3600 test lungs contained steel screws as part of its assembly and it was effected by the magnetic core and required support to complete the test.

Parameter	Set value*	Bench test		
(non-MRI environment)	MRI with extension line	MRI without extension line		
RATE	10 bpm	10 bpm	9 bpm	10 bpm
	12	12	11	12
	20	20	19	20
	30	30	28	29
	40	40	38	40
	50	50	47	49
	60	60	59	59

\*set value set prior to entry to MRI, unit set & then disconnected from gas source and reconnected in MRI.  
50psi direct connection, no flowmeter used.



# High Flow Nasal Cannula Therapy in Neonatology

Thomas L. Miller, PhD

## List of Terms

**High Flow Nasal Cannula (HFNC):** generic description for using nasal cannula flow rates which are greater than convention.

**High Flow Therapy (HFT):** The use of HFNC in a specified way to accomplish specific objectives pertaining to defined mechanisms of action.

**Mechanism of Action:** Process by which an intervention interacts with physiology to accomplish a specified effect.

**Mechanistic Research:** Research that is conducted in such a way as to demonstrate which specific aspects of an intervention are associated with the desired outcome (eg pressure vs flushing CO<sub>2</sub> vs humidification, etc). This concept differs from observational studies where an intervention is introduced and clinically relevant outcomes are recorded with no means to identify the specific mechanisms of action. Often, mechanistic research requires pre-clinical translational models that allow for thorough instrumentation, whereas clinical studies are often limited to observational models.

**Continuous Positive Airway Pressure (CPAP):** A pressure-based therapy wherein a nasal or mask interface is sealed to a patient's face and pressure within the device circuit is controlled.

**Dead Space (DS):** Region of the conducting airways that does not contribute to gas exchange. Under normal circumstances, the DS inadvertently serves as a reservoir of end-expiratory gas that is re-breathed at the onset of a subsequent inhalation.

**Anatomical Reservoir:** the dead space volume of the upper air passages including the nasal, oral and pharyngeal areas.

**Ventilation:** The circulation of air or a prescribed respiratory gas mixture into the pulmonary air spaces with an intention to replace expiratory gas that has already exchanged oxygen and carbon dioxide with the blood. In mammalian physiology, this process involves tidal volume exchanges because of the presence of dead space.

**Alveolar Ventilation ( $V_A$ ):** The total volume of gas exchanged

in the region of the respiratory tract where gas exchange can take place with the blood.  $V_A = (\text{tidal volume} - \text{DS})$  multiplied by respiratory rate.

**Minute Ventilation ( $V_E$ ):** The total volume of gas exchanged in and out of the respiratory tract each minute.  $V_E$  differs from  $V_A$  as a function of dead space where  $V_E$  is always greater than  $V_A$  by DS multiplied by breathing rate.  $V_E = \text{tidal volume}$  multiplied by respiratory rate.

## Introduction

Over the past several years, there has been a marked increase in the use of nasal cannulae to deliver high flows of humidified respiratory gas to neonatal patients. During this period, research has been conducted and published examining safety and efficacy as well as exploring means of optimizing the therapeutic impact of high flow nasal cannula. This review provides definitions, an overview of the therapeutic approach and mechanisms of action, as well as a review of published research. Some key terms are listed on this page which are important to distinguish specific concepts in discussing this therapy.

## High Flow Therapy (HFT) Defined

Fundamentally, HFT is the delivery of respiratory gas through a nasal cannula at flow rates that exceed a patient's demand, whereby this definition pertains to both the inhalation and exhalation phases of breathing. The technological advances that allow for HFT are related to precise heating and humidification; however, the resultant efficacy is a function of more efficient oxygen therapy and an impact on ventilation by way of dead space washout. The foundational premises of HFT are that cannula flow rates of respiratory gas exceed a patient's spontaneous inspiratory flow rate as well as be sufficient to purge anatomical dead space during exhalation. In this regard, a patient will not entrain room air while taking in a breath, making each breath composed of ideally conditioned gas with a precise fraction of oxygen. Moreover, when the gas flow is adequate, the nasopharyngeal region is purged during exhalation so as to improve ventilation by the elimination of expiratory CO<sub>2</sub>. In adults, both objectives are typically accomplished by a similar flow rate making flow a matter of exceeding inspiratory flow rate; however, infants are more complex because of the relative differences in the extrathoracic dead space. This will be discussed in greater detail below.

In the current literature, definitions of HFNC are inconsistent, particularly as it pertains to comparisons to other therapies.

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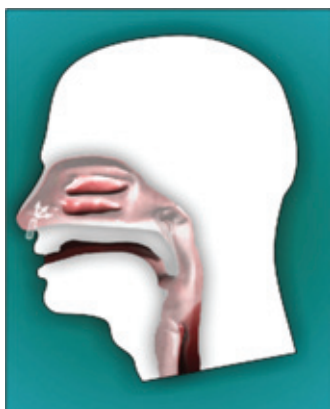


Figure 1. During inhalation the cannula flow needs to be adequate to meet inspiratory flow demand.



During exhalation the cannula flow needs to be adequate to purge the nasopharyngeal dead space volume between breaths.

Some investigators define the application of a HFNC therapy as simply using cannula flows greater than convention, which in neonatal medicine is greater than 2 L/min, or in some cases greater than 1 L/min.<sup>1</sup> However, based on the mechanistic research that has demonstrated how HFT affects respiratory function, HFT is correctly defined as the application of flow rates that accomplish the two aforementioned objectives. Again, these objectives pertain to meeting inspiratory demand as well as purging anatomical dead space in the window of time between breaths.

A widespread assumption is that HFNC provides for a continuous positive airway pressure (CPAP) effect. Whereas pressure will develop in the delivery of HFT, mechanistic studies suggest that pressure is not the primary mechanism of action responsible for observed physiologic outcomes. A more detailed comparison of HFT to CPAP is found in a later section of this paper.

An example of why we need agreement on the definition of HFT is the 2011 Cochrane review on the use of “High flow nasal cannula for respiratory support in preterm infants.”<sup>1</sup> These authors reviewed four studies and concluded that high flow nasal cannula may result in a higher rate of reintubation compared to CPAP. However, these reviews defined HFNC as flow rates greater than 1 L/Min, which may not exceed every infant’s inspiratory flow demand and certainly would not be sufficient to purge nasopharyngeal dead space during exhalation. The evidence cited to support that CPAP outperforms HFNC comes from the one study by Campbell and colleagues.<sup>2</sup> These authors administered HFNC as if it were a CPAP therapy, and used an equation to assign flow rates. Specifically, this equation was proposed to predict flow needed to achieve a certain airway pressure, and as such, the mean cannula flow rate used in this study was only 1.8 L/min.

It is fair to conclude from these data, as well as years of experience with nasal cannulae, that flow at rates less than 2 L/min may not be as effective as CPAP. However, this finding has little relevance to true high flow nasal cannula therapy (ie HFT) which is defined by the mechanistic literature to facilitate purging of the entire volume of nasal, oral and pharyngeal dead space. In this regard, the findings of Campbell and colleagues should not be unexpected and should not be used to represent the efficacy of HFT per its mechanistic definition.

## Multiple Mechanisms of Action

There are a number of mechanisms by which HFT can improve respiratory function in patients, including the neonatal population. In subsequent sections of this paper, the principle mechanisms of action are described in detail within the context of therapeutic application. Here, these mechanisms are briefly introduced to note the complex, multifactorial impact of HFT.

Essentially, HFT makes the nasopharyngeal region a reservoir of fresh gas by way of purging the end-expiratory gas from this space during exhalation. Therefore, the patient’s subsequent breath is more efficient in that it is composed of more fresh gas and less end-expiratory gas. With this improvement in efficiency, a patient can achieve adequate alveolar ventilation ( $V_A$ ) with less minute ventilation ( $V_E$ ), compared to pressure therapies that force greater lung expansion to achieve greater  $V_E$ . Vapotherm recommends that HFT should not be used to produce a substantial distending airway pressure, although some pressure inevitably is generated. Rather, HFT should be used so as to minimize resistance to gas exhausting from the nasopharynx around the cannula and through the mouth. In other words, HFT should be used to maximize the purging of the nasopharynx with the least amount of flow and associated pressure. A recent publication validating the dead space washout concept as the principal mechanism of action showed that the least occlusive cannula geometry resulted in an optimal efficacy with less than 75% of the flow and pressure required when snug fitting prongs are used to generate distending pressure.<sup>3</sup> Additional studies have shown how flow dynamics and heated humidification contribute to other mechanisms of action that reduce work of breathing and support airway function. These other mechanisms are summarized below and described in a review paper by Dysart et al.<sup>4</sup>

## HFT in the Context of Current Practices in Neonatal Respiratory Care

Since the 1980s, there has been a focus on developing strategies for noninvasive ventilation subsequent to the defining of bronchopulmonary dysplasia (BPD), the relationship to lung bio-inflammatory potential and the recognition of the need for lung protective ventilation strategies. Along these lines, there has been a major emphasis on CPAP and other noninvasive forms of ventilation, such as bilevel CPAP, that have reduced the need for mechanical ventilation.<sup>12</sup> Other major developments have surfaced in the last few decades, such as exogenous surfactant replacement therapy and inhaled nitric oxide, which have been widely adopted and used in conjunction with noninvasive respiratory support. For example, the INSURE technique (INtubate, SURfactant, Extubate) has allowed surfactant delivery to be combined with noninvasive ventilation with notable success.<sup>13</sup> Together these combinations of therapies have fostered tremendous improvements in infant mortality, but occurrence of BPD remains high.

In the context of this push for noninvasive ventilation strategies, dead space elimination, and thus HFT, is not a novel concept. Dead space elimination contributes to improved alveolar ventilation without forcing greater tidal volumes. In this regard, we need to reinforce that the term ventilation should not necessarily be synonymous with artificial breathing machines that deliver tidal breaths, but can encompass other, less invasive ways to facilitate exchange of respiratory gases within the lungs. Optimal gas conditioning capabilities have allowed for gas delivery by nasal cannula to exceed the conventional limits without degradation of the nasal tissues.<sup>14</sup>

MECHANISM	DESCRIPTION
Dead space washout	Reduce dead space making minute ventilation more efficient. <sup>3,5</sup>
Reduce inspiratory work of breathing	Exceed inspiratory flow thus eliminating nasal resistance. <sup>6</sup>
Improved lung mechanics	Warmed, humidified gas has been shown to improve conductance, compliance and lung elasticity. <sup>7</sup>
Eliminate metabolic work associated with gas conditioning	Attenuates the energy and water loss associated with conditioning inspiratory gas.
Provision of mild distending pressure	Flow can be restricted such as to provide positive distending pressure for lung recruitment. <sup>8-10</sup>
Improve secretion mobilization	Ideal humidification of the inspired gas has been shown to restore mucociliary function and reduce symptoms of airway exacerbations. <sup>11</sup>

This advancement has opened the door for a noninvasive way to eliminate anatomical dead space, making ventilation more efficient.

HFT, as we term the use of HFNC in a specified way so as to maximize the elimination anatomical dead space, has many peripheral advantages that are associated with the patient interface being easier to manage than a sealed CPAP system. These include patient tolerance, ease in nursing management, and accessibility for kangaroo care, as well as physiologic concerns such as prone positioning to support spontaneous breathing.<sup>15,16</sup> As we better define and optimize HFT as primarily a therapy to eliminate dead space, and understand the coinciding ability to generate mild pressure and hydrate the air passages, HFT holds promise to emerge as a significant advancement in neonatal respiratory support.

### HFT: A Unique Noninvasive Respiratory Support Modality

The act of ventilation refers to the circulation of air so as to replace stale or noxious air with fresh air. In mammalian physiology this process involves tidal volumes and lung compliance because of our anatomical dead space. In other words, if we were to remove dead space entirely by putting our alveolar surface on the outside of our body (eg gills on a fish), we would not need to have tidal volume excursions to expose the alveolar surface to adequate VA in support of respiration. Obviously, this is not practical for numerous reasons, including the need to condition gas before coming into contact with the blood, and our adaptation to use dead space for retaining CO<sub>2</sub> as our innate pH buffering mechanism.

Nonetheless, by reducing dead space we can reduce the V<sub>E</sub> needed to accomplish adequate V<sub>A</sub> and therefore reduce work of breathing. Dead space elimination tactics have been used for years in the form of tracheal gas insufflation<sup>17,18</sup> and transtracheal oxygen delivery.<sup>19</sup> In the last 10 or more years, advancements in heated humidification devices have made it possible to accomplish ventilation by way of dead space elimination with a nasal cannula.

Translational research has shown that the primary mechanism of action for HFT is purging anatomical dead space, thus achieving V<sub>A</sub> with lesser V<sub>E</sub>. A pivotal mechanistic study was done using neonatal piglets with a severe respiratory distress induced by central venous oleic acid delivery.<sup>3</sup> In this model, three conditions were compared: HFT with a low leak around the prongs (ie snug fit in the nares), HFT where no more than 50% of the nares were occluded (ie non-occlusive prongs) and conventional mask CPAP. The low leak condition was created to mimic the situations where clinicians try to get a CPAP effect, whereas the ≤50% occlusion condition fits our recommendation for the application of HFT. Under these conditions, the model

evaluated titration of flow/CPAP pressure on CO<sub>2</sub> removal, oxygenation and pressure development.

As shown in Figure 2, under both HFT conditions, arterial CO<sub>2</sub> inversely correlated with flow rate wherein arterial CO<sub>2</sub> tension (PaCO<sub>2</sub>) in these spontaneous breathers could be reduced back to pre-injury levels. Moreover, the PaCO<sub>2</sub> in the <50% occlusion condition was significantly reduced at lower flow rates compared to the low leak condition, indicating that a less occlusive prong design facilitates nasopharyngeal purge. CPAP alone was never able to achieve this ventilation effect. With CPAP, PaCO<sub>2</sub> was slightly reduced with a mild pressure increase, but then PaCO<sub>2</sub> rose as CPAP pressure went above 4 cmH<sub>2</sub>O, presumably due to overdistension.

As shown in Figure 3, regarding oxygenation, under both HFT conditions a flow dependent increase in arterial oxygen tension (PaO<sub>2</sub>) was demonstrated until a plateau was reached. This saturation pattern is indicative of dead space washout and fits the hypothesis of the study based on the background modeling of tracheal gas insufflation.<sup>20</sup> The concept behind dead space purge techniques is that there is a finite amount of time (late stage exhalation and end-expiratory pause) to purge the space and a finite amount of dead space volume that can be purged. As flow is increased, more of the volume can be purged until flow is sufficient to purge all of the volume in the allotted time, after which additional flow produces no additional effect. With respect to oxygenation, CPAP was as effective as HFT although not a function of pressure titration.

Pressure in this study was measured by direct perpendicular placement of a pressure catheter in the trachea through an anterior cervical cut-down. As shown in Figure 4, the pressure data from this study shows a direct relationship between flow and baseline pressure shift, which is in agreement with the clinical studies. Here the pressure from the low leak condition is always greater than the ≤50% occlusion condition. Importantly, there was dissociation between oxygenation and the pressure response where pressure continues to rise beyond the flow rate at which oxygenation response reaches a plateau. This dissociation between pressure and physiologic oxygenation response supports dead space flush as the primary mechanism of action. Moreover, because the cannula fit impacted the flow rate needed to accomplish optimal efficacy (ie flow rate where PaO<sub>2</sub> plateaued and PaCO<sub>2</sub> reached baseline levels), pressure was actually inversely related to physiologic improvement if we consider cannula design as a categorical variable. In other words, the less occlusive prong design accomplished maximal efficacy with approximately 60% of the flow needed to do so with the occlusive prong design, which translates to approximately one-half of the inadvertent distending pressure. Optimized prong fit translates to better outcome with less pressure.



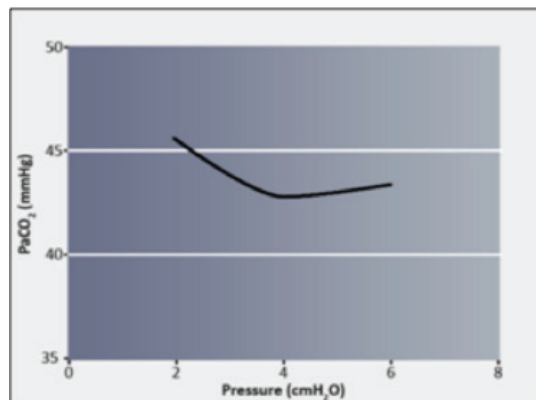
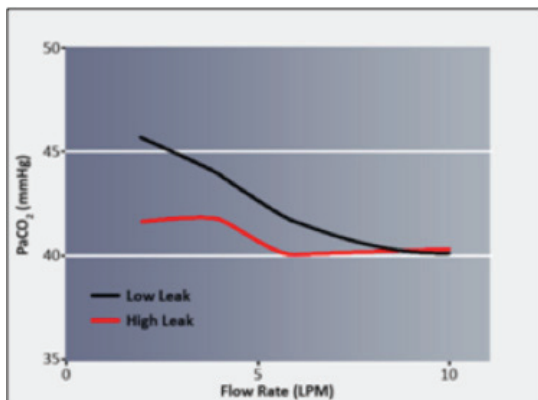


Figure 2. These graphs adapted from Frizzola et al.<sup>3</sup> show that high flow therapy (HFT) provides a ventilation effect (impact on arterial CO<sub>2</sub> tension) not seen with continuous positive airway pressure (CPAP). Moreover, the effect is more pronounced and occurs at lower flows when the cannulae are fitted to allow a high degree of leakage around the nasal prongs.

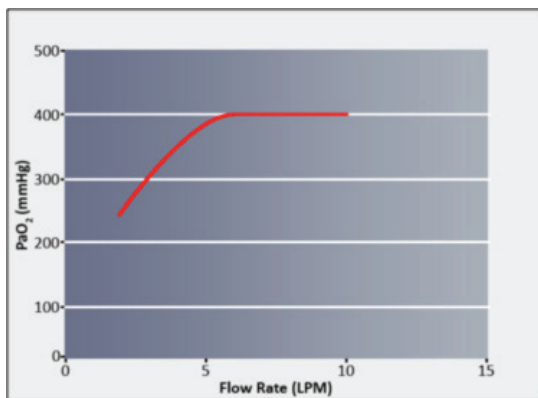


Figure 3. This graph adapted from Frizzola et al.<sup>3</sup> shows the oxygenation relationship with HFT titration. Arterial oxygen tension rises with increased flow to a plateau, after which more flow has no further effect. This inflexion point is explained in the tracheal gas insufflation literature as the point where flow is adequate to purge all available dead space.

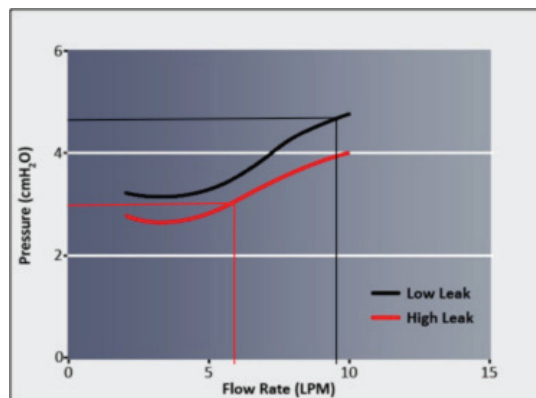


Figure 4. This graph adapted from Frizzola et al.<sup>3</sup> shows the end-distending pressure response to nasal prongs which occlude the nares (low leak) versus prongs that occlude no more than 50% of the nares (high leak). In each case pressure rises with increased flow, dissociating this relationship from the oxygenation curve (Figure 3). Referring back to Figure 2, note that the non-occlusive prongs facilitated better ventilation, accomplishing optimal effect at a lower flow, seen here where the extrapolation bars cross the x-axis. By following these bars to the y-axis, note the non-occlusive prongs accomplish this efficacy with significantly less distending pressure.

The clinical side to this translational modeling was done in COPD patients (data presented at the 2011 CHEST meeting and in review for publication). Adults were examined because they can be compliant in ways that an infant cannot, but the resulting evidence regarding ventilation is fundamental to the concept of dead space and translates to the infant as well. This study shows that HFT with room air results in at least a 13% reduction in  $V_E$  while maintaining the same PaCO<sub>2</sub> compared to both no support and supplemental oxygen conditions. As discussed later, this ventilation effect is potentially greater in infants because of the greater relative extrathoracic dead space volume compared to adults.<sup>21</sup>

### CPAP versus HFT

CPAP systems are specifically designed to be a closed system in conjunction with the infant's respiratory tract. The proposed mechanisms of action for CPAP are complex and multifactorial, but include the concept that pressure is able to recruit lung

alveoli by increasing FRC, thus improving compliance so that a greater  $V_E$  can be achieved to account for the necessary  $V_A$ .<sup>22</sup> From a mechanical perspective, CPAP supports spontaneous breathing by making it less taxing to stretch the lung and by minimizing atelectrauma during lung stretch. HFT, on the other hand, is aimed at achieving  $V_A$  with a lesser  $V_E$  so as to reduce the necessary lung stretch. Nonetheless, the accompanying humidification and mild pressure effects with HFT would attenuate atelectrauma as well.<sup>7,23</sup>

HFT is designed to be an open system, wherein the gas is not intended to be contained for the development of a pressurized patient airway. In an HFT system, pressure inside the device circuit is by necessity quite high, in the range of nearly 400 cmH<sub>2</sub>O.<sup>24</sup> This is the result of pushing high flow through the substantial resistance of the relatively tiny nasal prong orifices. Because of this relatively enormous cannula resistance and the fact that the system circuit is not sealed with the patient's

airway, physics dictates that circuit pressure does not transmit to the patient. The development of patient airway pressure is a coinciding effect during HFT and is a function of the resistance to the flow exiting from the patient's nasopharynx through the oral cavity and nose.

To keep the coinciding nasal pressure from reaching levels that would need to be monitored, the literature dictates that a cannulae should not occlude more than 50% of the nares. This recommendation is based on the work of Dr Locke and colleagues who showed that nasal prongs having an outside diameter that is no more than 50% of the internal diameter of the nares does not result in distending pressure during low flow O<sub>2</sub> therapy. Conversely, cannula having an outside diameter that was three-quarters of the inside nare diameter resulted in significant pressure at low flows. The message here is that keeping nares open by 50% of the diameter represents adequate anatomic release. Note that this 50% diameter rule ensures that the surface area of the unoccluded region of the nares is greater than the surface area of the occluded area, based on the nonlinear, direct relationship between surface area and distance from the center of a circle. Vapotherm's recommendations and cannulae offerings are consistent with this requirement.

When applied correctly, mild airway pressure does develop during HFT and is considered a mechanism of action based on the rationale for CPAP.<sup>22</sup> This pressure is a function of both the rate of flow through the patient's upper air space and the anatomical resistance to this flow as it passes through the anatomy;<sup>25</sup> however, the pressure is not at the level of closed CPAP system and varies regionally as a function of the gas flow patterns (preliminary data). From a review of the research related to airway pressures in neonates during HFT, data shows that airway pressure with HFT can be expected to be less than or approximately equivalent to airway pressure when a CPAP of 6 cmH<sub>2</sub>O is applied,<sup>8-10,23,24,26</sup> and equally as variable as airway pressure during CPAP.<sup>24</sup> In interpreting these data it is important recognize that some investigators were trying to create CPAP by minimizing the leak through the nose and mouth. Nonetheless, the data showed only modest pressures.

### **Application of HFT in the NICU: Flow Rate Titration and Rationale**

Despite the inconsistency in the literature defining the flow rates needed for HFT, when used appropriately reports indicate improved extubation success and potentially a reduction in intubation rates.<sup>27,28</sup> In addition, the simplicity of the cannula interface with loose fitting nasal prongs reduces facial skin and nasal abrasions associated with more intense therapies. HFT is simple to administer and manage compared to positive airway pressure therapies that require intense monitoring to ensure that the patient interface remains properly placed.

The range of flows to be used in infants is between 1-8 L/min. While infants have a very small tidal volume, in the range of 4-6 mL/kg, their respiratory rates are quite high. In sick children, respiratory rates can approach 100 breaths per minute, making peak inspiratory flows very high relative to minute volumes. Another consideration with infants, which pertains to the mechanisms of dead space purge, is the relative size of the anatomical reservoir which consists of the extra-thoracic dead space volume of the nasal, oral and pharyngeal cavities. Infants have a much larger anatomical reservoir compared to older children and adults.<sup>21</sup> Small infants have an extrathoracic

dead space volume around 2.3 mL/kg, whereas in children over six years of age and into adulthood this value drops to approximately 0.8 mL/kg. Therefore, as compared to an adult, an infant may need greater relative flow rates to realize the full benefits of purging the anatomical reservoir in the window of opportunity between breaths (flow rates that go beyond simply meeting inspiratory demand). This three-fold greater anatomical reservoir volume in small infants translates to dead space making up a much greater fraction of their tidal volume as compared to larger children and adults.

As a result of these factors, small infants have a greater propensity to benefit from HFT in that these patients are much more sensitive to changes in dead space. However, cannula flow rates needed to maximize efficacy typically begin at greater than 3 L/min.

### **Cannula Research in Optimizing HFT: Fluid Dynamics and Flow Patterns**

With an understanding that the mechanisms of action are based on creating an internal reservoir of conditioned gas, work has been done to refine the patient interface to optimize this effect. Some of the work that is currently underway involves using computation fluid dynamics modeling to learn more about gas flow characteristics in the nasopharynx with HFT. Using this model, we have already confirmed what is suggested by animal data, that a less occlusive prong design allows for more rapid purge of the nasal cavity at any flow rate. Therefore, as we saw in the animal data, the nasopharynx can be purged in the time between breaths with a lesser flow rate when cannula design is optimized; in this case smaller prong diameter (data being prepared for publication).

Another topic addressed using the computational fluid dynamics modeling pertains to sheer force (or strain rate) on the walls of the nasopharynx as a result of the gas flow velocity from the cannula nozzle (commonly referred to as "jetting effect"). With this model we learned that the strain rate is absorbed between laminae of the gas, and with a smaller cannula dissipates before impacting the wall.

However, with the larger cannula, the strain rate impacts the wall just by nature of its closer proximity (data being prepared for publication). Thus, the larger cannula is more likely to result in a jetting effect. To put this concept in another way, this "jetting effect" is often described as similar to turning a fire hose on a wall; however, this analogy is very much incorrect because it involves jetting one medium (water) though another less dense medium (air). In the case of cannula gas flow, air is jetting through air, and thus a more appropriate analogy would be similar to water jets that are under water such as in a hot tub. In this analogy, you can probably imagine that you would only experience significant strain if you were to hold your hand directly on or around the water jet.

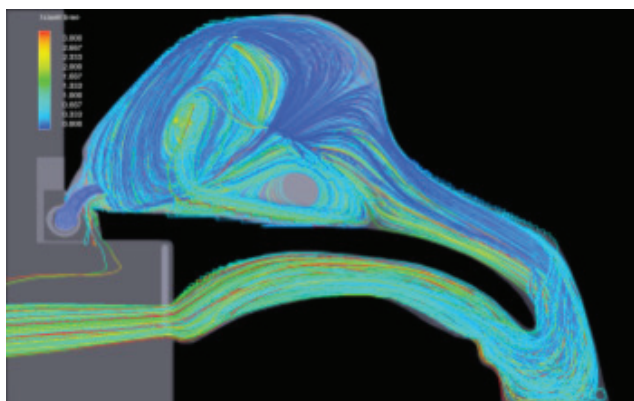


Figure 5. This image from computational fluid dynamics modeling shows the patterns of gas flow through the nasopharynx from the cannula. Note the vortices and varied directionality of flow. These patterns define pressure and other forces throughout the cavity.

## Summary

HFT is a unique noninvasive respiratory support modality in the NICU. It is based on the concepts of dead space elimination for breathing efficiency and the delivery of ideally conditioned respiratory gases to an already fragile lung. A misconception that stifles the adaptation of HFT is that it is an uncontrolled form of CPAP. The mechanistic literature, however, does not support this presumption and a significant amount of clinical data suggests that pressure is not a concern when HFT is applied correctly. Importantly, the neonatal community would benefit from the uniform adaptation of a definition that is based on research and guides the cannula design aspects and flow requirement. These studies suggest that cannula fit should not occlude more than 50% of the nares and that flows should be between 3 and 8 L/min.

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# Intubating Laryngeal Airway in Children

The journal *Pediatric Anesthesia* recently published the article *Prospective Evaluation of the Self-pressurized air-Q Intubating Laryngeal Airway in Children*.<sup>\*</sup> [The product referred to throughout this paper as the air-Q ILA SP or ILA-SP has been rebranded as the air-Q SP.] The objective of the authors was to assess the clinical efficacy of the self-pressurized air-Q ILA (ILA-SP) (Mercury Medical). The purpose of their prospective audit was to evaluate the feasibility of the ILA-SP in clinical practice and generate data for future comparison trials. The ILA-SP is a new first-generation supraglottic airway for children with a self-adjusting cuff that does not require balloon. Over a 4-month period, 352 children with an ASA physical status of I–III, newborn to 18 years of age, undergoing various procedures, were studied. Data points assessed included insertion success rates, airway leak pressures, quality of ventilation, and perioperative complications associated with the use of this device. In 349 of the 352 patients in this study, the ILA-SP was used successfully as a primary supraglottic airway device in a variety of patients. Three patients required conversion to a standard laryngeal mask airway or a tracheal tube. The mean initial airway leak pressure for all patients was  $17.8 \pm 5.4$  cm H<sub>2</sub>O, and  $20.4 \pm 5.5$  cm H<sub>2</sub>O when re-checked at 10 min, which was statistically significant ( $P < 0.001$ ). Complications were limited to 14 patients and related to reflex activation of the airway (coughing, laryngospasm, and bronchospasm) ( $n = 10$ ), sore throat ( $n = 3$ ), and blood staining on removal of the device ( $n = 1$ ). There were no episodes of regurgitation, aspiration, or hoarseness. The authors concluded: Acceptable clinical performance was demonstrated with the ILA-SP for a variety of procedures in infants and children with spontaneous and positive pressure ventilation. Future studies comparing this device to other supraglottic airways may provide useful information regarding the safety of the ILA-SP in pediatric clinical practice.

The authors used a newer version of the ILA self-pressurized air-Q, the ILA-SP, which was introduced into their practice for routine airway maintenance in children. According to the authors, “This device shares structural similarities with the original ILA, including the ability to provide a reliable conduit for tracheal intubation.” The new distinguishing features of the ILA-SP are the absence of a pilot balloon and continuity between the airway tube and the cuff through an inner aperture at their conjunction.

According to the authors, these features may allow for several clinical benefits, in that intra-cuff pressures are determined by the airway pressures, because of the equalization of pressures with the movement of gas between the cuff and airway tube. Also, lower intra-cuff pressures are maintained overall as a result of being limited by the peak airway pressures, with the highest pressures exerted during inspiration. Finally, by not exceeding peak airway pressures, the balance between intra-cuff pressures

and the airway seal of the device may be optimized at lower pressure. As such, the risk of sore throat, neuropraxic injury, and gastric insufflation seen with overinflation of traditional cuffed supraglottic devices may be reduced.

The study sought to assess insertion success rates, airway leak pressures, quality of ventilation, and perioperative complications. The authors recorded the type of inductions, the size of the ILA-SP inserted, and the number of attempts required for successful insertion. The authors wrote: “The airway leak pressure was observed with the head in a neutral position... The expiratory valve was immediately released when the leak pressure was determined by the onset of audible noise or if airway pressure reached 40 cm H<sub>2</sub>O without an audible leak. A second airway leak pressure was taken at least 10 minutes later to observe whether there was a change in the airway seal.”

Participants were 221 male and 131 female pediatric patients of various weights and ages (mean age  $5 \pm 4$  years). The ILA-SP insertion resulted in subsequent ventilation in 351 patients, and successful placement at first attempt was achieved in 336 patients, while 13 needed a second attempt, typically requiring a change in the size of the ILA-SP. “Spontaneous ventilation was reported in 203 patients, mechanical ventilation in 144, and 5 received pressure support ventilation,” per the authors, who noted that the design modification of the ILA-SP had clinical advantages, in that insertion techniques were similar to other such devices but there was no need for cuff manipulation, the pressure in the cuff being self-regulated and no longer a closed air space. While ease of placement was similar to the original ILA and LMA, the ILA-SP was found to fit better in infants, in that the wider mask bowl and curved airway tube of the latter may have provided greater lateral stability and better seating of the hypopharynx. The authors wrote: “The ILA-SP may improve the applicability of supraglottic airway devices for the anesthetic management of smaller children.” Also, “An improvement in airway leak pressures was seen in the 10-min leak pressure testing, potentially indicating an improvement in airway seal across all cohorts.” It was noted that “as a result of the ILA-SP design, airway seals may also have been optimized at lower intra-cuff pressures.”

The authors concluded that “the airway leak pressures and ventilation parameters achieved for a variety of procedures were clinically acceptable throughout all patient sizes, even with the use of positive pressure ventilation.”

<sup>\*</sup> Prospective evaluation of the self-pressurized air-Q intubating laryngeal airway in children. Narasimhan Jagannathan, Lisa E. Sohn, Ravinder Mankoo, Kenneth E. Langen, Andrew G. Roth & Steven C. Hall, Department of Pediatric Anesthesiology, Children’s Memorial Hospital, Northwestern University Feinberg School of Medicine, Chicago, IL. *Pediatric Anesthesia* 21 (2011) 673-680 © 2011 Blackwell Publishing Ltd.

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# The No-Bite V: Proving to be a more comfortable suctioning method in Hospice & Palliative Care for “The Death Rattle”

## Abstract

To understand The No-Bite V, one must understand some difficulties and contraindications to nasopharyngeal and nasotracheal suctioning:

- Occluded Nasal Passages/Deviated Septum<sup>1</sup>
- Nasal Trauma/Bleeding<sup>1</sup>
- Recent Nasal Fractures/Sinus Surgery<sup>1</sup>
- Elevated Coagulation Times from Blood Thinners<sup>1</sup>
- Coagulopathy or Bleeding Disorders<sup>1</sup>
- Frequent Coiling of Suction Catheters Upon Insertion<sup>1</sup>
- Basal Skull Fracture/Transphenoidal Neurosurgery (absolute contraindications)<sup>1</sup>

Hospice and palliative care provides humane and compassionate care for people in the last phases of an incurable disease. The focus is on patient comfort and symptom management. One symptom, the death rattle, which refers to the gurgling noise of excessive secretions, can be misinterpreted as the sound of gagging or choking to death.<sup>2</sup> The death rattle occurs in up to (92%) of people actively dying and can be an unnerving experience for the patient’s family as well as the caregivers.<sup>3</sup>

The standard of care is repositioning of the patient and also the use of muscarinic receptor blockers (anti-cholinergic drugs), but these do not always work.

Another way to treat the death rattle is gentle oropharyngeal, nasopharyngeal, or nasotracheal suctioning. But during oral insertion of the suction catheter, the patient can bite down and stop the process. The catheter can also be ineffective because it cannot reach the secretions due to non-directional method of inserting catheter orally. During nasal insertion of the suction catheter, it can have a tendency to coil in the back of the throat, leading to multiple unsuccessful attempts and nasal bleeding. Compound these issues with a dying patient, a grieving family, fragile mucous membranes, low platelets, or a patient previously on blood thinners, and the situation can go from bad to worse.

Clinicians are all too familiar with situations where a patient is in need of suctioning but the nasal passageways prove to be either difficult or even contraindicated. Never before did an alternative option exist to perform pharyngeal or tracheal suctioning while avoiding the nasal pathways. In the following report, we described two cases of more comfortable suctioning experiences with The No-Bite V in patients where the nasal approach to suctioning was contraindicated and unable to be done.

## Case #1

Cardiac ICU, 83 y/o male, pmHx of HTN, CAD, prostate cancer s/p chemotherapy, pancytopenia. Patient was found down in field, resuscitated and brought to CCU. Several days later in CCU, patient diagnosed with severe brain damage and terminal weaning protocol initiated with palliative care team. Post extubation, patient developed death rattle despite the use of anti-cholinergic drugs. Wife and family members were so disturbed by the noises of the death rattle that they had to leave the room. Oropharyngeal suctioning proved ineffective due to the inaccuracy of the catheter placement; caregivers were unable to reach secretions in the vocal cord area, which were causing the noises. The nasal route was contraindicated due to low platelet count and high INR. Respiratory therapist and ICU nurse initiated the use of The No-Bite V, and successfully suctioned out the secretions that were causing the death rattle.

Conclusion: With The No-Bite V the patient could be suctioned directionally, in an effective yet respectful manner, avoiding painful nasal trauma and bleeding. More importantly, the wife and family were able to come back to the room and spend the last peaceful moments with their loved one.

## Case #2

Home hospice in a rural area, 77 y/o female, pmHx: end stage pancreatic CA, currently w/ pneumonia, patient in end stages of life and has been enrolled in the Home Hospice program for approximately 7 days. Patient deteriorated more rapidly on her last day due to complications of pneumonia, patient developed the death rattle and secretions were too thick for anti-cholinergic medication to be effective. A nasal trumpet was placed but coiling of the suction catheter occurred frequently so it had to be removed. The family was also uncomfortable with the idea of a rubber device permanently placed in the nose. The patient was in need of suctioning more frequently in her last phase of life so the hospice nurse initiated the use of The No-Bite V with the help of the family, and successfully suctioned the secretions that were causing the death rattle.

Conclusion: With the help of The No-Bite V, the family members suctioned their mother several times throughout the night and she passed away peacefully. The nasal approach was avoided altogether, therefore preventing any nasal trauma and bleeding. In teaching the family how to suction their dying mother, the family stated, “They no longer felt helpless and were grateful that they could take part in their  
*Continued on page 46...*”

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This article was provided by NJR Medical.

# To Compensate or Not To Compensate

John Newton, RRT-NPS; Paul Garbarini, MS, RRT

The creation of additional airway resistance as a result of artificial airways is an ever-present issue with invasive mechanical ventilation. This increase in airway resistance can lead to increased work of breathing imposed upon the patient, cause muscle fatigue and complicate or lengthen the weaning process.<sup>1</sup>

Automatic tube compensation is available on various mechanical ventilators, and can have various names, such as automatic tube compensation, tube resistance compensation, etc. Since the development and availability of automatic tube compensation, many mechanical ventilators have the ability to offload the artificial airway resistance as they have become more responsive to the variable flows of pressure supported breaths, typically used during spontaneous breathing trials.<sup>2-6</sup> These algorithms increase inspiratory pressure proportional to flow since resistance and flow have a direct relationship through a fixed resistance orifice. Unlike pressure support which provides a fixed pressure level during inspiration, tube compensation varies the applied pressure during inspiration.

While this makes perfect sense in vitro with a “clean” artificial airway, once this airway is in vivo, inspissated secretions and tube distortion can eventually decrease the inner diameter of the airway. Many studies have demonstrated that within a week in vivo, the airway resistance from the artificial airway can increase the equivalent to having the next smaller size endotracheal (ET) tube inserted. This unaccounted for increase in airway resistance will then not be fully compensated for with automatic tube compensation alone. Either additional work will be required on the part of the patient, or some additional pressure support from the ventilator will be required to help fully compensate for the increased airway resistance.

Some practitioners may view this as a failure of automatic tube compensation, as it may not always provide sufficient support independently. However, it should be viewed as only partially correcting the problem created from the artificial airway that has been in place for an extended period of time.

In the past, it was not always possible to provide automatic tube compensation and pressure support simultaneously and the practitioner had to decide between either dynamic

automatic tube compensation or a static pressure support, but that is no longer the case as some ventilator platforms allow the practitioner to apply both simultaneously. Consideration of additional pressure support in addition to automatic tube compensation may be required relative to the length of time the artificial airway is in place. Tube compensation does not off load resistive work of breathing increases due to secretions or bronchospasm nor does it compensate for increased elastic work...decreased lung and/or chest wall compliance.

Some advocate the minimum that should be done for the patient is 100% automatic tube compensation to remove “baseline” airway resistance which will be proportional to flow rates. The assumption is that eliminating the endotracheal tube imposed work of breathing will mimic the patients post-extubation work of breathing.

However, several studies have reported that work of breathing increases post extubation, presumably due to upper airway edema post-extubation. Patients with autopeep due to obstructive airways disease or chronic heart failure may lose the benefits of positive pressure ventilation post extubation.

Additionally, studies have not provided conclusive evidence of any difference in outcomes whether performing a spontaneous breathing trial with low level pressure support vs automatic tube compensation vs a T-piece vs CPAP.

There is one circumstance where automatic tube compensation could be misleading. If tube compensation is active with a small tracheostomy tube in place, the tube compensation may provide a false positive spontaneous breathing trial as the patient will still have the tracheostomy tube in place when off the ventilator. So, it may be advisable to assess the patient with a small tracheostomy tube with tube compensation off.

In conclusion, if the goal is to eliminate the artificial airway resistance, rather than applying a fixed level of pressure support as a “best guess,” it would seem reasonable to use tube compensation since it tailors the level of pressure support to the size of the artificial airway and actual measured flow. That said, the clinician is obligated to understand the limitations of automatic tube compensation systems.

## References

- 1 Jun Oto, Hideaki I, Emiko N, et al. Potential inadequacy of *Continued on page 52...*

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Newton is Clinical Support Specialist, Hamilton Medical; Garbarini is VP, US Research & Development, Hamilton Medical. This article appeared in Hamilton Medical's Newsletter, Intelligent Ventilation.



# Inadequate Treatment of Ventilator-associated and Hospital-acquired Pneumonia

Nihal Piskin, Hande Aydemir, Nefise Oztoprak, Deniz Akduman, Fusun Comert, Furuzan Kokturk, Guven Celebi

## Abstract

**Background:** Initial antimicrobial therapy (AB) is an important determinant of clinical outcome in patients with severe infections such as pneumonia; however, well-conducted studies regarding prognostic impact of inadequate initial AB in patients who are not undergoing mechanical ventilation (MV) are lacking. In this study we aimed to identify the risk factors for inadequate initial AB and to determine its subsequent impact on outcomes in both ventilator associated pneumonia (VAP) and hospital acquired pneumonia (HAP).

**Methods:** We retrospectively studied the accuracy of initial AB in patients with pneumonia in a university hospital in Turkey. A total of 218 patients with HAP and 130 patients with VAP were included. For each patient clinical, radiological and microbiological data were collected. Stepwise multivariate logistic regression analysis was used for risk factor analysis. Survival analysis was performed by using Kaplan-Meier method with Log-rank test.

**Results:** Sixty six percent of patients in VAP group and 41.3% of patients in HAP group received inadequate initial AB. Multiple logistic regression analysis revealed that the risk factors for inadequate initial AB in HAP patients were; late-onset HAP (OR = 2.35 (95% CI, 1.05-5.22;  $p = 0.037$ ) and APACHE II score at onset of HAP (OR = 1.06 (95% CI, 1.01-1.12);  $p = 0.018$ ). In VAP patients; antibiotic usage in the previous three months (OR = 3.16 (95% CI, 1.27- 7.81);  $p = 0.013$ ) and admission to a surgical unit (OR = 2.9 (95% CI, 1.17-7.19);  $p = 0.022$ ) were found to be independent risk factors for inadequate initial AB. No statistically significant difference in crude hospital mortality and 28-day mortality was observed between the treatment groups in both VAP and HAP. However we showed a significant increase in length of hospital stay, duration of mechanical ventilation and a prolonged clinical resolution in the inadequate AB group in both VAP and HAP.

**Conclusion:** Our data suggests that the risk factors for inadequate initial AB are indirectly associated with the acquisition of resistant bacteria for both VAP and HAP. Although we could not find a positive correlation between adequate initial AB and survival; empirical AB with a broad spectrum should be initiated promptly to improve secondary outcomes.

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## Background

Nosocomial pneumonia, which is usually defined as hospital-acquired pneumonia (HAP), is the second most frequent nosocomial infection but the first in terms of morbidity, mortality and cost. It occurs in 8-20% of intensive care unit (ICU) patients, with an increased frequency and mortality if the patients are mechanically ventilated.<sup>1-4</sup> Over the past decade, several risk factors associated with mortality have been detected in HAP and ventilator-associated pneumonia (VAP). One of the most consistent and evident prognostic factor throughout the literature is the accuracy of initial antibiotic treatment (AB). By contrast, early aggressive therapy with adequate broad-spectrum regimens that optimize therapy against the likely pathogens is associated with lower mortality rates and shorter hospital stay.<sup>4-8</sup> However, despite numerous studies some controversies continue to exist about the genuine prognostic impact of initial AB.<sup>9-14</sup>

In recent years, international societies and most recently, the American Thoracic Society jointly with the Infectious Diseases Society of America, have developed guidelines for the management of HAP and VAP.<sup>2,3</sup> In spite of the presence of practice guidelines, the percentage of inadequate AB varies in the literature from 10% to 73%.<sup>8-11,13-18</sup> The presence of multidrug-resistant bacteria is the primary reason that patients with VAP and HAP receive inadequate AB,<sup>5</sup> however other factors that contribute to inadequate AB are not well defined. Therefore, we aimed to identify the possible risk factors for inadequate initial AB in both HAP and VAP and to determine its subsequent impact on outcomes.

## Methods

**Patients and setting:** This retrospective cohort study was conducted at Zonguldak Bulent Ecevit University Hospital, a 524 bed referral and tertiary hospital, from January 2005 to January 2008. Patients were enrolled in the study if they were >16 years of age and diagnosed with VAP or HAP irrespective of the diagnosis at admission. Only the first episode of pneumonia was taken into account and no community acquired pneumonia cases were included. The study was approved by the Zonguldak Bulent Ecevit University Hospital Ethics Committee. The need for informed consent was waived due to the retrospective observational nature of the study.

For each patient clinical, radiological and microbiological data were collected. The following characteristics were retrieved from patient records: age, sex, underlying diseases, antibiotic usage in the previous three months, Acute Physiological Score

**Table 1 Characteristics of 218 patients with HAP with regard to the adequacy of empirical antibiotic treatment**

Characteristics	Adequate treatment n = 128	Inadequate treatment n = 90	p
Age (years)	61.84 ± 14.66	64.44 ± 13.49	0.189
Sex (male)	84 (65.6)	58 (64.4)	0.857
Surgical unit	24 (68.6)	11 (31.4)	0.269
Underlying diseases			
Diabetes mellitus	26 (20.3)	14 (15.6)	0.474
COPD	32 (25.0)	19 (21.1)	0.613
Chronic renal failure	14 (10.9)	10 (11.1)	1.000
Congestive heart failure	15 (11.7)	16 (17.8)	0.287
Cerebrovascular disease	7 (5.5)	10 (11.1)	0.203
Malignancy	24 (18.8)	22 (24.4)	0.398
Central venous catheterization	37 (28.9)	35 (38.9)	0.123
Urinary catheterization	88 (68.8)	66 (73.3)	0.464
Late-onset pneumonia	78 (60.9)	72 (80.0)	<b>0.003</b>
Acquisition of other site infection	21 (16.4)	20 (22.2)	0.365
Previous antibiotic usage	42 (32.8)	34 (37.8)	0.449
Culture proven pneumonia	43 (33.6)	51 (56.7)	<b>0.001</b>
MDR bacteria	29 (22.7)	38 (42.2)	<b>0.002</b>
Polymicrobial etiology	1 (0.8)	8 (8.9)	<b>0.004</b>
Length of stay before HAP	7.09 ± 5.07	8.52 ± 5.26	<b>0.003</b>
APACHE II score	12.68 ± 5.79	14.63 ± 6.59	<b>0.024</b>

Chronic Health Evaluation (APACHE) II at onset of pneumonia, length of hospital and ICU stays, presence of invasive procedures, duration of mechanical ventilation, presence of an other site infection, microbiological culture results, fever and/or other clinical symptoms resolution dates and mortality.

**Definitions:** Hospital-acquired pneumonia was diagnosed on the basis of Centers for Disease Control and Prevention clinical criteria.<sup>19</sup> Pneumonia was considered ventilator associated when it occurred 48 hours after starting mechanical ventilation and it was known to have not been incubating before the initiation of MV. Pneumonia was defined as early-onset if it started within 4 days of admission, in accordance with the American Thoracic Society/Infectious Disease Society of America guidelines.<sup>2,3</sup> Quantitative cultures of respiratory samples obtained at the time of diagnosis were used to diagnose pneumonia. Inadequate AB was defined as, at least one bacterial isolate not covered by any initial antibiotic, or when the pathogen was resistant to all initial empiric antimicrobial agents. In culture negative cases, patients' records were evaluated and appropriateness of AB was decided according to resolution of clinical and laboratory signs of pneumonia with the initial regimen that had been pursued or changed. AB was modified as soon as susceptibility testing results were available or if the clinical and radiological signs of pneumonia did not improve, mainly within 48–72 hours. The total number of deaths within 28 days after the onset of pneumonia and during hospitalization were defined as 28-day mortality and in-hospital mortality respectively.

**Microbiological data:** Microbiological data for the patients was obtained from cultures of sputum, transendotracheal aspirates (TA), blood, pleural fluids and bronchoalveolar lavage (BAL) fluids. The bacteriological diagnosis required the following criteria: Sputum and TA cultures growing  $\geq 10^5$  colony-forming units (cfu)/ml of bacteria, BAL cultures growing

$10^4$  cfu/ml of bacteria, blood or pleural fluid cultures revealing the same pathogen with the respiratory samples. Appropriate specimens of sputum and TA to be taken into consideration for diagnostic testing required a white blood cell count of  $>25$  and  $<10$  epithelial cells per low-power examination field. Bacterial identification and susceptibility testing were performed by standard methods. The identification of "mouth flora" was considered as culture negative.

**Statistical analysis:** Statistical analysis was performed with SPSS 18.0 software (SPSS, Inc., Chicago, IL, USA). Continuous variables were expressed as mean  $\pm$  standard deviation and categorical variables as numbers and percentages. Continuous variables were compared with the Independent Sample T test or Mann–Whitney U test and categorical variables were compared using Pearson's Chi-square test or Fisher's Exact Chi-square test. A P value of less than 0.05 was considered statistically significant for all tests. Forward stepwise logistic regression model was performed to assess the independent risk factors for inadequate initial antibiotic treatment in both HAP and VAP patients. Survival analysis was performed using Kaplan-Meier method with Log-rank test.

## Results

During the study period 348 patients met the inclusion criteria in whom 218 patients developed HAP and 130 patients developed VAP. The mean age of the patients was  $63.56 \pm 15.17$  and 62.9% were male. The most frequent admission diagnoses included respiratory diseases (namely COPD, ARDS or acute respiratory failure) (32.3%), neurological diseases (17.7%), malignancy (13.1%) in VAP patients and respiratory diseases (34.9%), malignancy (20.2%) and metabolic diseases (27.1%) in HAP patients. Eighty six (66%) patients in VAP group and 90 (41.3%) patients in HAP group received inadequate initial AB. Characteristics of patients with HAP and VAP with regard to the adequacy of empirical AB are summarized in Tables 1 and 2

**Table 2 Characteristics of 130 patients with VAP with regard to the adequacy of empirical antibiotic treatment**

Characteristics	Adequate treatment n = 44	Inadequate treatment n = 86	p
Age (years)	65.64 ± 16.42	64.15 ± 16.83	0.628
Sex (male)	29 (65.9)	48 (55.8)	0.358
Surgical unit	22 (45.8)	26 (54.2)	<b>0.044</b>
Underlying diseases			
Diabetes mellitus	6 (13.6)	13 (15.1)	1.000
COPD	15(34.1)	18 (20.9)	0.156
Chronic renal failure	1 (2.3)	4 (4.7)	0.672
Congestive heart failure	7 (15.9)	15 (17.4)	1.000
Cerebrovascular disease	5 (11.4)	16 (18.6)	0.418
Malignancy	6 (13.6)	13 (15.1)	1.000
Central venous catheterization	34 (77.3)	62 (72.1)	0.671
Urinary catheterization	43 (97.7)	84 (97.7)	1.000
Late-onset VAP	36 ( 81.8)	75 (87.2)	0.575
Presence of other site infection	12 (27.3)	42 (48.8)	<b>0.030</b>
Previous antibiotic usage	12 (27.3)	39 (45.3)	0.071
Culture proven pneumonia	37 (84.1)	80 (93.0)	0.128
Polymicrobial etiology	2 (4.5)	6 (7.0)	0.186
MDR bacteria	32 (72.7)	60 (69.8)	0.883
Length of stay before VAP	12.61 ± 11.20	14.31 ± 10.348	0.138
APACHE II score	16.39 ± 6.71	16.81 ± 6.63	0.730

respectively. Age, sex, comorbidities and admission diagnosis were not statistically different between treatment groups in either HAP or VAP patients.

In all VAP cases TA and/or BAL cultures were performed. While for the HAP group, TA cultures were performed in 45 patients and BAL cultures were performed in 7 patients, the remaining samples were all sputum cultures. Of the 130 patients with VAP, 13 (10%) were culture negative, eight patients (6.1%) had polymicrobial infection and 92 (78.6%) patients were infected by a multi-drug resistant pathogen. The number of cultures which grew non-fermenting gram-negative bacilli was higher in the inadequate AB group but the difference was not statistically significant (Table 3). Of the 218 patients with HAP, 124 (56.9%) were culture negative, nine patients (4.1%) had polymicrobial infection and 67 (30.7%) patients were infected by a multi-drug resistant pathogen. Totally 103 pathogens were isolated from 94 patients. The isolated pathogens are presented in Table 3.

The regimens of empiric antibiotics are summarized in Table 4. Thirty three (25.4%) patients in VAP group and 13 (5.9%)

patients in HAP group received an antibiotic combination with a glycopeptide antibiotic. Among the patients who received inadequate initial AB, antibiotic therapy was modified  $4.84 \pm 2.49$  and  $3.80 \pm 2.49$  days after the onset of pneumonia in VAP and HAP patients respectively.

As the number of culture negative pneumonias were high especially in the HAP group, we also performed the analysis in “culture positive patients only” in both HAP and VAP to determine whether the risk factors differed based on culture positivity. The results are presented in Table 5.

To define the independent risk factors for inadequate initial AB in both HAP and VAP; multiple logistic regression analysis was performed and age, gender, type of ICU and/or general ward, presence of underlying diseases, presence of central venous catheterization and mechanical ventilation, duration of intubation (for VAP patients only), duration of hospitalization before onset of pneumonia, previous antibiotic usage in the previous three months, APACHE II score at onset of pneumonia, diagnosis of pneumonia (late-onset) and presence of multi-

**Table 3 Microorganisms recovered from patients with HAP and VAP**

Bacteria	HAP (n = 103)*			VAP (n = 125)*		
	Adequate n = 49	Inadequate n = 54	p	Adequate n = 41	Inadequate n = 84	p
Acinetobacter spp	8 (7.8)	13 (12.6)	0.499	13 (10.4)	37 (29.6)	0.383
Pseudomonas spp	10 (9.7)	14 (13.6)		9 (7.2)	21 (16.8)	
S. aureus	12 (11.6)	7 (6.8)		10 (8)	13 (10.4)	
S.pneumoniae	6 (5.8)	5 (4.8)		1 (0.8)	5 (4)	
K. pneumonia	3 (2.9)	3 (2.9)		3 (2.4)	2 (1.6)	
E.coli	6 (5.8)	5 (4.8)		2 (1.6)	4 (3.2)	
Others	4 (3.9)	7 (6.8)		3 (2.4)	2 (1.6)	

n = Number of microorganisms in patient groups.



**Table 4 Antimicrobial agents used in patients with HAP and VAP**

Empiric antibiotic	HAP (n = 218)			VAP (n = 130)		
	Adequate (n = 128)	Inadequate (n = 90)	p	Adequate (n = 44)	Inadequate (n = 86)	p
Carbapenems	31 (24.2)	16 (17.8)	0.004	20 (45.5)	18 (20.9)	<0.001
Third generation cephalosporine	31 (24.2)	27 (30.0)		4 (9.1)	20 (23.3)	
β-lactam + β- lactamase inhibitor	35 (27.3)	21 (23.3)		14 (31.8)	26 (30.2)	
Quinolone	21 (16.4)	16 (17.8)		0	10 (11.6)	
β-lactam in combination with quinolone	1 (0.8)	9 (10.0)		0	9 (10.5)	
Aminoglycoside in combination with carbapenem or β-lactam	9 (7.0)	1 (1.1)		6 (13.6)	3 (3.5)	

drug resistant bacteria were included to the model. There were no multicollinearity in the variables included in the regression model. Multiple logistic regression revealed that the risk of inadequate initial AB in HAP patients was more than twice as large among patients with late-onset HAP (OR = 2.35 (95% CI, 1.05-5.22; p = 0.037) and the risk was also found to be significantly associated with the higher APACHE II score at the onset of HAP (OR = 1.06 (95% CI, 1.01-1.12); p = 0.018). In VAP patients; antibiotic usage in the previous three months (OR = 3.16 (95% CI, 1.27-7.81); p = 0.013) and admission to a surgical unit (OR = 2.9 (95% CI, 1.17-7.19); p = 0.022) were found to be independent risk factors for inadequate initial AB.

Sixty eight (31.2%) patients out of 218 died in the HAP group and 88 (67.7%) patients died in the VAP group. In the HAP group 95 (43.6%) patients were admitted to an ICU during their hospital stay and 54 (56.8%) of these died. The remaining 123 patients were followed in other wards and 14 (11.4%) of these died. The difference was statistically significant (p < 0.001). The outcome

measures of patients who did and did not receive adequate initial AB are summarized in Table 6. No statistically significant difference in crude hospital mortality was observed between the groups in both VAP and HAP (Table 6). The pneumonia related mortality also did not reach statistical significance by day 28 after the diagnosis of pneumonia in either HAP or VAP [25.2% (30/119) with adequate initial AB versus 39.5% (32/81) with inadequate initial AB in HAP patients (p = 0.519) (Figure 1) and 75.0% (30/40) with adequate initial AB versus 71.2% (42/59) with inadequate initial AB in VAP patients (p = 0.847) (Figure 2)]. In VAP patients median survival time after VAP onset was 13 days with adequate initial AB and 14 days with inadequate initial AB (Figure 1). In HAP patients median survival time after HAP onset was 26 days with adequate initial AB and 22 days with inadequate initial AB (Figure 2).

## Discussion

Despite numerous studies in the literature, most of our knowledge about the risk factors and prognostic impact of inadequate initial

**Table 5 Characteristics of culture positive patients with HAP and VAP with regard to the adequacy of empirical antibiotic treatment**

Characteristics	HAP (n = 94)			VAP (n = 117)		
	Adequate treatment n = 43 (%)	Inadequate treatment n = 51 (%)	p	Adequate treatment n = 37 (%)	Inadequate treatment n = 80 (%)	p
Age (years)	60.67 ± 16.04	65.14 ± 13.75	0.167	63.59 ± 16.65	63.85 ± 17.07	0.907
Sex (male)	32(74.4)	37 (72.5)	1.000	24 (64.9)	45 (56.3)	0.497
Surgical unit	9 (20.9)	8 (15.7)	0.697	21 (56.8)	25 (31.3)	<b>0.015</b>
Underlying diseases						
Diabetes mellitus	5 (11.6)	8 (15.7)	0.789	5 (13.5)	11 (13.8)	1.000
COPD	13 (30.2)	10 (19.6)	0.341	11 (29.7)	17 (21.3)	0.443
Chronic renal failure	5 (11.6)	4 (7.8)	0.727	0 (0)	3 (3.8)	0.551
Congestive heart failure	4 (9.3)	9 (17.6)	0.386	6 (16.2)	13 (16.3)	1.000
Cerebrovascular disease	1 (2.3)	9 (17.6)	<b>0.019</b>	3 (8.1)	15 (18.8)	0.227
Malignancy	6 (14.0)	9 (17.6)	0.838	6 (16.2)	11 (13.8)	0.944
Central venous catheterization	16 (37.2)	22 (43.1)	0.710	30 (81.1)	58 (72.5)	0.442
Urinary catheterization	33 (76.7)	37 (72.5)	0.820	37 (100)	78 (97.5)	1.000
Late-onset pneumonia	34 (79.1)	46 (90.2)	0.223	34 (91.9)	72 (90)	1.000
Acquisition of other site infection	12 (27.9)	11 (21.6)	0.637	11 (29.7)	42 (52.5)	<b>0.036</b>
Previous antibiotic usage	20 (46.5)	23 (45.1)	1.000	11 (29.7)	36 (45.0)	0.173
MDR bacteria	29 (67.4)	38 (74.5)	0.599	32 (86.5)	60 (75)	0.243
Polymicrobial etiology	1 (2.3)	8 (15.7)	<b>0.036</b>	2 (5.4)	6 (7.5)	1.000
Length of stay before HAP	7.6 ± 4.3	9.18 ± 5.8	0.194	13.89 ± 11.56	14.88 ± 10.34	0.313
APACHE II score	12.7 ± 5.83	14.92 ± 5.83	<b>0.031</b>	16.08 ± 6.94	16.69 ± 6.72	0.654
Exitus	16 (37.2)	24 (47.1)	0.452	27 (73)	53 (66.3)	0.608

**Table 6 Outcome of patients who did and did not receive adequate antimicrobial therapy**

	HAP (n = 218)			VAP (n = 130)		
	Adequate (n = 128)	Inadequate (n = 90)	p	Adequate (n = 44)	Inadequate (n = 86)	p
In hospital mortality (n,%)	32 (25.8)	35 (38.9)	0.056	32 (72.7)	56 (65.1)	0.497
Length of total hospital stay	19.61 ± 14.40	24.22 ± 13.70	<b>0.001</b>	28.57 ± 23.66	45.00 ± 49.30	<b>0.0091</b>
Length of stay after the diagnosis of pneumonia	12.52 ± 11.14	15.70 ± 11.21	<b>0.010</b>	16.45 ± 18.23	30.71 ± 46.21	<b>0.034</b>
Duration of intubation				19.11 ± 19.74	32.14 ± 49.51	<b>0.050</b>
Resolution of fever and other symptoms	2.40 ± 2.91	4.96 ± 7.79	<b>&lt;0.001</b>	5.70 ± 5.50	9.09 ± 10.33	<b>0.044</b>

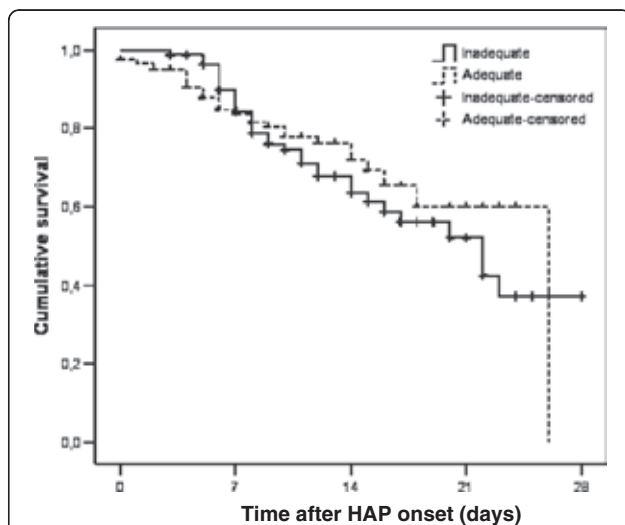
AB was based on studies of VAP because well-conducted studies involving patients who are not undergoing mechanical ventilation are lacking. Similarly the American Thoracic Society/Infectious Diseases Society of America evidence-based guidelines for nosocomial pneumonia are mainly based on studies of VAP but it is recommended to treat patients who were not intubated or undergoing mechanical ventilation in the same manner as those with VAP.<sup>3</sup> Although treatment alternatives are similar, in our study we planned to evaluate the risk factors for inadequate initial AB and the impact of adequacy of initial AB on the prognosis of patients with HAP and VAP separately.

In this study 66.6% of patients in VAP and 41.3% of patients in HAP received inadequate initial AB. The percentage of patients who received inadequate initial AB is quite variable in the previously published studies and ranges from 10% to 73%.<sup>8-11,13-18</sup> Knowledge regarding the colonization of patients, the need to limit selection pressure and the sensitivity profile of the suspected pathogens may influence the frequency of inappropriateness of initial AB.

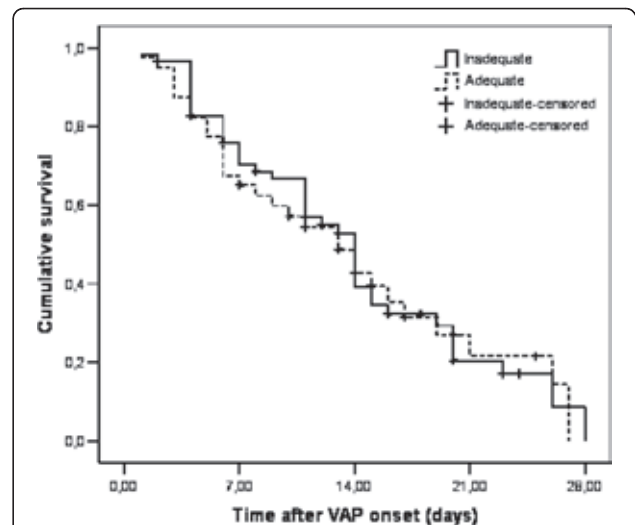
We identified higher APACHE II score and late-onset pneumonia as independent risk factors for inadequate initial AB for patients with HAP. Although severity indices are not always mentioned in studies regarding the adequacy of AB of pneumonia, patients with higher severity are considered to be at high risk of poor outcome and they are also likely to be infected by more resistant bacteria.<sup>10,11</sup> Similarly, late-onset nosocomial pneumonia is caused most frequently by hospital-acquired and often MDR pathogens.<sup>20-22</sup> The potential involvement of more

resistant bacteria in the late-onset pneumonia is more likely to lead to inadequate treatment with traditional antibiotic regimens.<sup>4,6,8,22</sup> However, we did not find such association in late onset pneumonia regarding the adequacy of initial AB and susceptibility patterns of the isolated pathogens when we performed the analysis in culture positive patients only. This conflicting result may be explained by the distribution of MDR bacteria within the groups. In our study cohort the presence of MDR bacteria was higher in the inadequate treatment arm in HAP patients and this was statistically significant. But this significance could not be shown when only culture positive HAP patients were analyzed. So we may conclude that the causative pathogens in late-onset pneumonia in culture negative HAP patients were resistant to the initial empiric AB. Although the presence of polymicrobial etiology were found to be associated with inadequate initial AB in HAP patients both in general and in the subgroup analysis of the culture positive patients, it was not determined as an independent risk factor. We believe that this may be due to the small number of patients with polymicrobial etiology.

For patients with VAP, previous antibiotic usage and admission to a surgical unit were found to be independent risk factors for inadequate AB. Previous antibiotic exposure is one of the most evident risk factors for nosocomial infections due to antibiotic-resistant bacteria, and it was reported as an independent risk factor for inadequate AB in most of the previously published studies.<sup>6,10,22-24</sup> "Admission to a surgical ICU" as being a risk factor for inadequate AB is more difficult to explain. The separation of patients into medical and surgical units without identifying the



**Figure 1** Kaplan-Meier analysis of empirical antimicrobial treatment of HAP according to 28-day mortality ( $p = 0.519$ ) log rank test.



**Figure 2** Kaplan-Meier analysis of empirical antimicrobial treatment of VAP according to 28-day mortality ( $p = 0.847$ ) log rank test.

performed surgical procedure may have affected the analysis of risk factors.

In our study cohort, all of the identified risk factors were shown to be indirectly associated with the acquisition of resistant bacteria for both VAP and HAP. However, in contrast to the results of other previously published studies, multivariate analysis showed that presence of MDR bacteria was not an independent risk factor for both of the groups.<sup>5,8</sup> This contradictory finding may be due to the MDR *Acinetobacter* spp. outbreak which had just begun early in the study period in our ICUs. This could also be a possible explanation of high rates of inadequate therapy in our study population in general. We reevaluated the empiric treatment choices after the antibiotic susceptibility profile of the epidemic clone had been identified. For some of the isolates colistin was the only drug of choice but since colistin was unavailable in the market in Turkey at the time of the study, we were not able to use it as an empirical treatment option. As a result, the presence of MDR bacteria was high in both of the treatment groups and the difference regarding the frequency of MDR bacteria between groups did not reach statistical significance. In patients with HAP, presence of MDR bacteria was associated with inadequate AB but in the final multivariate model this was not significant. Although we have included both culture positive and culture negative patients in the risk factor analysis, the impact of presence of MDR bacteria did not change when the analysis was performed in culture proven patients only.

In this study, we were not able to find any statistically significant difference in mortality rates between patients who received inadequate initial AB and patients who received adequate initial AB for both HAP and VAP. Available studies evaluating the impact of empirical AB have produced conflicting results; some found positive correlation between adequate empirical AB and survival, whereas others did not.<sup>8-15</sup> These contradictory results are probably ascribable to differences in patients and pathogens responsible for pneumonia; since in the studies that found higher mortality rates when AB was inadequate, the patients who received inadequate AB were the ones with pneumonia caused by the most difficult to treat microorganisms.<sup>5,11</sup> In a prospective study of patients with late-onset VAP; it was reported that infection due to non-fermenting gram-negative bacilli was the most important predictor of in-hospital mortality.<sup>22</sup> These pathogens were also the most common isolates in our study. However, the frequency of non-fermenting gram-negative bacilli in the inadequate and adequate AB groups was not significantly different and this may have affected the survival results. Another reason may be the difference in the definition of adequate AB as in some studies adequate AB was defined as AB with a favorable clinical response and in others it is described as microbiological recovery of susceptible organisms to the empirical antibiotic regimen. In the present study we used both of these definitions; in culture positive patients the adequacy of antibiotics were defined according to the results of the antimicrobial susceptibility testing whereas in culture negative patients clinical response to the empiric antibiotic regimen was taken into consideration. However the association between the adequacy of the initial AB and survival did not change when the analysis was performed in culture positive patients only for both VAP and HAP.

In our study cohort, although we could not find a positive correlation between adequate initial antimicrobial therapy and

survival, we showed a significant increase in ICU length of stay, duration of mechanical ventilation and a prolonged clinical resolution in the inadequate AB group for both VAP and HAP. Other researchers also reported an increased length of stay and increased duration of mechanical ventilation when initial AB was inadequate in comparison with adequate AB.<sup>6,10</sup> Only in one study evaluating the outcome of patients with VAP, length of ICU and hospital stays were found to be similar in patients who did and did not receive adequate initial AB.<sup>11</sup> For patients receiving adequate AB, it was reported that clinical resolution of pneumonia usually begins during the first several days of treatment.<sup>6,25</sup> Our results were correlated with the literature, besides we showed a significant prolongation of the clinical resolution when the initial antibiotic therapy was inadequate.

The present study has several limitations. Its retrospective design is a limitation, since it was not possible to conduct an accurate analysis of any changes in the empirical AB regimens. On the other hand, the retrospective feature could have been an advantage, as the prescription of initial AB was not influenced by a prospective evaluation during which a large spectrum initial AB could have been chosen. Another limitation is the impact of specific pathogens on the adequacy of initial AB and survival could not be performed because stratification into smaller groups would complicate entry in the logistic regression model, as each group would have a very small number of cases.

## Conclusions

In the present study, late-onset pneumonia and APACHE II score at the onset of HAP were found to be independent risk factors for inadequate initial AB in patients with HAP, whereas previous antibiotic usage and admission to a surgical unit were found to be associated with inadequate initial AB in VAP. Our data suggests that the risk factors for inadequate initial AB were indirectly associated with the acquisition of resistant bacteria for both VAP and HAP. Moreover, patients who received inadequate initial AB with VAP or HAP had a longer duration of hospital stay and an increased clinical resolution time. Our findings support the importance of investigating the local ecology by active surveillance cultures and follow-up of susceptibility patterns to establish adequate empirical AB. Therefore, consideration should be given to the empirical use of a broader-spectrum antibiotic that has not previously been administered, especially for the coverage of resistant gram-negative bacteria in order to minimize the occurrence of inadequate AB.

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*The No-Bite V...continued from page 38*

mother's care." The family also felt that suctioning their mother was easier and more comfortable with The No-Bite V.

## Discussion

Although some hospice and palliative care professionals do not believe in suctioning a dying patient due to the uncomfortable nature of suctioning, sometimes it is unavoidable. All should agree that in cases where a death rattle is so loud that the family cannot stand to be in the room or where copious secretions persist despite the use of anti-cholinergic drugs, suctioning must be done. To those professionals that think suctioning should never be done on the dying patient, it is recommended that they research The No-Bite V as a more comfortable new option.

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# Respiratory Viral Infections in Children with Asthma: do they matter and can we prevent them?

Hamid Ahanchian, Carmen M. Jones, Yueh-sheng Chen

## Abstract

**Background:** Asthma is a major public health problem with a huge social and economic burden affecting 300 million people worldwide. Viral respiratory infections are the major cause of acute asthma exacerbations and may contribute to asthma inception in high risk young children with susceptible genetic background. Acute exacerbations are associated with decreased lung growth or accelerated loss of lung function and, as such, add substantially to both the cost and morbidity associated with asthma.

**Discussion:** While the importance of preventing viral infection is well established, preventive strategies have not been well explored. Good personal hygiene, hand-washing and avoidance of cigarette smoke are likely to reduce respiratory viral infections. Eating a healthy balanced diet, active probiotic supplements and bacterial-derived products, such as OM-85, may reduce recurrent infections in susceptible children. There are no practical anti-viral therapies currently available that are suitable for widespread use.

**Summary:** Hand hygiene is the best measure to prevent the common cold. A healthy balanced diet, active probiotic supplements and immunostimulant OM-85 may reduce recurrent infections in asthmatic children.

## Background

Asthma is a major public health problem with a huge social and economic burden affecting 300 million people worldwide. Viral respiratory infections are the major cause of acute asthma exacerbations and contribute to asthma inception in high risk young children with susceptible genetic background. A history of wheeze associated with respiratory viral infections early in life is one of the major risk factors for the later development of asthma, together with sensitization to aeroallergens in early life and a family history of asthma and allergies, reflecting a genetic predisposition. Respiratory viral infections are also the principal cause of asthma exacerbations in children and adults. However,

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The authors are with The Queensland Children's Medical Institute, The University of Queensland; Australia Allergy Reserch Center, Mashad University of Medical Sciences, Mashad, Iran; and the Royal Children's Hospital, Brisbane, Australia. Reprinted from BioMed Central, BMC Pediatrics, © 2012 Ahanchian et al; licensee BioMed Central Ltd. This is an open access article distributed under the terms of the Creative Commons Attribution License. This article has been slightly edited for our readers. For references please visit BioMed Central and type the full title.

the question of whether viral infections “select” susceptible hosts or whether viral infections may induce asthma de novo by “damaging” airways is not settled. In other words, do viruses cause or simply unmask asthma?

**Viral infections and innate immune responses:** Respiratory viruses first infect nasal epithelial cells which triggers an antiviral response. This response is driven by type I ( $\alpha/\beta$ ) and III ( $\lambda$ ) interferons (IFN) that are induced following recognition of viral ribonucleic acid (RNA) by pattern recognition receptors (PRRs). Toll-like receptors (TLRs) are cell surface and endosomal PRRs, whilst the RNA helicase receptors (RIG-I and MDA-5) and NOD-like receptors (NOD2), detect viral RNA in the cytoplasm. Signaling via the PRRs activates transcription factors (IRF-3, IRF-7, NF- $\kappa$ B), which lead to the production and secretion of type I and III IFN. The IFNs then bind to cell surface receptors to activate a separate pathway leading to the production of interferon stimulated genes (ISGs) which encode antiviral proteins that combat infection, as well as PRRs and transcriptional factors which further amplify IFN production. The respiratory syncytial virus (RSV), human meta-pneumovirus (hMPV) and human rhinovirus (HRV) are all single stranded RNA viruses but engage differently with cell signaling pathways. In airway epithelial cells RSV and hMPV RNA are primarily detected by RIG-I in the cytoplasm. RSV can also be detected by NOD2. HRV is endocytosed by epithelial cells, and is therefore primarily detected by TLR3 in the endosome early in the infection process and by RIG-I and MDA-5 later in infection following up regulation of these PRRs. The fusion (F) protein of RSV is recognized by TLR4 at the epithelial cell surface.

A successful antiviral response would see the infection limited to the upper airway, as is the case clinically with the majority of viral infections in healthy individuals. Should such a response be deficient, then predominantly upper-airway viral infections, such as HRV, may spread to the lower airways, causing lower respiratory symptoms and an exacerbation of asthma in predisposed individuals.

**Abnormal innate antiviral immunity in asthmatics:** While definitive data are yet to be produced, experimental HRV infections in adult volunteers initially suggested that asthmatics were more likely to develop lower respiratory infections (LRI) than healthy adults, ie less likely to be able to limit viral replication to the upper airways. Subsequent in vitro infection of primary airway epithelial cells from asthmatic and healthy adults with HRV have demonstrated that asthmatic cells

**Table 1 The processes of rhinoviral infection and preventive strategies**

Process	Preventive strategies
Rhinoviral transmission	Hand hygiene, isolation
Attachment to respiratory epithelium	HRV neutralizing antibodies, anti-receptor antibodies Second generation antihistamines, zinc vaccines
Entry, RNA and protein synthesis	Anti-rhinoviral therapies (Pleconaril, Rupintrivir)
Enhancing immunity	Balanced diet, interferons, immunostimulants, probiotics, breast milk, Echinacea, garlic, zinc, ginseng

produce less IFN- $\beta$  and IFN- $\lambda$  making them potentially more susceptible to infection, slower to clear infection, and more susceptible to virus-induced cell cytotoxicity. Deficiencies in the IFN- $\alpha$  response of peripheral blood mononuclear cells and plasmacytoid dendritic cells from asthmatic adults and children has also been observed, in these particular studies, in response to RSV, HRV and Influenza A. It is likely that the overall impaired innate immune response of the asthmatic airway epithelium is a result of deficiencies in the antiviral response of both epithelial cells and immune cells. Childhood, especially infancy, is characterized by developmentally-regulated deficiencies in innate and adaptive immunity. Such deficiencies are likely to increase the risk of viral LRI in children, especially in those at high risk for asthma and allergies.

**Viral infections in children with asthma:** Each year, at the end of summer, parents of asthmatic children are concerned about acute asthma exacerbations following a common cold, asking how to minimize the risk during the winter viral season. It is a valid concern as up to 70% of asthmatic children have an intermittent or wheeze which is mostly symptomatic after viral infections. Asthmatics with exacerbation-prone phenotype are susceptible to acute exacerbations requiring hospitalization or an unscheduled visit for medical attention. Major risk factors for acute exacerbations include previous acute exacerbation, allergy, young age, poorly controlled asthma, and, in particular, viral respiratory infections. Moreover, recent data suggests an interaction between allergies and viral infections occurs to increase the risk of asthma exacerbation. Acute exacerbations are associated with decreased lung growth or accelerated loss of lung function and, as such, add substantially to both the cost and morbidity associated with asthma. Viral respiratory infections are the main cause of asthma exacerbations in children (80-85%) and are a major risk factor for admission in hospital every autumn. HRV are the most common viral agents; Other respiratory tract viruses detected in children with an asthma exacerbation include RSV, influenza, coronavirus, hMPV, parainfluenza virus, adenovirus, and bocavirus. Current drugs for the prevention and treatment of virus-induced exacerbation of asthma are poorly effective and novel alternative therapies are needed.

**Role of respiratory viral infections in asthma inception:** Much research interest has focused on the potential role respiratory viral infections play in the inception of asthma. It is well established that hospitalization for RSV bronchiolitis is a risk factor for asthma during childhood. Epidemiological studies have shown an increased risk of asthma with LRI caused by HRV. In the Childhood Origin of Asthma (COAST) birth cohort study,

wheezing with RSV (odds ratio [OR], 2.6), HRV (OR, 9.8), or both HRV and RSV (OR, 10) was associated with increased asthma risk at age six years.

The Childhood Asthma Study (CAS) in Perth, Australia showed that wheezing with HRV or RSV in the first year of life was a risk factor (OR, 2.5) for current wheeze at five years of age. Infant birth about four months before the winter virus peak carried the highest risk of developing asthma compared with birth 12 months before the peak. The risk of asthma is increased by severe LRI (sLRI), especially in the presence of allergic sensitization in early life. There appears to be a synergistic interaction between viral infection and allergic sensitization, suggesting a “two hit” model for induction of persistent asthma. These data also provide a series of novel strategies for the primary prevention of asthma by prevention of either allergic sensitization or of sLRI in high risk children. This strategy is also supported in a study by Simoes et al, in which the use of palivizumab to prevent RSV infection decreased the risk of recurrent wheezing in nonatopic premature infants.

The crucial period, with respect to asthma initiation, appears to be the first two to three years of life during which the growth and remodeling of lung and airways proceeds at maximum rates. Pulmonary inflammation resulting from atopy and sLRI occurring during this vulnerable time is hypothesized to perturb underlying tissue differentiation programs, resulting in deleterious long term effects on respiratory functions. As a result, there is widespread belief amongst the pediatric respiratory community that intervention measures that can lower the frequency and/or intensity of sLRI in early life amongst the high risk atopic subgroup of children are likely to be successful at preventing asthma. If successful, these strategies would have major implications for reducing the high impact of this chronic disease on the community.

Recent studies using culture-independent techniques have challenged the long-held dogma that lungs are sterile and have demonstrated that a microbiota community exists in the lung. The implications of these new data are not clear, however new concepts and more research is required. The resident microbiome is different in the presence of respiratory disease; therefore interactions between respiratory viruses and the resident pulmonary microbiome are postulated. The pulmonary and gastrointestinal microbiota influence the immune system and interventional approaches (by bacterial immunostimulants, prebiotics and/or probiotics) to create a healthy gut and respiratory microbiota are potential strategies for the prevention of viral infections.

**Preventing viral infections by non-immunologic methods:** Children are important vectors for HRV transmission to family members particularly siblings. HRV shedding peaks two to four days after infection and decreases sharply thereafter, although nasal samples can be positive for rhinovirus for up to five weeks after a symptomatic infection.

There are three ways of common cold transmission in children. First, inhalation of small particles aerosolized by coughing; second, large particle droplets from saliva expelled while sneezing; and third, self-inoculation of one's own conjunctivae or nasal mucosa after touching a person or object contaminated with the cold viruses. The first two methods are inefficient, while the third is the most important method of transmission. The



**Table 2 Summary of interventions to prevent rhinoviral infection in asthmatic children**

Effectiveness	Interventions
<b>Most likely to be beneficial</b>	Hand Hygiene Immunostimulants (OM-85) Probiotics (specific strains), Prebiotics and Synbiotics Breast milk
<b>Likely to be beneficial</b>	Regular exercise, balanced diet, adequate sleep, low psychological stress Prevention of air pollutions and environmental tobacco smoke (ETS) Second generation of antihistamines Monoclonal antibodies: Anti IgE, Anti IL-5 Vitamin D, Vitamin A Garlic, zinc, ginseng Interferons
<b>Unknown effectiveness</b>	Montelukast Vitamin C Macrolides Echinacea Antiviral drugs
<b>Unlikely to be beneficial</b>	Mask Vaccination
<b>Likely to be ineffective or harmful</b>	Antibiotics Intensive exercise

mode of transmission could differ with age of the index case, duration of contact, and other factors. Moreover, there is some evidences that the daily activities of infected people can lead to the contamination of environmental surfaces with HRV eg light switches, telephone dial buttons and handsets.

Meticulous hand hygiene is the best measure to prevent the common cold; frequent hand washing and avoid touching one's nose and eyes. The use of alcohol-based hand sanitizers is also effective. The promotion of hand washing was associated with a 12- 34% reduction in respiratory-tract infections and colds in child-care centers in the USA Canada and Australia and a 21% decrease in absences due to respiratory illness in the school setting. Hand hygiene campaigns were also successful in reducing absenteeism caused by influenza-like illnesses among schoolchildren in Egypt. Similar programs within families would be expected to reduce transmission of HRV between family members.

A recent Cochrane review which included data from 67 randomized controlled trials and observational studies, investigated the effectiveness of physical interventions to reduce the spread of respiratory viruses. The authors concluded that respiratory virus spread can be reduced by hygiene measures (such as hand washing), especially around younger children and can reduce transmission from children to other family members. Controversy still exists and a newly published study showed that an antiviral hand treatment used by adult volunteers, recruited from a university community, did not significantly reduce RV infection or RV-related common cold illnesses.

Asthmatic children should avoid close contact with people who have colds especially during the first three days of their illness. There is little evidence to support the effectiveness of face masks to reduce the risk of viral respiratory infections and consequently, the use of mask is generally not recommended for prevention of common cold.

**General immunologic strategies:** Immune function and anti-viral defenses have a number of components, both specific and non-specific. Asthmatic children can improve their immune function by following some simple advice including a healthy life style with regular exercise, a balanced diet, adequate sleep and avoiding environmental tobacco smoke, stress and unnecessary antibiotics.

**Exercise:** Exercise has anti-inflammatory effects and in the long term can protect the development of chronic diseases and obesity. Regular exercise of moderate-intensity is associated with a reduced incidence of upper respiratory tract infection. However, long hours of intensive training appear to make children more susceptible to upper respiratory tract infections. The recommended means of aerobic exercise is walking, with an optimal frequency of three to five days a week and an optimal duration of 20 to 30 minutes of continuous activity. In a recent study, the IgA secretion rate was negatively correlated with the incidence of infections. A recent randomized trial comparing meditation and exercise with wait-list control among adults aged 50 years and older found significant reductions in ARI illness.

**Diet:** Malnutrition is the most common cause of immune deficiency worldwide and a balanced diet is fundamental for a healthy immune system. Vitamin D deficiency has been associated with increased risk of infections, early-life wheeze and reduced asthma control. Vitamin A derivatives are involved in the regulation of the immune system and tissue inflammation as well as prevention of respiratory infections. Zinc, selenium and other trace elements are necessary for function of both innate and adaptive immune function. A high intake of fruit and vegetables ensures adequate consumption of nutrients and antioxidants and appears to be beneficial for asthma. Although recent reviews have shown that zinc, garlic, Echinacea purpurea or Ginseng supplementation for several months may reduce cold incidence, there is insufficient evidence to recommend any vitamin or mineral supplementation in the management of asthmatic children without nutrient deficiency. However, a large controlled trial showed Echinacea was ineffective in reducing infection rate or symptom severity of HRV infection in healthy young adult volunteers. Vitamin C supplementation failed to reduce the incidence of colds in the general population except in those exposed to short periods of extreme physical stress. Finally, it is worth remembering that infants who are not breastfed have significantly higher risk of respiratory, gastrointestinal, and other infections, as breast milk is a biologically active substance containing antimicrobial and immunomodulatory elements.

**Sleep:** Sleep and the circadian system exert a regulatory influence on immune functions. Sleep deprivation can affect immune function in several ways including reduced natural killer cell activity, suppressed interleukin-2 production and increased levels of circulating proinflammatory cytokines. There is also evidence for an enhanced susceptibility to the common cold and pneumonia with poor sleep efficiency.

**Air pollution:** Air pollutants (nitrogen dioxide, ozone, particulate matter) and environmental tobacco smoke (ETS) have long been correlated with multiple adverse effects on the immune system and susceptibility to viral respiratory tract infections in children. Studies in Europe and the United States have shown that 40% of children live with a smoker and they have approximately twice the risk of contracting a serious respiratory tract infection in early life. Cigarette smoking leads to a longer duration of cough, greater frequency of abnormal

auscultatory findings during acute respiratory tract illness and higher risk for severe exacerbations. Urinary leukotriene E4 levels identify children exposed to ETS at high risk for asthma exacerbation.

**Specific immunologic strategies:** There is strong evidence that some pharmacological preparations can help prevent viral infection by specific effects on immune system. These results have been promising with a hope that using these strategies can attenuate the role of viruses in asthma inception.

**Probiotics and prebiotics:** Ancient physicians of the Middle East prescribed yogurt for curing disorders of the stomach, intestines and for stimulation of appetite. It is written in the old Persian Testament that "Abraham owed his longevity to the consumption of sour milk." The popularity of probiotics and intestinal microbiota significantly increased when the Nobel Prize-winning Russian scientist Eli Metchnikoff suggested in 1908 that the long life of Bulgarian peasants resulted from their consumption of fermented milk products. The term probiotic, meaning "for life," is used for live microorganisms (typically of the bifidobacterium and lactobacillus species) administered in adequate amounts which confer a beneficial physiological effect on the host. Prebiotics are nutrients, in particular oligosaccharides, which foster the growth of probiotics in the colon. The term synbiotics is used when a product contains both probiotics and prebiotics .

Up to 100 trillion bacteria from different species colonize the human gut. This microbiota participates in: host metabolism, vitamin synthesis, control of epithelial cell growth, protection from infectious microbes, and helps proper development and function of the immune system. There is constant cross-talk between microbiota and gut-associated lymphoid tissue (the largest lymphoid tissue of the human body which contains more than 60% of all body lymphocytes) to establish mucosal immune tolerance in the gut. Common mucosal immunity describes the phenomenon where immune cells, especially regulatory T-cells, traffic to and influence responses at other mucosal surfaces, including the lungs. Alteration in the microbiota composition (dysbiosis) results in immunological dysregulation that may underlie many human diseases such as inflammatory diseases, obesity, allergy and autoimmunity.

Reduced bacterial diversity in the infant's gastrointestinal tract has been associated with an increased risk of allergic sensitization and allergic rhinitis but not asthma or atopic dermatitis. In the first year of life, especially the first few weeks, the microbiota of the newborn is highly variable during this critical time of post-natal maturation of the immune system. Microbiota is shaped by genetic and environmental factors including: mode of delivery, neonates born by means of vaginal delivery are exposed to mothers gut, skin, and vaginal flora; breast feeding and diet; farm or urban living; vitamin D status; and antibiotic consumption. This knowledge stimulated interest in the use of probiotics and prebiotics as the intentional introduction or encouragement of specific microbes to shape immune system development. Specifically, the microbiota can activate distinct tolerogenic dendritic cells in the gut and through this interaction can drive regulatory T-cell differentiation that modulates both Th1 and Th2 responses inside and outside the gut. Probiotics have been successfully used for the treatment of several gastrointestinal disorders (viral and antibiotic-associated diarrhea, inflammatory bowel disease). However, attempts to

prevent or treat allergic disorders such as eczema, asthma and allergic rhinitis have had inconsistent results.

There are a growing number of clinical trials using probiotics for the prevention and management of respiratory infections. While the precise mechanisms are largely unknown, speculations include: probiotics compete against pathogens; increase the barrier function in respiratory epithelium; immunostimulatory effects by enhancing cellular immunity with increased activity of natural killer cells and macrophages in airways. Probiotics reduce the frequency of gastrointestinal and respiratory tract infections in children who attend day care centers. They have also been found to reduce the incidence of ventilator-associated pneumonia, respiratory infections in healthy and hospitalized children, and reduce the duration of common cold symptoms.

One study demonstrated that that daily probiotic supplementation for six winter months in children three to five years of age reduced the incidence of fever, coughing and rhinorrhea by 32-43% with no notable adverse events. Probiotic combination with vitamins and minerals also reduced the duration and severity of common cold. A recent Cochrane review of 14 randomized controlled trials showed that probiotics were better than placebo in reducing the number of episodes of acute upper respiratory infections (URIs) and reducing antibiotic use, while there were no differences in the mean duration of an episode and no increase in adverse events. Probiotic foods such as probiotic milk or yogurt (functional foods) containing well-defined probiotic strains may reduce the risk of catching the common cold and represent a simple, safe, effective, available and affordable method for preventing respiratory infections in children.

Although there are several clinical trials that showed the preventive effect of probiotic, prebiotic or synbiotics treatments on respiratory infections, not all studies are positive with some failing to show any significant preventive effect. To explain the different results in clinical trials, it is of particular importance to point out that the immunomodulatory capabilities of probiotics are strain-dependent. Difference in dosage, duration of intervention, population and environmental background may also affect the results. One major limitation in this field is that it is not possible to test just how "probiotic" a particular preparation is. Technical advances will be required before some of the apparent discrepant results of studies can be resolved.

**Immunostimulants:** Several immunostimulants, including herbal extracts, bacterial extracts, synthetic compounds, have been promoted as increasing the immune defenses of the respiratory tract. A recent Cochrane review included data from 35 placebo-controlled trials including 4060 participants below the age of 18 years in which various types of "immunostimulants" were used to reduce acute respiratory tract infections, involving either upper or lower airways. The authors concluded that immunostimulants reduced the incidence of acute respiratory infections by 40% on average in susceptible children, but that trial quality was generally poor and a "high level of statistical heterogeneity was evident". A subgroup analysis focusing on bacterial immunostimulants, including OM85, produced similar results with lower statistical heterogeneity.

OM-85 BV (Broncho-Vaxom) is an immunostimulant extracted from eight common bacterial pathogens of the upper respiratory tract: Haemophilus influenzae, Diplococcus pneumoniae, Klebsiella pneumoniae and ozaenae, Staphylococcus aureus,

*Streptococcus pyogenes* and *viridans*, *Neisseria catarrhalis* and has been used in several countries around the world for as long as 20 years. Recent studies showed that OM-85 BV can reduce the number of acute respiratory infections by 25% to 50% compared with placebo in children with a history of recurrent infection. Of particular interest, Razi et al showed that children between the age one and six years with recurrent wheezing who were given OM-85 BV had a 40% reduction in the rates of wheezing over the subsequent 12 months, compared to placebo ( $p < 0.001$ ). In addition, the duration of each wheezing attack was two days shorter in the group given OM-85 BV than in the group given placebo ( $p = 0.001$ ).

Again, direct evidence of the mechanisms involved are lacking from human studies. However, recent data from rodents shows that baseline regulatory T lymphocyte activity in the airways can be boosted by microbe-derived stimulation of the gut. Bacterial immunostimulants were also shown to enhance innate immunity (i.e. intensification of phagocytosis) and adaptive immunity.

**Interferons:** As discussed above, evidence exists for an impaired innate immune response to respiratory viral infections in asthmatics. Entry of rhinovirus into normal epithelial cells initiates a vigorous innate immune response with IFN- $\beta$  secretion and apoptosis induction. In asthma, IFN- $\beta$  and IFN- $\lambda$  responses are impaired, resulting in viral replication, cell cytotoxicity, enhanced virion shedding and increased susceptibility to common cold. Epithelial cells of asthmatic patients responded to exogenous treatment with IFN- $\beta$  exhibiting reduced rhinovirus release (Cakebread, Xu et al 2011; Jackson, Sykes et al 2011). If the proposed deficiency of type I and III contribute to asthma exacerbations, correcting this deficiency with exogenous interferons would be a logical approach. The advantages of interferon application include the broad spectrum of activity with low risk of resistance development. Prophylactic intranasal recombinant IFN- $\alpha$  and IFN- $\beta$  have been shown to be effective against rhinovirus infection in humans. The results of these clinical trials are awaited with interest. However, the systemic symptoms associated with severe viral infections, eg influenza, are associated with interferons, so careful dosing may be required. Considering the occurrence of the local side effects, neutropenia and cost, the use of long-term prophylaxis with daily, intranasal administration of interferons is not feasible. However, randomized clinical trials using similar strategies are currently underway in adults with chronic respiratory disease and the results are keenly awaited.

**Vitamin D:** Vitamin D deficiency is a common worldwide problem. Beside importance for bone health, vitamin D plays an important role in adequate function of both the innate and adaptive immune systems including development of dendritic cells and regulatory T lymphocytes, production of antimicrobial proteins by airway epithelium, modifying the effect of intestinal flora on inflammatory disorders, and modulation of the inflammatory response to viral infections. Recent reports suggest that vitamin D might play a role in the recent increase in allergic disease. Vitamin D insufficiency has been associated with a higher incidence of respiratory tract infection, wheezing illness in children, reduced asthma control, emergency department visits, severe asthma exacerbations and hospitalizations. In a recent study of 48 children from five to 18 years of age, with newly diagnosed asthma, vitamin D supplementation during the northern hemisphere winter months (September to July) prevented declining serum concentrations of 25(OH) D and reduced the risk of asth-

ma exacerbation triggered by acute respiratory tract infections.

**Macrolides:** Macrolides possess anti-inflammatory and immunomodulatory properties extending beyond their antibacterial activity. Indeed, they can attenuate pro-inflammatory cytokine production by bronchial epithelial cells, neutrophils and macrophages that may contribute to clinical improvement in many patients with chronic airway inflammation. Azithromycin has anti-rhinoviral activity and can reduce HRV replication and release by increasing interferon production from epithelial cells. Macrolide antibiotics inhibit RSV infection in human airway epithelial cells. A three weeks treatment with clarithromycin in RSV bronchiolitis had statistically significant effects on hospital length of stay and rate of readmission to the hospital within six months after discharge. However, direct evidence of macrolides preventing respiratory viral infection in children is lacking.

**Anti-viral therapies:** As the majority of respiratory viral infections in young children are caused by HRV or RSV, we will briefly discuss anti-viral strategies to prevent HRV or RSV infections in asthmatic children. Because there are more than 100 serotypes of HRV, antiviral drugs are considered to be more effective than vaccination. Antiviral agents have been designed to inhibit rhinovirus attachment, entry to the cell, viral uncoating, and RNA and protein synthesis. Table 1 shows how intervention strategies can be targeted to various steps in the infective process.

### Rhinovirus structure

HRV has the icosahedrally shaped capsid formed by 60 identical copies of viral capsid structural proteins VP1-4. The capsid protects the single-stranded, positive sense RNA genome. While HRV-A and -B most often induce a self-limited upper respiratory infection, the recently discovered HRV-C was associated with sLRIs in infants, bronchiolitis, and asthma exacerbations in children.

Prevention of attachment, entry and uncoating: HRV deposits on nasal or conjunctival mucosa and is transported to the posterior nasopharynx by mucociliary action of epithelial cells. The so-called major group of HRV uses intercellular adhesion molecule-1 (ICAM-1) as their receptor and the minor group attach to low density lipoprotein (LDL) receptor and very-LDL (VLDL) receptors on epithelial cells in the adenoid area to bind and enter cells. Viral attachment can be prevented by specific anti-HRV neutralizing antibodies, anti-receptor antibodies and soluble receptor molecules.

Endothelial cells express histamine receptors and increased adhesion molecule expression, such as ICAM-1, was demonstrated by histamine infusion. Second-generation H1-antihistamines decrease expression of ICAM-1 on cultured bronchial epithelial cells. Zinc may also act as an antiviral agent by reducing ICAM-1 levels.

The monoclonal antibody to the cellular ICAM-1 was not effective. CFY196 (Coldsol) is a nasal spray multivalent Fab fusion proteins against ICAM-1 with a better avidity and in vitro potency against HRV. Tremacamra, a soluble intercellular adhesion molecule 1 reduced the severity of experimental rhinovirus infection. Pleconaril, an orally administered antiviral drug, acts by binding to a hydrophobic pocket in viral protein 1, and stabilizes the protein capsid so that the virus cannot release its RNA genome into the target cell. Outcomes of clinical trials



with pleconaril have revealed mixed results and new compounds are currently being developed.

Prevent RNA and protein synthesis: Despite extensive research, no agent has been approved for prevention and/or therapy of rhinovirus-induced diseases so far. Ruprintrivir selectively inhibits HRV 3C protease and shows potent, broad-spectrum anti-HRV activity in vitro. Ruprintrivir nasal spray (2% solution) prophylaxis reduced the proportion of subjects with positive viral culture by 26% and reduce viral titers, but did not decrease the frequency of colds. HRV RNA synthesis during replication can be blocked by deoxyribozymes, morpholino oligomers, and small interfering ribonucleic acids. The novel antiviral therapies that have been discovered recently, may one day add significantly to the armamentarium of antiviral agents, against respiratory viral infections in asthmatic children.

**Monoclonal antibodies:** Maternally-derived RSV neutralizing antibodies help to protect infants against RSV hospitalization. Palivizumab, a humanized monoclonal antibody against the RSV fusion protein is effective against RSV and wheezing in children and reduces hospitalization in high-risk individuals. RSV prophylaxis with palivizumab significantly reduced the relative risk of subsequent recurrent wheezing in nonatopic premature infants. Motavizumab is another monoclonal antibody against RSV, with an approximately 20-fold increase in ability to neutralize RSV and 100 fold increase in ability to reduce viral titers compared to palivizumab. Motavizumab was also found to be superior to palivizumab in reducing outpatient medically attended lower respiratory illness by 50%.

**Vaccination:** Vaccination against HRV and RSV have been in development for quite some time, but there are no safe and effective vaccines at present. High rates of exposure to viruses in early life, presence of more than 100 serotypes of HRV, the presence of maternal antibodies, the risk of vaccine induced disease and relative immaturity of the infant immune system make effective vaccination difficult.

## Discussion

Respiratory viral infections are major contributors to the global burden imposed by asthma. In early life, they contribute to the inception of asthma and are responsible for most of the acute exacerbations for asthma in childhood. While the debate is not completely settled, children at high risk of developing asthma and those with established asthma may be at increased risk of acquiring respiratory viral infections and may be less able to contain these to the upper airway. Several simple general strategies can be used to help prevent respiratory viral infections in asthmatic children (Table 2), with good personal hygiene, hand-washing and avoidance of cigarette smoke likely to reduce respiratory viral infections. General immuno-stimulatory strategies, such as eating a healthy balanced diet, active probiotic supplements and bacterial-derived products, e.g. OM-85, may reduce recurrent infections in susceptible children.

## Summary

While research continues on specific anti-viral therapies, including vaccination, there are no currently available practical therapies that are suitable for widespread use. The role of preventative strategies in primary prevention of asthma in high risk children is of considerable academic interest and a number of studies are currently in the pipeline. The results are awaited with interest.

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# Vital Capacity and Inspiratory Capacity as Additional Parameters to Evaluate Bronchodilator Response in Asthmatic Patients: a cross sectional study

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## Abstract

**Background:** Bronchodilator response in patients with asthma is evaluated based on post-bronchodilator increase in forced expiratory volume in one second (FEV1) and forced vital capacity (FVC). However, the need for additional parameters, mainly among patients with severe asthma, has already been demonstrated.

**Methods:** The aim of this study was to evaluate the usefulness of vital capacity (VC) and inspiratory capacity (IC) to evaluate bronchodilator response in asthma patients with persistent airflow obstruction. The 43 asthma patients enrolled in the study were stratified into moderate or severe airflow obstruction groups based on baseline FEV1. All patients performed a 6-minute walk test before and after the bronchodilator (BD). A bipolar visual analogue scale post-BD was performed to assess clinical effect. The correlation between VC and IC and clinical response, determined by visual analogue scale (VAS) and 6-minute walk test (6MWT), was investigated.

**Results:** Patients in the severe group presented: 1) greater bronchodilator response in VC (48% vs 15%,  $p = 0.02$ ), 2) a significant correlation between VC variation and the reduction in air trapping ( $R_s = 0.70$ ;  $p < 0.01$ ), 3) a significant agreement between VC and VAS score ( $\kappa = 0.57$ ;  $p < 0.01$ ). There was no correlation between IC and the reduction in air trapping or clinical data.

**Conclusions:** VC may be a useful additional parameter to evaluate bronchodilator response in asthma patients with severe airflow obstruction.

## Background

Asthma is a serious worldwide health issue, but its clinical manifestations can be controlled with appropriate treatment.<sup>1</sup>

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Currently, a positive bronchodilator response is established based on an increase  $\geq 12\%$  and 200 ml in forced vital capacity (FVC) and/or forced expiratory volume in one second (FEV1) compared with baseline values following administration of bronchodilators.<sup>2</sup> However, in clinical practice, patients with moderate or severe asthma may refer clinical improvement after bronchodilator use despite a negative bronchodilator test. In patients with chronic obstructive pulmonary disease (COPD), in whom the bronchodilator test is frequently negative, vital capacity (VC) and inspiratory capacity (IC) variation are used as complementary tools in order to evaluate bronchodilator response.<sup>3-6</sup> COPD patients have a persistent airway obstruction that may also be observed in moderate or severe asthma; however, only a few studies so far have evaluated the usefulness of VC and IC to assess bronchodilator response among asthmatic patients.<sup>7-13</sup> The aim of this study was to analyze the usefulness of VC and IC as additional parameters to assess bronchodilator response in asthma patients with moderate or severe airflow obstruction.

## Methods

This study prospectively enrolled patients aged 15 years and older diagnosed with asthma and persistent airway obstruction according to Global Initiative for Asthma (GINA) criteria, and who were clinically stable at the time of enrollment.<sup>14</sup> Subjects were not eligible if they were current or former smokers ( $\geq 20$  packs) or had clinical and/or radiographic evidence of heart failure, uncontrolled systemic arterial hypertension, pregnancy, focal fibrous scarring on chest X-ray with total area  $\geq 1$  pulmonary lobe, chest wall deformity or articular or neuromuscular disease, morbid obesity or previous lung resection. Also excluded were patients who used short-acting  $\beta_2$ -agonist spray, long-acting  $\beta_2$ -agonist spray or oral theophylline 8 h, 12 h or 48 h respectively before the pulmonary function tests, and patients experiencing an asthma crisis or exacerbation during the week before the pulmonary function tests. All patients were referred from the Outpatient Asthma Clinic at the Federal University of Rio de Janeiro Institute of Thoracic Diseases (ITD). They were evaluated at the ITD Pulmonary Function between June 19, 2006 and July 30, 2008. Written informed consent was obtained from all participants (or a legally responsible representative when applicable) and the study was approved by the Federal University of Rio de Janeiro Ethics Committee.

All patients answered a standardized interview and underwent physical examination as well as lateral decubitus and posteroanterior chest x-ray before the bronchodilator test.<sup>14</sup>

**Table 1 Demographic and clinical characteristics of asthma patients**

Parameters	Moderate airflow obstruction (n = 20)	Severe airflow obstruction (n = 23)	P
Age (years)	50 (37–61)	56 (45–65)	0.32
Height (cm)	156 (152–163)	156 (153–161)	0.76
Weight (kg)	70.6 (58.7–78.9)	67.6 (54.7–72.2)	0.38
Male/Female	6/14	4/19	0.33
Dyspnea score (Borg scale)	0 (0–3.3)	3 (0–5)	0.12
Treatment (Standard/Others)	13/7	20/3	0.09

Standard treatment: regular inhaled corticosteroids and long-acting  $\beta_2$ -agonists.

*p* value – Mann Whitney test for quantitative data and Chi-square for qualitative data. Quantitative data are expressed as median (25<sup>th</sup> percentile–75<sup>th</sup> percentile).

Pulmonary function tests (PFTs) and a 6-minute walk test (6MWT) were performed before and 15 minutes after the bronchodilator test. Only one 6MWT was done before and after the bronchodilator. A bipolar visual analogue scale (VAS) was used to assess the perceived effect of the bronchodilator test on shortness of breath. The bronchodilator test was performed with salbutamol/400  $\mu$ g spray under physician supervision (KRSA). PFTs included flow-volume and volume-time curves, inspiratory slow vital capacity maneuver and determination of static lung volumes using a Jaeger spirometer (model MasterScreen-

PTF, Hoechberg, Germany), and were conducted according to American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines.<sup>15,16</sup> Static lung volumes were calculated using the closed-circuit helium dilution method. For He-derived TLC, the end-of-test criterion (equilibration) was defined as helium concentration change of 0.02% or less during 30s rebreathing. The predicted normal values for spirometry and lung volumes were those of Knudson et al.<sup>17</sup> Polgar/Promadhat and Goldman/Becklake<sup>18,19</sup> respectively. The 6MWT was performed following ATS guidelines, with dyspnea score based on a Borg scale.<sup>20</sup>

**Table 2 Pulmonary function before and after bronchodilator of asthma patients**

Parameters % P or L	Moderate airflow obstruction (n = 20)	Severe airflow obstruction (n = 23)	P (Mann Whitney)
VC			
Pre-BD (%P)	93.2 (86.5–101.0)	75.7 (67.3–85.2)	<0.01
Post-BD (%P)	102 (91.4–104.7)	84.9 (76.5–96.7)	0.01
P (Wilcoxon)	0.01	<0.01	
IC			
Pre-BD (L)	1.94 (1.63–2.43)	1.56 (1.24–1.88)	0.01
Post-BD (L)	2.1 (1.73–2.63)	1.76 (1.50–1.94)	0.01
P (Wilcoxon)	0.02	<0.01	
FVC			
Pre-BD (%P)	96.2 (88.1–104.3)	76.6 (65.5–93.9)	<0.01
Post-BD (%P)	105.2 (92.3–109.7)	87.7 (76.8–87.7)	0.02
P (Wilcoxon)	<0.01	<0.01	
FEV <sub>1</sub>			
Pre-BD (%P)	68.2 (65.3–77.5)	48.8 (42.7–55.7)	<0.01
Post-BD (%P)	78.9 (70.7–86.3)	60.8 (51.2–65.2)	<0.01
P (Wilcoxon)	<0.01	<0.01	
TLC			
Pre-BD (%P)	95.8 (91.4–113.5)	92.8 (82.3–105.9)	0.19
Post-BD (%P)	99.2 (89.9–109.4)	95.8 (87.4–104.0)	0.40
P (Wilcoxon)	0.8	0.4	
RV/TLC			
Pre-BD (%P)	108.1 (97.6–123.9)	124.8 (105.0–145.0)	0.06
Post-BD (%P)	101.0 (79.7–122.4)	111.0 (91.9–125.4)	0.18
P (Wilcoxon)	0.1	<0.01	
RV			
Pre-BD (% P)	105.2 (90.0–136.6)	113.0 (103.3–145.4)	0.42
Post-BD (% P)	97.3 (76.3–135.6)	102.6 (87.6–124.3)	0.39
P (Wilcoxon)	0.3	0.05	

BD = bronchodilator, FEV<sub>1</sub> = forced expiratory volume in one second, FVC = forced vital capacity, IC = inspiratory capacity, L = liters, P = predicted, RV = residual volume, TLC = total lung capacity, VC = vital capacity. Results are expressed as median (25<sup>th</sup> percentile–75<sup>th</sup> percentile). *p* value for paired sample – Wilcoxon test.



**Table 3 6-minute walk test results before and after bronchodilator of asthma patients**

Parameters	Moderate airflow obstruction (n = 20)	Severe airflow obstruction (n = 23)	P (Mann Whitney)
6WTD			
Pre-BD (m)	515 (479–570)	501 (468–537)	0.26
Post-BD (m)	555 (511–588)	519 (480–570)	0.26
P (Wilcoxon)	<0.01	<0.01	
Borg Scale			
Pre-BD	5 (0–6)	5 (3–7)	0.35
Post-BD	3 (0–5)	3 (1–4)	0.86
P (Wilcoxon)	0.03	<0.01	

6WTD = 6 minute walk test distance, m = meters, BD = bronchodilator. Results are expressed as median (25<sup>th</sup> percentile–75<sup>th</sup> percentile). *p* value for paired sample – Wilcoxon test.

For the VAS, patients were asked to indicate on a 100 mm horizontal line, labeled “very much worse” on the left end (–100), “very much better” on the right end (+100) and “no change” (zero) in the middle, after the bronchodilator test.<sup>21</sup> Bronchodilator response was defined as an increase in FEV<sub>1</sub> or FCV ≥ 12% of the baseline value plus 200 ml,<sup>2</sup> or a decrease in residual volume (RV) ≥ 20% of the predicted value and 300 ml compared with baseline.<sup>22</sup> Clinical bronchodilator response was defined as 6MWD ≥ 50 meters or at least 30 meters associated with a reduction greater than 2 points in the Borg scale score,<sup>5,20</sup> or any positive value in VAS. For VC and IC, an increase ≥ 12% and 200 ml compared with baseline indicated a positive bronchodilator test.

Asthma patients were stratified into two groups according to the value of FEV<sub>1</sub>: moderate (60% < FEV<sub>1</sub> < 80% of predicted values) and severe airflow obstruction (FEV<sub>1</sub> ≤ 60% of the predicted values), according to GINA criteria.<sup>14</sup>

Statistical analysis: The Mann-Whitney test was used for quantitative data, and the chi-square test for qualitative parameters. The correlation between the variation in VC and IC and the variation in residual volume-to-total lung capacity ratio (RV/TLC) was analyzed using Spearman’s correlation test. The agreement between VC and IC responses and clinical response was analyzed using the Kappa coefficient. The classification proposed by Chan and Byrt for the interpretation of Spearman and Kappa values respectively, was adopted.<sup>23,24</sup> The statistical package for the social sciences (SPSS) v. 13.0 was used, and a *p* < 0.05 was considered significant.

## Results

During the study period, 60 subjects were screened and 43 (72%) were enrolled: 20 had moderate airflow obstruction and 23 had severe airflow obstruction. Demographic, clinical and radiological parameters are presented in Table 1. Spirometry,

6MWT, and VAS were performed in all patients, while static lung volumes were analyzed in 37 patients. Functional data for patients with moderate and severe obstruction before (Pre) and after (Post) the bronchodilator (BD), test are depicted in Table 2. VC, IC, FVC, and FEV<sub>1</sub> were significantly lower in the group with severe airflow obstruction vs. the group with moderate airflow obstruction. Conversely, pre-BD RV/TLC ratio was increased in the presence of severe airflow obstruction. After BD, a significant increase in VC, IC, FVC and FEV<sub>1</sub> was observed in both groups as well as a significant reduction in RV/TLC ratio in severe group. A significant increase in 6MWT distance and a decrease in dyspnea score (Borg scale) were observed after the BD in both groups (Table 3).

If considering the ATS/ERS definition of obstructive abnormalities, FEV<sub>1</sub>/VC < 5th percentile of predicted value, only 2 patients did not fulfill this criterion, although they have FEV<sub>1</sub> values below 80%, respectively 79.3 and 69.0%.

VC response was observed in 11 (48%) patients with severe obstruction and three (15%) with moderate obstruction (*p* = 0.02). No significant changes were observed between the two groups in the percentage of bronchodilator response for the other parameters.

The correlations between the variation in spirometric parameters and the variation in RV/TLC (% predicted values) before and after BD were performed and we observed a significant negative correlation between VC and RV/TLC in the severe airflow obstruction group [Spearman’s rank correlation coefficient (Rs) = –0.70, *p* < 0.01], and between FVC and RV/TLC in patients with moderate obstruction (Rs = –0.55, *p* = 0.03). Conversely, there was no correlation between IC and RV/TLC. Agreement analyses for functional and clinical parameters after BD use are presented in Table 4. There was a fair agreement between VC (severe group) and FVC (moderate group) response and VAS scores. and

**Table 4 Analysis of agreement between functional and clinical positive responses after bronchodilator use**

Parameters	VAS		6WT	
	Moderate airflow obstruction (n = 20)	Severe airflow obstruction (n = 23)	Moderate airflow obstruction (n = 20)	Severe airflow obstruction (n = 23)
VC	0.20 (0.14)	0.57 (<0.01)	0.17(0.39)	0.13 (0.54)
IC	0.10 (0.61)	0.22 (0.17)	–0.33(0.14)	–0.15 (0.47)
FVC	0.40 (0.03)	0.34 (0.06)	0.00 (1.0)	0.04 (0.86)
FEV <sub>1</sub>	0.10 (0.65)	0.06 (0.75)	–0.05 (0.80)	–0.05 (0.83)
RV	0.10 (0.61)	0.32 (0.04)	0.20 (0.37)	0.12 (0.55)

6MWT = six-minute walk test, FEV<sub>1</sub> = forced expiratory volume in one second, FVC = forced vital capacity, IC = inspiratory capacity, RV = residual volume, VAS = visual analogue scale, VC = vital capacity. Results are expressed as Kappa coefficient and *p* value in parenthesis.

a slight agreement between RV response (severe group) and VAS score. There was no agreement between functional parameter responses and improvement in 6MWT. There was a poor correlation five patients with positive VC and/or IC response presented a negative FVC and/or FEV1 response.

## Discussion

In the present study with asthma patients with moderate and severe obstruction, we observed that VC may be a useful complementary parameter to FVC and FEV1 to assess bronchodilator response.

Asthma patients were assigned to a moderate or severe airflow obstruction group based on FEV1 analysis. In addition, because clinical improvement is the main goal of asthma therapy, VAS (subjective criterion) and 6MWT (objective criterion) were also used to evaluate clinical bronchodilator response in this study.<sup>20,21,25</sup>

Paré et al have described two patterns of response to bronchodilator therapy: predominant increase in expiratory flow rate (flow responders) or FVC (volume responders). Volume responders presented lower expiratory flows and greater degree of air trapping.<sup>7</sup> Newton et al, also reported similar results.<sup>22</sup> More recently, Sorkness et al, studying 287 patients with stable but severe asthma, demonstrated that this group presented prominent air trapping in contrast to individuals with non-severe asthma.<sup>12</sup> Our patients with severe airflow obstruction had both greater VC response in the group and greater air trapping (Table 2).

The 6MWT is considered a good parameter to estimate exercise tolerance in patients with moderate or severe pulmonary impairment, even though it has not been extensively used in asthma patients.<sup>20</sup> In our patients a significant increase in 6MWT as well as a decrease in Borg scale were observed in both groups (Table 3). We made only one 6MWT before and after the BD because the reproducibility of the 6MWT has been considered excellent.<sup>20</sup>

The post-BD response of VC was well correlated with the variation in RV/TLC ratio in the severe obstruction group. In this line, O'Donnell et al studied 84 patients with obstructive disease without response in FEV1 and found a good correlation between variation in VC and IC and FRC after use of bronchodilator.<sup>6</sup> Additionally, Newton et al demonstrated that lung volume improvement was independent of changes in maximal expiratory flows in patients with moderate and severe hyperinflation.<sup>22</sup>

Agreement between VAS scores and functional responses was statistically significant in only three parameters, VC and RV in the severe obstruction group and FVC in the moderate obstruction group, without agreement with IC response (Table 4). This is in accordance with previous studies reporting a better correlation between dyspnea and the volume of thoracic gas rather than FEV1.<sup>9,10,13</sup> A poor correlation ( $p = 0.35$ ) was observed between variations in VC versus variation in VAS in severe obstruction patients. Probably, the reduction in air trapping is not enough to improve exertional breathlessness without a simultaneous and marked decrease in end-expiratory lung volume. Moreover, the increase in VC and IC may represent unrelated effects of the bronchodilation. VAS has been shown to be sensitive to detect improvement in asthma patients.<sup>26</sup>

FEV1 is considered a good marker of improvement. However, in

patients with severe airflow obstruction, FEV1 presents a lack of sensitivity and is a poor predictor of improvement in exercise tolerance.<sup>22,27-29</sup> Moreover, Teeter and colleagues demonstrated that asthma symptoms were poorly correlated with FEV1 before and after therapy.<sup>30</sup> Therefore, in addition to FEV1, other physiologic parameters, such as lung elastic recoil, should be considered to characterize asthma severity.<sup>31</sup>

This study has some limitations that need to be addressed: 1) we were not able to correlate the reduction in air trapping with the increase in IC measured in rest, as previously described during exercise tests<sup>3,9,29</sup> or during methacholine challenge testing<sup>8,11</sup> and 2) static lung volumes were measured using the helium dilution method, even though body plethysmography is considered the most sensitive method.<sup>25,32</sup> However, we opted to use more routine tests because ergospirometry, bronchoprovocation test and plethysmography are not available in most pulmonary function laboratories.

## Conclusions

The present findings suggest that VC may be useful in addition to FVC and FEV1 to identify bronchodilator response in asthma patients with severe airflow obstruction.

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*Guest Editorial...continued from page 4*

Many respiratory care departments have a Patient Driven Protocol in place, where the therapist can get the patient on the appropriate respiratory treatment and/or modality. Unfortunately this hasn't prevented the endless calls for prn bronchodilators. I am, along with a colleague, in the process of conducting a prn study in which we are tracking how many prn treatments are called for in a day. We are averaging about 20 calls in a 24 hour period, and approximately three-fourths of these prn calls are not indicated. In our institution, respiratory care provides nurses and residents with bronchodilator education on a routine basis, yet the calls for unnecessary treatments keep coming in. And I have a strong feeling this isn't happening in just one hospital, but in hospitals nationwide. So as respiratory therapists, how can we begin to deal with this problem? Ordering and giving drugs that are not indicated, no matter how minor the side effects can be, is not appropriate care for our patients, and our patients' best interest is of the utmost importance. At the completion of this prn study, I hope to have a protocol in conjunction with our Patient Driven Protocol, one that doctors and nurses have access to as well. It will state the indication for a bronchodilator to be ordered, the symptoms associated with this indication and an algorithm to follow. The goal is to decrease unnecessary bronchodilator use, to educate patients as well as doctors and nurses and to help reduce the cost of healthcare.

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# Diagnostic Aid to Rule Out Pneumonia in Adults with Cough and Feeling of Fever. A validation study in the primary care setting

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## Abstract

**Background:** We recently reported the derivation of a diagnostic aid to rule out pneumonia in adults presenting with new onset of cough or worsening of chronic cough and increased body temperature. The aim of the present investigation was to validate the diagnostic aid in a new sample of primary care patients.

**Methods:** From two group practices in Zurich, we included 110 patients with the main symptoms of cough and subjective feeling of increased body temperature, and C-reactive protein levels below 50 µg/ml, no dyspnea, and not daily feeling of increased body temperature since the onset of cough. We excluded patients who were prescribed antibiotics at their first consultation. Approximately two weeks after inclusion, practice assistants contacted the participants by phone and asked four questions regarding the course of their complaints. In particular, they asked whether a prescription of antibiotics or hospitalization had been necessary within the last two weeks.

**Results:** In 107 of 110 patients, pneumonia could be ruled out with a high degree of certainty, and no prescription of antibiotics was necessary. Three patients were prescribed antibiotics between the time of inclusion in the study and the phone interview two weeks later. Acute rhinosinusitis was diagnosed in one patient, and antibiotics were prescribed to the other two patients because their symptoms had worsened and their CRP levels increased. Use of the diagnostic aid could have missed these two possible cases of pneumonia. These observations correspond to a false negative rate of 1.8% (95% confidence interval: 0.50%-6.4%).

**Conclusions:** This diagnostic aid is helpful to rule out pneumonia in patients from a primary care setting. After further validation application of this aid in daily practice may help to reduce the prescription rate of unnecessary antibiotics in patients with respiratory tract infections.

## Background

The inappropriate prescription of antibiotics is an avoidable cause of the increasing problem of antibiotic resistance. Overuse of antibiotics for upper respiratory tract infections is common,

although guidelines recommend antibiotics only for patients with bacterial pneumonia or moderate to severe exacerbations of chronic bronchitis. However, in a recent publication also a benefit of antibiotic treatment has been demonstrated in patients with mild to moderate exacerbations. Physicians are aware of the recommendations in the guidelines, but they may have understandable concerns about missing pneumonia in patients with cough and increased body temperature, and when in doubt, physicians prefer to prescribe antibiotics.

In a recently published study<sup>6</sup> we reported the derivation of a fast and low-cost diagnostic aid to rule out pneumonia in patients with new onset of cough or worsening of chronic cough and the subjective feeling of increased body temperature. A total of 621 patients, almost all of them attending a primary care physician were included in the derivation study. The mean age of that patients was 48 years and half of them were males. The derivation study showed that three pieces of information are necessary to rule out pneumonia in these patients; C-reactive protein (CRP) level, dyspnea (no/yes), and daily feeling of increased body temperature since onset of cough (no/yes). Pneumonia could be ruled out in patients with CRP levels below 50 µg/ml who lacked dyspnea and daily subjective feeling of increased body temperature since onset of cough. At the time of publication, this diagnostic aid had not been validated in patients outside of the derivation sample.

Before integrating such a diagnostic aid into daily practice, the accuracy of the instrument should be tested in a new sample of patients. The aim of this study is to evaluate the accuracy of the diagnostic aid in patients with CRP levels below 50 µg/ml, no dyspnea and not daily subjective feeling of increased body temperature since onset of cough.

## Methods

The participating physicians asked patients about the presence of dyspnea and the duration and regularity (daily or not) subjective feeling of increased body temperature. Venous blood samples for measuring CRP levels were drawn from all patients, and blood was analyzed using standard procedures.

At a minimum of one week after the first consultation, physicians or physician assistants contacted the patients for follow-up. All patients were asked four questions: Have you received a prescription for antibiotics since the time of the consultation leading to inclusion in the study? Have you been hospitalized during this time? Has the severity of your cough decreased,

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increased, or remained stable since the first consultation? Has the subjective feeling of increased body temperature disappeared, remained stable, or worsened? When a patient had been hospitalized since inclusion in the study, we contacted hospitals to obtain the information whether pneumonia or another illness was the reason for the hospitalization.

When patients at the follow-up consultation reported that symptoms improved and no antibiotics had been prescribed to them since the first consultation we assumed that a clinically relevant pneumonia could be excluded with a high degree of certainty.

## Results

115 patients were eligible for this study. After exclusion criteria, 110 patients remained in the study. To obtain information about the proportion of patients with cough and increased body temperature fulfill the inclusion criteria, the practice assistants registered all potentially eligible patients with cough and feeling of increased body temperature during two weeks in January 2012. Within those two weeks, the practice assistants counted 34 potentially eligible patients; ten of these patients, a bit less than a third, were eligible for inclusion in the study.

The median age of the included patients was 39 years (range 16 to 86 years), and 73 (66%) were female. The median duration between new onset and worsening of chronic cough was 7 days (interquartile range 4 to 14) days. The median CRP level was 6.3 µg/ml (range 1 to 44 µg/l), 61% of the included patients had a CRP level below 10 µg/l, and 39% of participants had a CRP level between 11 µg/l and 50 µg/l. In two patients, chest x-rays at the time of the first consultation showed no pathological changes.

All 110 patients enrolled in the study were contacted a median of 13 days (interquartile range 11 to 15 days) after enrollment in the study. Cough had improved in 90 (81.8%) of participants, had worsened in 6 (5.5%), and had remained stable in 11 (10%) of patients. Subjective feeling of increased body temperature disappeared completely in 98% of the patients, and two patients reported that they still had intermittent increased measured body temperature. In none of the patients a chest x-ray was performed after the first visit.

Three patients received a prescription for antibiotics between the time of inclusion in the study and the phone call by the practice assistant.

In 107 out of 110 patients, pneumonia could be ruled out with a very high degree of certainty. In the remaining three patients, who received antibiotics after inclusion, we did not miss an apparent case of pneumonia; there could have been one or two potential cases of pneumonia, but it is unlikely. Based on these data, the maximum proportion of missed pneumonia cases is  $p = 2/110 = 0.018$  (95% confidence interval 0.005-0.064) as a worst-case scenario.

## Discussion

**Main results:** We validated a simple diagnostic aid for ruling out pneumonia in patients with cough and increased body temperature<sup>5</sup> in a new primary care population. In patients with cough, feeling of increased body temperature, and a CRP level below 50 µg/ml, but without dyspnea and daily subjective feeling of increased body temperature since the onset of cough, pneumonia can be ruled out safely as the underlying illness. The

predictive performance of the simple diagnostic aid was good, as no definite case of pneumonia was missed and only two potential cases of pneumonia appeared. If we rate both these cases as patients with missed pneumonia – the worst-case scenario – then the estimated proportion of falsely classified non-pneumonia cases is 1.8%.

**Clinical implications:** When physicians, after taking the patient history and performing the physical exam, are in doubt whether pneumonia could be present and therefore prescribe antibiotic treatment, the validated diagnostic aid is useful for two reasons. In patients with CRP levels below 50 µg/ml, no dyspnea, and no daily subjective feeling of increased body temperature since the onset of cough, pneumonia is very unlikely at the time of consultation. Unnecessary chest x-rays as well as unnecessary prescriptions of antibiotics can be avoided. However, symptoms could worsen in the days following the first consultation, making further tests and antibiotic treatment necessary.

Applying this diagnostic aid in daily practice may lead to a reduction in the overuse of antibiotics as well as a reduction in associated problems caused by this overuse. In our previous derivation study,<sup>7</sup> we demonstrated that use of the simple diagnostic aid would have led to a decrease in antibiotic prescriptions of approximately ten percent even in a population of patients with a low risk of pneumonia. Acute respiratory tract infections are the most common reason for inappropriate antibiotic therapy in primary care. In view of the increasing problem of antibiotic resistance, possible side effects, and costs, even a small reduction is desirable and will impact public health.

**Implications for further research:** In the future, the diagnostic aid should be validated in additional patient populations and in various health care settings. These validations will increase the reliability of this simple diagnostic instrument, and motivate physicians to apply it to their daily practice.

## Conclusion

Validation of the diagnostic aid in a new sample of primary care patients revealed that the instrument is highly accurate at ruling out pneumonia in patients with cough and subjective feeling of increased body temperature. The application of this rapid and low-cost instrument may support a change in physician behavior, reducing the rate of unnecessary chest x-rays and antibiotic prescriptions in patients with low risk of pneumonia. These improvements would markedly contribute to cost control and address the increasing problem of antibiotic resistance.

# Using Respiratory Rate and Thoracic Movement to Assess Respiratory Insufficiency in Amyotrophic Lateral Sclerosis: a preliminary study

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## Abstract

**Background:** Hypoventilation due to respiratory insufficiency is the most common cause of death in amyotrophic lateral sclerosis (ALS) and non-invasive ventilation (NIV) can be used as a palliative treatment. The current guidelines recommend performing spirometry, and recording nocturnal oxyhemoglobin saturation and arterial blood gas analysis to assess the severity of the hypoventilation. We examined whether the respiratory rate and thoracic movement were reliable preliminary clinical signs in the development of respiratory insufficiency in patients with ALS.

**Methods:** We measured the respiratory rate and thoracic movement, performed respiratory function tests and blood gas analysis, and recorded subjective hypoventilation symptoms in 42 ALS patients over a 7-year period. We recommended NIV if the patient presented with hypoventilation matching the current guidelines. We divided patients retrospectively into two groups: those to whom NIV was recommended within 6 months of the diagnosis (Group 1) and those to whom NIV was recommended 6 months after the diagnosis (Group 2). We used the Mann Whitney U test for comparisons between the two groups.

**Results:** The mean partial pressure of arterial carbon dioxide in the morning in Group 1 was 6.3 (95% confidence interval 5.6–6.9) kPa and in Group 2 5.3 (5.0–5.6) kPa ( $p = 0.007$ ). The mean respiratory rate at the time of diagnosis in Group 1 was 21 (18–24) breaths per minute and 16 (14–18) breaths per minute in Group 2 ( $p = 0.005$ ). The mean thoracic movement was 2.9 (2.2–3.6) cm in Group 1 and 4.0 (3.4–4.8) cm in Group 2 ( $p = 0.01$ ). We observed no other differences between the groups.

**Conclusions:** Patients who received NIV within six months of the diagnosis of ALS had higher respiratory rates and smaller thoracic movement compared with patients who received NIV later. Further studies with larger numbers of patients are needed to establish if these measurements can be used as a marker of hypoventilation in ALS.

## Background

Amyotrophic lateral sclerosis (ALS) is a form of degenerative motor neuron disease of unknown etiology. The disease is characterized by progressive muscle weakness and atrophy throughout the body. The prevalence is 4–8 in 100 000 and the annual incidence is 1–2 in 100 000. Prognosis is poor with a median survival from the onset of symptoms of 2–4 years. Despite extensive effort, no curative treatment is available and riluzole (a tetrodotoxin-sensitive sodium channel blocker) is the only drug that can slow the progression of the disease. Therefore, treatment following the diagnosis is palliative.

Hypoventilation due to respiratory insufficiency is the most common cause of death in patients with advanced ALS. Non-invasive ventilation (NIV) has been recommended for ALS patients when hypoventilation occurs because it relieves dyspnea, increases the quality of life, and may prolong survival in late stage ALS patients. The current guidelines recommend beginning NIV if the patient presents with dyspnea, orthopnea, disturbed sleep, tachypnea, nocturnal desaturation  $< 90\%$ , increased morning carbon dioxide partial pressure ( $p\text{CO}_2$ )  $> 6$  kPa, decreased sniff nasal pressure  $< 40$  cmH<sub>2</sub>O, decreased maximum inspiratory mouth pressure (MIP)  $< 60$  cmH<sub>2</sub>O, or decreased forced vital capacity (FVC)  $< 80\%$ . However, there is great international variation in the use of different diagnostic tests prior to initiation of NIV.

The onset of muscle weakness varies between patients and symptoms may appear first in the limbs or they may start from the bulbar area leading to dysphagia and speech difficulties. This wide variability in the clinical course of ALS can be challenging for the clinician because the progression of respiratory insufficiency also greatly varies among these patients. Because of this variability, the current guidelines recommend a clinical visit every 2–3 months. Although nocturnal desaturation and carbon dioxide tension can be recorded noninvasively, it is often not possible to perform these measurements outside the hospital because of lack of devices and health care providers to assist the patient. The measurement of increased morning  $p\text{CO}_2$  requires blood sampling by a health care professional. In addition, spirometric measurements require good facial function, as patients have to hold their lips tightly around the mouthpiece of the spirometer. In ALS patients with severe bulbar dysfunction, this measurement may be unreliable. We therefore wished to determine if we could use respiratory rate and thoracic movement as preliminary clinical signs in the development of respiratory insufficiency.

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## Methods

**Design:** A total of 77 patients fulfilled the El Escorial World Federation criteria for ALS. NIV treatment and other palliative treatments were offered to all the patients. The respiratory measurements were obtained within three months of the diagnosis in only 42 patients who were included in the per-protocol analysis of the data. Twenty-nine patients were excluded because respiratory measurements were not performed within the three-month period from the diagnosis. The three-month time window was assumed to reflect the respiratory function of the patients at the time of the ALS diagnosis.

We excluded an additional three patients because of lack of cooperation (frontotemporal dementia) and three patients declined follow-up for NIV. Although NIV was recommended for 42 patients, 29 of these 42 patients were able to use NIV. Based on earlier studies in which the course of the disease was rapid, we divided these 42 patients retrospectively into two groups: those for whom NIV was recommended within 6 months from the diagnosis (Group 1;  $n = 22$ ) and those for whom NIV was recommended after 6 months from the diagnosis (Group 2;  $n = 20$ ). Before the NIV trial, we asked the patients if they were willing to start the treatment. Each patient made the final decision whether to begin NIV.

**Data collection:** An experienced respiratory physiotherapist performed the respiratory function tests. The respiratory rate was assessed before any other measurements with the patient awake, in a supine position and following a one-hour rest. A specialized nurse observed and calculated the respiratory rate during one minute. We measured forced vital capacity (FVC) and forced expiratory volume exhaled in 1s (FEV 1) using a hand-held MicroPlus spirometer (Cardinal Health, Chatham, UK), and expressed each as a fraction of the predicted values in percent. Respiratory muscle tests included assessments of peak cough flow (PCF), maximum inspiratory mouth pressure (MIP), maximum expiratory mouth pressure (MEP), and sniff nasal pressure (SNP), all measured with MicroRPM (Cardinal Health, Chatham, UK). We performed each measurement three times with the patient in a sitting position and submitted the best value for the analyses. We measured the thoracic movement at the mammillary level with the patient in a sitting position and recorded the difference in the thoracic circumference between the maximal inspiration and expiration. The respiratory rate was expressed as breaths per min (BPM) at rest. An arterial blood gas sample was drawn from the radial artery in the morning just after waking and with the patient in a supine position.

We assessed the subjective symptoms of hypoventilation using a set of visual analogue scales (VAS) using a 10 cm long line with opposite extremes at each end, where 0 indicated no symptoms and 10 indicated the worst imaginable symptoms; assessing dyspnea, cough weakness, sleep disturbances, morning headaches, and daytime sleepiness. If a patient was not able to tick the line on the VAS because of impaired motor function of his/her hand, the physiotherapist marked the patient's response.

**Ventilatory support:** NIV was provided using a pressure-targeted ventilator (VPAP III ST, ResMed, Bella Vista, Australia). Both a pulmonologist and an anaesthesiologist assessed the need for NIV. The primary criteria for recommendation for an NIV trial were dyspnoea at rest, increased  $p\text{CO}_2 > 5.5$  kPa or decreased  $p\text{O}_2 < 10$  kPa in the morning arterial blood gases or decreased FVC under 50 % of the predicted value. The secondary criteria for recommendation for an NIV trial were  $\text{MIP} < 60$  cmH<sub>2</sub>O, or  $\text{SNP}$

$< 40$  cmH<sub>2</sub>O. We interpreted a VAS score  $> 5$  for dyspnoea as an indication to recommend an NIV trial. The remainders of the measurements were used as supportive criteria to recommend an NIV trial.

## Results

The records for 42 patients with ALS (20 male, 22 female) were adequate for analysis. The age and the duration of the symptoms before the diagnosis of ALS did not differ between the groups.

The mean  $p\text{CO}_2$  and  $p\text{O}_2$  in the morning arterial blood gas samples at the time of diagnosis in Group 1 were 6.3 (5.6–6.9) and 9.8 (9.3–10.4) kPa, respectively. The mean  $p\text{CO}_2$  and  $p\text{O}_2$  at the time of diagnosis in Group 2 were 5.3 (5.0–5.6) and 10.7 (9.4–12) kPa, respectively. The mean  $p\text{CO}_2$  was significantly higher in Group 1 ( $p = 0.007$ ) whereas the values for mean  $p\text{O}_2$  did not differ between the two groups ( $p = 0.4$ ). The mean respiratory rate at the time of diagnosis in Group 1 was 21 (18–24) BPM and 16 (14–18) BPM in Group 2 ( $p = 0.005$ ). The mean thoracic movement at the time of diagnosis in Group 1 was 2.9 (2.2–3.6) cm and 4.0 (3.4–4.8) cm in Group 2 ( $p = 0.01$ ). We observed no other differences between the two groups.

## Discussion

This was a retrospective study to clarify if we could use the respiratory rate and thoracic movement as preliminary clinical signs for the development of significant respiratory insufficiency in ALS patients. The main finding in our study was that patients who received NIV within six months of the diagnosis of ALS had higher respiratory rates and smaller thoracic movement at diagnosis compared with patients who received NIV later.

Among healthy subjects, a respiratory rate under 15 BPM allows a physiologically optimal level of work of breathing. In advanced ALS, thoracic compliance is usually decreased, resulting in decreased tidal volume, increased respiratory rate and work of breathing. NIV can help patients compensate for the decreased thoracic compliance and thus decrease the respiratory frequency and the work of breathing. Although the retrospective study design and small number of patients did not allow the calculation of positive and negative predictive values and cut-off values for respiratory rate and thoracic movement in the assessment of respiratory insufficiency in ALS, it appears that NIV was initiated within six months from diagnosis for those patients who had a respiratory rate at least of 20 BPM at the moment of diagnosis.

Another result of interest was that we failed to show any difference in dyspnea between the two study groups. The patients scored only mild symptoms of dyspnea with no morning headaches at the initiation of NIV in both groups. The same was true for sleep disturbances and daytime sleepiness. In a previous study with 36 ALS patients, respiratory complaints did not occur until the vital capacity, MIP, or MEP were severely impaired. In that study, the strongest correlation with dyspnea was a decline in vital capacity. The authors suggested that a small reduction in vital capacity does not cause any symptoms except in heavy exercise. The patients decrease their physical activity because of skeletal muscle weakness, and thus may not feel dyspneic during their daily activities unless more strenuous exercise is required. Our results are similar as our patients complained of very little dyspnoea at the time of diagnosis. Nevertheless, as our patients were aware of the possibility of initiating NIV, they might have been reluctant to disclose the severity of their

symptoms and intentionally underestimated their response in our VAS query. A larger sample size might show a difference in dyspnea.

FVC and FEV<sub>1</sub> are commonly used to assess pulmonary function in lung diseases and in ALS patients. Previously, FVC, SNP, MIP and MEP were determined in 16 ALS patients monthly over a period of 18 ± 10 months. The SNP, MIP and MEP were severely reduced even though the FVC remained normal. In addition, the measurement of MIP and MEP was difficult in these advanced ALS patients because they had difficulties tightly holding the mouthpiece of the recording device. This led to air leaks and reduced the values of MIP and MEP. A reduced SNP of under 40 cmH<sub>2</sub>O has been suggested as the most sensitive and easiest test to perform in ALS patients. However, although we found that the SNP was severely reduced in both groups, only those with an increased respiratory rate in Group 1 were ready to start NIV.

Our study has limitations. First, the retrospective design compared the respiratory measurements between two different patient groups at one single time point. Thus, we cannot draw definitive conclusions for the cut-off values for respiratory rate or thoracic movement to indicate the need for NIV. Further studies are needed. In addition, the only inclusion criterion was the respiratory assessment within three months from diagnosis. Thus, we did not evaluate other pulmonary or heart diseases which might have biased the results. Second, the ideal is a randomized prospective trial in which the initiation of NIV is blinded and the subjects are observed from an asymptomatic stage until severe hypoventilation occurs. However, because NIV is established in palliative care in ALS, ethical aspects have to be considered in randomized study designs, especially if the initiation of NIV is somehow blinded. Moreover, the diagnosis of ALS is often delayed and the patients often have reduced ventilation capacity at the time of diagnosis. We saw this in our patients as the median time from the first symptoms until diagnosis ranged from 11 to 13 months. During this time, the patients' symptoms were evaluated at the primary care level or not at all. Thus, when we met the patients, half already showed moderately to severely reduced FVC (60%), SNP (24 cmH<sub>2</sub>O), MIP (29 cmH<sub>2</sub>O), or MEP (41 cmH<sub>2</sub>O) and NIV was recommended based on a single measurement without follow-up. Third, we dealt with severely ill patients, whose NIV initiation was based on both the clinical measurements and the patient's own desire. The fact that NIV was based on the patient's own desire may have biased the answers in the hypoventilation questionnaire if the patients reported no or only mild symptoms of hypoventilation even if they had severely reduced respiratory measurements.

## Conclusions

The use of NIV as palliative treatment has previously been shown to relieve symptoms as well as to improve survival in ALS patients. However, the optimal timing for initiating NIV is not yet well established. Most of the available methods used to evaluate the degree of hypoventilation and the need for NIV require well-trained health care professional and special devices. In contrast, assessing resting respiratory rate or thoracic movement can be performed in a patient's home by primary care nursing staff and could be a feasible screening tool for detecting hypoventilation. However, further studies are needed to define the positive and negative predictive values and cut-off values for respiratory rate and thoracic movement in the assessment of respiratory insufficiency in ALS.



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**References:** 1. Castro M, et al, for the AIR2 Trial Study Group. *Ann Allergy Asthma Immunol.* 2011;107:65-70. 2. Castro M, et al, for the AIR2 Trial Study Group. *Am J Respir Crit Care Med.* 2010;181:116-124.

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