



Education

Jan./Feb. '99

Bulletin

3

1999 Listing of Acquisitions Editors for Respiratory Care Textbooks

4

AARC 1999 Education Committee Charges

Inhaled Nitric Oxide Therapy and Persistent Pulmonary Hypertension of the Newborn

8

Hot List Topics: AARC Times Wants Your Input

American Association for Respiratory Care

Notes from the Editor

by Arthur Jones, EdD, RRT

David Chang has completed this, his final issue as editor of the *Education Bulletin*. Those among us who have benefited from his hard work and expertise over the past few years owe him a debt of gratitude. So thanks, David, and good luck as Education Section Chair.

Now that I am assuming the editorial responsibilities for this publication for the next two years, I am hoping that you will continue to support the *Bulletin* as a source of information and ideas. The publication cannot exist without contributors, and RC educators with ideas and a few writing skills are needed to submit articles, reviews, or other items of interest. Perhaps there are student papers that warrant publication here. In addition to articles, the *Bulletin* will continue Dr. Chang's practice of publishing guest edi-

torials. So, if there is a topic that you would like to address in that manner, please feel free to do so.

The success of any publication ultimately depends on its readers; that is, whether they read it, and how they perceive its value. So, it is vital that I gain insight into what you want to read in the *Bulletin*. Even if you are not inclined to write for the *Bulletin*, you can still participate by providing information on the kinds of things you would like to read about in these pages. Your ideas for article topics or editorials are quite welcome. Finally, we are also seeking comments on the contents of the *Bulletin*. Please let us know how we are doing – and what we are not doing that we should. Truly, it is your publication. We only work here. ■

1999 Calendar Deadline

March 13, 1999 CRTT Exam.....	January 1
June 5, 1999 RRT Exam	February 1
June 5, 1999 CPFT Exam.....	April 1
Summer Forum Abstract & Poster Presentations.....	April 1
Summer Forum (Phoenix, AZ).....	July 16-18

Notes from the Chair

by David W. Chang, EdD, RRT

Education is not preparation for life, education is life itself.
-John Dewey

At the International Respiratory Congress in Atlanta this past November, the AARC Board of Directors passed on the second reading of the revised bylaws that would provide a Board seat for each specialty section having 1,000 or more active members. This change would provide a direct link between the qualified specialty sections and the governing body of our association.

At the end of 1998, the Education Section had slightly less than the required 1,000 active members needed to qualify our section for a seat on the Board. The

good news is that this new provision will not go into effect until the year 2000 or later. Debbie Lierl, chair of our Long-range Planning Committee, is developing a plan for membership recruitment and retention. Information on this effort is forthcoming. In the meantime, you may help us attain our goal by asking your colleagues to become active members of the AARC (some of them may be associate members) and to join the Education Section.

The simplest way to join the section is to call the membership services department at the AARC at (972) 243-2272 and charge the specialty section fee to a cred-

"Notes" continued on page 2

"Notes" continued from page 1

it card. It is important to point out to your colleagues that this can be done anytime – it is not necessary for them to wait for their annual AARC membership renewals.

The Education Section is please to announce three new committee chairs, each of whom will be serving a two-year term (1999 to 2000). They are Arthur Jones (Publications), Gudrun Pryor (Abstract and Poster Presentations), and Terry LeGrand (Practitioner of the Year). I am also grateful to our three current chairs for their willingness to serve an additional year in 1999: Tim OptHolt (Program), Linda Van Scoder (Education Annual), and Debbie Lierl (Long-range Planning).

There are many opportunities for our members to participate in the section. All

six of our committees have memberships available in 1999. As always, the committee chairs are looking for volunteers to bring in new ideas and help the section develop strategic plans for the enhancement of RC education. I urge you, as active members of the section, to participate in one or more of these six committees.

Take a minute to look over the functions of each committee that are listed on the form below and then submit your name to us. Since these committee memberships are two-year appointments, all current members must re-submit their preferences for 1999. The only requirement is that you are a current, active member of the AARC and the section.

Thank you for your continuing support of the Education Section. I look forward to working with you during the next two years. If you have suggestions and/or comments, please feel free to send them to me. (My contact information appears on page 2.)

1999-2000 Education Section Committees: Sign-Up form and Committee Information

Name _____
 Phone _____
 Address _____

E-mail _____
 _____ I would like to serve on the following committee(s) in 1999 and 2000, or
 _____ I would like to nominate _____

to serve as chair (in the year 2000) of the following committee. (Please provide address and phone number of nominee).

Committee	Member	Chair
Publications	_____	Filled
Abstract and Poster Presentations	_____	Filled
Practitioner of the Year	_____	Filled
Program	_____	_____
Education Annual	_____	Filled
Long-range Planning	_____	_____

(Return Form before April 1, 1999 to David Chang, Chair, AARC Education Section, Columbus State University, 4225 University Ave, Columbus, GA 31907)

Publications Committee
 Arthur Jones
 Department of Respiratory Care
 The University of Texas Health Science Center at San Antonio

7703 Floyd Curl Drive
 San Antonio, TX 78284
 (210) 567-8857
 FAX (210) 567-8852
 Committee members: Arthur Jones (Chair), David Chang, Sharon McGenity-Hatfield, Jackie Rogers, David Shelledy, Steve Wehrman

Program Committee
 Tim Op't Holt, EdD, RRT
 Associate Professor
 Cardiorespiratory Care
 University of South Alabama
 1504 Springhill Ave.
 Mobile, AL 36604
 (334) 434-3405
 FAX (334) 434-3941
 email: topholt@jaguar1.usouthal.edu
 Committee members: Tim Op't Holt (Chair), Karen Milikowski, F. Ross Payne, Bill Galvin, Andrew Mazzoli, Pat Munzer, Kathleen Sheely, Barbara Fedak, Carolyn O'Daniel, Carole Smith, Phil Hoberty, Jane Boulanger, Margaret Swanson

The Program Committee meets twice a year to discuss ideas for the following year's educational programs at the Summer Forum and AARC Congress. In advance of each meeting, the committee members are asked to formulate ideas and bring them to the meeting. During the meetings, we discuss those ideas in relation to what is happening in respiratory therapy education. Most recently, we have discussed how to incorporate hospital educators' interests into our programs. During our last meeting at the AARC Congress in Atlanta, committee members were assigned topics to develop into proposals for submission to the AARC Program Committee. The chair acts as a liaison to the AARC Program Committee. Section members are welcome to submit their ideas to any member of the section's Program Committee.

Respiratory Care Education Annual
 Linda Van Scoder, EdD, RRT
 Allied Health Education
 Ball State University, Clarian
 1701 N. Senate Blvd.
 Indianapolis, IN 46202
 (317) 929-8475
 FAX (317) 929-2102
 email: lvanscoder@clarian.com
 Mailing Address for submissions to the Annual:
 Education Department
 AARC
 11030 Ables Lane
 Dallas, TX 75229
 1998 Committee Members: Linda Van Scoder (Chair), Will Beachey, William Clark, Phillip Hoberty, Arthur Jones, Paul Mathews, Sharon McGenity-Hatfield, David Rice, Christine Romeo-Hamilton, David Shelledy

Education Bulletin

is published by the
**American Association
 for Respiratory Care**
 11030 Ables Lane
 Dallas, TX 75229-4593
 (972) 243-2272
 FAX (972) 484-2720
 e-mail: info@aarc.org

Kelli Hagen
 AARC communications coordinator

Debbie Bunch
 Bulletin managing editor

Edwards Printing
 Bulletin typesetting

Chair
David Chang, EdD, RR T
 Respiratory Therapy
 Columbus State University
 4225 University Avenue
 Columbus, GA 31907
 (706) 568-2130
 FAX (706) 569-3101
 e-mail: chang_david@colstate.edu

Bulletin Editor
Art Jones, EdD, RR T
 Department of Respiratory Care
 The University of Texas Health Science Center at San Antonio
 7703 Floyd Curl Drive
 San Antonio, TX 78284-7784
 (210) 567-8857
 FAX (210) 567-8852
 e-mail: jonesap@uthscsa.edu

Medical Advisor
Richard Sheldon, MD (ATS)
 (909) 792-7563

"Notes" continued on page 3

"Notes" continued from page 2

Committee functions include encouraging educators to submit scholarly articles, reviewing papers for possible publication, providing feedback to authors, publishing a refereed journal each spring, and maintaining CINAHL listing. Submissions for the 1999 Annual have already been received and the review process began at the beginning of January. Volume 8 will be ready for publication in the spring. We encourage educators to begin preparing their papers for Volume 9, which will be published in the spring of 2000. The submission deadline for Volume 9 is December 1.

Long-range Planning Committee

Debbie Lierl, RRT
 Program Chair, Respiratory Care
 Cincinnati State Technical & Community College
 3520 Central Parkway
 Cincinnati, OH 45223-2690
 (513) 569-1690
 email: lierld@cinstat.oh.edu
 Committee members: Debbie Lierl (Chair), Wayne Lawson, Karen Milikowski

The main 1999 goal of the Long-range Planning Committee (previously the Strategic Planning Committee) is to increase membership in the Education

Section. We will also continue to gather information on a core curriculum. The committee is looking for members to help achieve these goals. If you do not want to serve on this committee, but would like to help the section's membership drive, you can do so by encouraging one or two of your colleagues to join the section. Please let them know that they do not have to wait until their annual renewal date to join the section. They can call the AARC at anytime and sign up.

Practitioner of the Year Committee

Terry S. LeGrand, PhD
 Director of Clinical Education
 Department of Respiratory Care
 The University of Texas Health Science Center at San Antonio
 7703 Floyd Curl Drive
 San Antonio, TX 78284
 (210) 567-8855
 FAX (210) 567-8852

Committee members: Terry S. LeGrand (Chair), Thomas J. Butler, Kerry Jean Connor, Bruce Feistner, Kenny McGowen, Jackie Rogers, McIver Rountree

The Practitioner of the Year Committee develops and updates the appropriate criteria for nominating and selecting an individual who, based on contributions made during the previous year, embodies the characteristics of an exemplary educator.

The committee's goal for 1999 is to refine the method for selecting an individual for this recognition to better reflect the broad cross-section of respiratory therapy educators making unique contributions to the field.

Poster and Abstract Presentations Committee

Gudrun Pryor
 Washburn University
 School of Applied Studies
 1700 SW College
 Topeka, KS 66621
 (785) 231-1010, ext. 1287
 FAX (785) 231-1027
 e-mail: zzpryor@washburn.edu
 Committee members: Gudrun Pryor (Chair), Ellen Becker, Thomas Butler, David Chang, Clarissa Craig, Nancy Colletti, Kerry Jean Connor, Christine Fitzgerald, David Gordon, Phillip Hoberty, Arthur Jones, Lori Krueger, Paul Matthews, Karen Milikowski, Pat Munzer, Carolyn O'Daniel, Tim Op't Holt, Karen Schell, David Shelledy, Lisa Stillerman, James Taylor, Lynda Thomas-Goodfellow

The committee establishes the deadline for submission of abstract and poster presentations to the Summer Forum, reviews the submissions, and makes recommendations regarding their acceptance. ■

1999 Listing of Acquisitions Editors for Respiratory Care Textbooks

Editor's Note: The acquisitions editors listed in the table below welcome textbook ideas and proposals from RC educators and practitioners. You are invited to call or write for a copy of the respective submission guidelines. For those interested in contacting an acquisitions editor, see the related article in the summer 1995 issue of the Bulletin: "The Publishing Process: From Concept to Reality" (Listing updated December 1, 1998)

Publishers

Delmar Publishers

3 Columbia Circle
 P.O. Box 15015
 Albany, NY 12212-5015

F.A. Davis Company

Philadelphia, PA 19103

Lippincott Williams and Wilkins

227 East Washington Square
 Philadelphia, PA 19106-3780

McGraw-Hill Health Professions Division

1221 Avenue of the Americas
 New York, NY 10020-1095
 stephen_zollo@mcgraw-hill.com

Mosby

11830 Westline Ind. Dr.
 St. Louis, MO 63146

Prentice Hall-Simon & Schuster Education Group

One Lake Street
 Upper Saddle River, NJ 07458

W.B. Saunders Company

85 Marty Street
 Redlands, CA 92373

Acquisition Editors

Dawn F. Gerrain
 (518) 464-7022
 (800) 998-7498 ext. 7022
 FAX (518) 464-0358
 dgerrain@delmar.com

Lynn Borders Caldwell
 (215) 568-2270

(800) 523-4049
 FAX (215) 568-5065
 lbc@fadavis.com

Larry J. McGrew
 (215) 238-4325
 lmcgrew@lww.com

Stephen Zollo
 (212) 337-6034
 stephen_zollo@mcgraw-hill.com

Janet Russell
 (800) 325-4177 ext. 4471
 FAX (312) 726-6075
 janet.russell@mosby.com

Mark Cohen
 (201) 236-7906
 FAX (201) 236-7759
 mark_cohen@prenhall.com

Andrew Allen
 (215) 238-7833
 (800) 523-1649
 aallen@wbsaunders.com

AARC 1999 Education Committee Charges

Editor's Note: The 1999 AARC Education Committee charges are listed below, along with the members who have agreed to address them. If you would like to participate in accomplishment of, or comment on, any of these charges, please contact Debbie Lierl at (513) 569-1690 or lierld@cinstat.oh.us

1. Concern itself with continuing programs and special education projects as directed by the president. (Debra Lierl)
2. Monitor and document changes occurring in the educational system as a result of the associate degree entry level. (F. Herbert Douce & Patricia Fisher)
3. In collaboration with CoARC, oversee the development and implementation of the new standards for accreditation of respiratory care educational programs. (William Clark & F. Herbert Douce)
4. In collaboration with the Executive Office, develop new IISPs and revise current IISPs. Report to the Board of Directors at the March 1999 meeting the committee's recommendations for same. (Karen M. Boudin & Wesley Granger)
5. Identify and present to the Board of Directors at the March 1999 meeting published sources of age-specific educational materials and competency testing. (George Gaebler & William Clark & Deborah Cullen)
6. Investigate avenues for documenting continuing competency of respiratory therapists. Report the committee's recommendations at the fall 1999 meeting. (Terry LeGrand & Wayne Lawson)
7. Develop new age-specific educational materials in the categories approved by the Board of Directors at the July 1998 meeting. (William Clark)
8. Identify two future postgraduate educational courses dealing with the expanded role of the respiratory therapist. (Ruth Rinker & Wayne Lawson)
9. Recommend cross training and multi-skilling opportunities for respiratory therapists and develop strategies for implementation into entry level and advanced practice programs. (Completed in 1998)
10. Look at the educational needs of training a respiratory therapist in the year 2010 and make recommendations to the Board about what the entry level of education will need to be at that time. (Patricia Fisher & Wesley Granger)
11. In collaboration with the Cultural Diversity Committee, address the inclusion of cultural awareness training in entry and advanced practice educational programs. (Gwen Valentine) ■

Inhaled Nitric Oxide Therapy and Persistent Pulmonary Hypertension of the Newborn

by Michael E. Lobby

Editor's Note: Michael E. Lobby was the recipient of the ARCF William W. Burgin, Jr. MD Education Recognition Award. He was recognized at the AARC International Respiratory Congress held last November in Atlanta, GA. Michael is a student in the respiratory care program at NMSU Dona Ana Branch Community College in Las Cruces, NM. To obtain information on this and other competitive awards for RC students, contact the American Respiratory Care Foundation at (972) 243-2272.

As a disease without recognizable cause, or as a secondary complication of congenital defect, persistent pulmonary hypertension of the newborn (PPHN) is one of the most common causes of failure of conventional ventilator therapy in neonates. (1) PPHN occurs when the normally high pulmonary artery pressures, typical of the fetal circulatory system, do not decrease after birth and the normal decrease in pulmonary vascular resistance does not occur. (2) Since the discovery more than ten years ago that nitric oxide (NO) is a naturally produced major endothelium derived relaxing factor (EDRF) (3), NO has been studied extensively and thought to be an effective alter-

native to invasive therapies such as extracorporeal membrane oxygenation (ECMO) for the treatment of PPHN. (4) Because ECMO is expensive and invasive and may result in negative long-term neurological effects, NO therapy is proving to be a promising therapy for the treatment of cardiac disease, acute respiratory distress syndrome (ARDS), pulmonary hypertension and PPHN. (5)

Persistent pulmonary hypertension of the newborn

In the most severe cases of PPHN, the result is respiratory failure. Severe PPHN affects approximately 4,500 term infants each year in the United States. When a decrease in the high pulmonary artery pressures and pulmonary vascular resistance typical of in utero fetal circulation does not occur, PPHN may develop. These high pulmonary artery pressures serve to maintain the fetal circulation and continue the right-to-left shunting of blood across the patent ductus arteriosus and foramen ovale. (2) Most infants with PPHN are full term or post mature and have experienced perinatal asphyxia. Other clinical associations include hypothermia, meconium aspiration syndrome (MAS) (6), hyaline membrane disease, polycythemia, neonatal group B streptococcal sepsis (7), chronic intrauterine hypoxia, pulmonary hypoplasia (2), pneumonia, asphyxia, respiratory distress

syndrome, and premature closure of the ductus arteriosus in utero (6).

Physiology

When separating these infants based on developmental stages, they can be divided into three groups: 1) acute vasoconstriction caused by perinatal hypoxia, 2) prenatal increase in pulmonary vascular smooth muscle development, and 3) decreased cross-sectional area of the pulmonary vascular bed caused by inadequate vessel number. In group one, a rapid onset of a perinatal event leads to hypoxia, and pulmonary vascular resistance fails to drop. In the second group, abnormal muscularization of the pulmonary resistance vessels results in PPHN after birth. The third group includes infants with pulmonary hypoplasia (e.g., diaphragmatic hernia). (2) Other causes include bacterial or viral pneumonia, septicemia, meconium aspiration, transient tachypnea with hypoxemia, and intraventricular hemorrhage. (8) PPHN affects term and post-term newborns and is characterized by severe respiratory distress and severe hypoxemia and presents itself with the symptoms of cyanosis and tachypnea a few hours after birth. Right-to-left shunting, secondary to pulmonary hypertension is present. Clinically, the

"Newborn" continued on page 5

"Newborn" continued from page 4

cyanosis and tachypnea are often unresponsive to increases in the Fraction of Inspired Oxygen (FIO₂), respiratory distress persists, and onset is within 24 hours after birth. There is evidence of right ventricular overload, systemic hypotension, and acidosis, and no evidence of structural heart disease. PPHN occurs as a result of the ductus arteriosus and foramen ovale failing to close or reopening after closure. No apparent lung disease is noted. (8)

In fetal circulation, the placenta rather than the fetal lung acts as the organ of gas exchange. The pulmonary blood vessels of the fetus are normally relatively constricted. This constriction causes the majority of the fetal blood volume to bypass the lungs. After birth, this pulmonary vascular resistance (PVR) decreases. This is appropriate for the fetus since PPHN of the newborn is the result of a sustained elevation of the PVR after birth, preventing transition to the normal extrauterine pattern of circulation. When this pulmonary hypertension occurs, causing this increased PVR, hypoxemia further increases PVR and reduces pulmonary blood flow even more. With the resultant hypoxemia, the ductus arteriosus opens, shunting blood from the pulmonary artery to the aorta and resulting in an increased right-to-left shunt. Because of the increased PVR and shunting, pulmonary venous return to the left side of the heart is reduced, reducing the left arterial filling pressure. Heart pressure on the right side exceeds heart pressure on the left side, reopening the foramen ovale and causing right-to-left shunting. Blood gases show severe hypoxemia and acidosis with a normal CO₂ level. (8) This pattern of circulation is referred to as right-to-left shunting because blood is diverted from the venous circulation on the right side of the heart to the arterial circulation on the left side of the heart without going through the pulmonary vascular system. Severe prolonged hypoxemia progresses to hypoxia and results in metabolic acidosis and worsening pulmonary vasoconstriction. (6)

PPHN may be a condition without a clear recognizable cause, due either to abnormal development of pulmonary vessels or a circumstance secondary to the aforementioned clinical associations. Infants with PPHN make up the majority of patients who are treated in some centers with ECMO. In recent years, new modes of treatment have been introduced that are decreasing the need for invasive procedures such as ECMO, most notably inhaled gas nitric oxide (NO), which is very similar to EDRF. NO has been shown to be a very promising and specific pulmonary vasodilator. (9)

Diagnosis

When diagnosing PPHN, it is necessary to differentiate between respiratory distress syndrome, persistent fetal circulation (PFC) or PPHN, and a congenital heart disease. (8) Different methods are used to determine and confirm a diagnosis.

One method is the use of echocardiography findings showing right-to-left shunting of blood across the ductus arteriosus or the foramen ovale, tricuspid regurgitation, and diastolic interventricular septal flattening. Many of the criteria included for the diagnosis and subsequent use of inhaled NO therapy are taken from those defined for the use of ECMO. (1) Some of these criteria include: at least 35 weeks of gestational age, severe hypoxemia despite optimized ventilator therapy and conventional supportive management, PaO₂ < 40 mmHg for > 2 h or PaO₂ < 50 mmHg for > 4 h, and oxygenation index (OI) > 40 for > 1 h. Oxygenation index (OI) = mean airway pressure (cmH₂O) x fractional inspired oxygen x 100/ arterial oxygen tension (mmHg). (1)

Three different tests may be conducted to confirm the diagnosis of PPHN. The first is a hyperoxia test. The infant is placed on 100% oxygen for five to ten minutes, after which time the PaO₂ is determined. If the PaO₂ is more than 100 mmHg, lung disease is present. If the PaO₂ is less than 50 mmHg, a large right-to-left shunt is present or either PFC or cyanotic congenital heart disease is present.

To differentiate PFC or PPHN from other anomalies, the second test is performed: Preductal and postductal arterial blood gas (ABG) comparison. For this test the patient breathes 100% oxygen, and blood gases are obtained from both the preductal arteries (right radial, brachial, and temporal) and the postductal arteries (left radial, posterior tibial, and umbilical). A preductal and postductal PaO₂ difference of more than 15 mmHg is an indication of ductal shunting. A preductal and postductal PaO₂ difference of less than 15 mmHg indicates no significant ductal shunting.

The third test is the hypoxemia-hyperventilation test and is considered the most definitive test to determine PPHN. It may be performed on intubated and nonintubated patients. The patient is hyperventilated with 100% oxygen using an ambu bag. Respiratory rates of 100 to 150 breaths per minute are delivered. During these respirations, the rise and fall of the chest are observed and the breath sounds are auscultated to determine ventilation. If the patient is hyperventilated with 100% oxygen, the PaCO₂ will decrease and the PaO₂ will increase, thus reducing PVR and pulmonary hypertension. If

blood gases show a reduced PaCO₂ (20-25 mmHg) and a significant increase in PaO₂ (more than 100 mmHg) and cyanosis either diminishes or disappears, then PPHN is present. No significant change in the PaO₂ will occur with congenital heart diseases. (8) When these specific criteria are met and tests performed, the diagnosis of persistent pulmonary hypertension can be made.

The next step is the plan of treatment. Depending on the severity of the case, the availability of necessary equipment, and the knowledge of therapy, the use of inhaled NO therapy may be warranted.

Nitric oxide gas

NO is a common air pollutant formed by combining nitrogen and oxygen during a series of high temperature combustion processes. It is produced commercially by the combination of sulfuric acid and sodium nitrite. (10) NO gas is highly diffusible, with a density similar to air. Until recently, NO was known only for its industrial applications. For many years, it has been used as the inert gas in electrical systems (11), in the semiconductor industry, in the production of catalysts, and as an ozone scavenger in welding shield gases. (10) When clinicians first used NO during initial trials, the techniques necessary to produce gas mixtures containing low concentrations were already available.

NO is a nonflammable, colorless gas that will support combustion. As a combustible product it can be present as an environmental pollutant in extremely small concentrations. High concentrations of vapors are a strong irritant to the pulmonary tract. The vapor is highly toxic and hazardous because of its ability to cause delayed pneumonitis and pulmonary edema. Much of the information on NO toxicity has been gained from studies addressing the safety of NO exposure.

In the body, NO is an endogenous vasodilator, produced by endothelium in response to both chemical and physical stimuli. (10) In 1987, NO was discovered to be a major EDRF of the vascular muscles. (1,4,11) The NO molecule is made within the endothelial cell from the amino acid L-arginine through the action of at least three isoforms of the enzyme NO synthase, one of which is endothelial nitric oxide synthase (eNOS). The component part eNOS generates NO continuously and maintains the cardiovascular system in a state of constant active vasodilation. The ensuing activation of its receptor and further enzymatic reactions cause the smooth muscle relaxation.

It is believed that decreased NO generation, caused by a genetic defect or some

"Newborn" continued on page 6

“Newborn” continued from page 5

type of acquired inhibition of the NO synthase or reduced sensitivity of its receptor, plays a major part in the etiology of the various forms of hypertension. (12) Since the discovery of NO to be EDRF, it has been employed in many clinical situations to induce pulmonary vasodilation. The therapeutic goal of most of these situations is to improve pulmonary blood flow and enhance arterial oxygenation; NO offers the unique ability to affect pulmonary circulation without producing adverse systemic effects. (11)

Several clinical studies conducted since NO's discovery as a pulmonary vasodilator have suggested that inhaled NO may be beneficial for patients with a variety of acute or congenital disorders. (13) It has been shown to be effective in the treatment of ARDS (14) and respiratory failure of both the neonatal and pediatric patient (15), the treatment of patients with congenital mitral stenosis (9), and treatment of patients after cardiac surgery with other congenital heart diseases (16,17).

In a study published in the *British Heart Journal* in 1995, researchers showed that inhalation of NO reduced pulmonary artery pressure in children with severe pulmonary hypertension after cardiac surgery, and this effect was maintained over several days at concentrations carrying little risk of toxicity. (18) NO has also been shown to cause a decrease in pulmonary vascular resistance in patients with pulmonary embolism. (19) Inhaled NO, a powerful vasodilator selective for pulmonary vasculature, has been shown to be beneficial in the treatment of PPHN. (20)

Endothelium-Derived Relaxing Factor (EDRF)

The vasoactive substance known as endothelium-derived relaxing factor (EDRF) (4, 21) was recognized and studied as a potent vascular smooth muscle relaxant as early as 1979. (22) EDRF is a potent vasodilator released by normal vascular endothelium. It is released in response to a high blood flow rate and signaling molecules such as acetylcholine and bradykinin (and the vasodilator nitroglycerin). EDRF, which acts via a cyclic GMP second-messenger system, promotes reflex (systemic) and highly localized vasodilation. However, EDRF is quickly destroyed and its potent vasodilator effects are very brief. Until now, it has been accepted that sympathetic nervous system activity “rules” blood vessel diameter. It now appears that EDRF plays a major role in causing vasodilation and when its synthesis is inhibited, blood pressure skyrockets. (21)

In 1987, two separate research teams identified EDRF and NO as being the

same substance. (3, 11) Since that time EDRF has come to be known and discussed using the name NO. (21) NO plays a role in the renin-angiotensin mechanism by acting as an antagonist substance to the potent vasoconstrictor angiotensin II, contributing to renal autoregulation. However, studies have shown that the use of inhaled NO is not related to the formation of transpulmonary angiotensin II, nor does it have a positive effect of inhibiting its formation. (22) A study conducted in 1996 tested the hypothesis that the decrease in pulmonary vascular resistance (PVR) caused by inhaled NO is accompanied by a change in transpulmonary angiotensin II formation in ARDS patients, because NO and the renin-angiotensin system (RAS) are counteracting systems to regulate vascular tone. The study concluded that a decrease in PVR by short-term NO inhalation in ARDS patients was not accompanied by changes in transpulmonary angiotensin II formation. (24)

NO is thought to be a “retrograde messenger” involved in long-term potentiation (learning and memory). It travels back from the post-synaptic neuron to the presynaptic neuron, where it activates guanyl cyclase. Excessive release of NO is responsible for much of the brain damage seen in stroke patients. In the myenteric plexus of the intestine, NO causes relaxation of the intestinal smooth muscle. (21) It also acts synergistically with prostacyclin, a compound formed from the metabolism of arachidonic acid, to inhibit platelet aggregation. (25) Since the discovery that EDRF and NO are identical compounds, they have been the subject of extensive research, revealing their importance in a vast number of physiological functions, such as smooth muscle relaxation, enhancement of bacterial killing, influence on central and autonomic neurotransmission, hormonal release, platelet inhibition, and tumor cell lysis. It has also been demonstrated that NO is an essential link in the transition from fetal circulation to neonatal circulation. (26) It may be that NO is just the first of a soon-to-be discovered class of signaling gases that pass swiftly into cells, where they bind briefly to metal-containing enzymes and then vanish. (21)

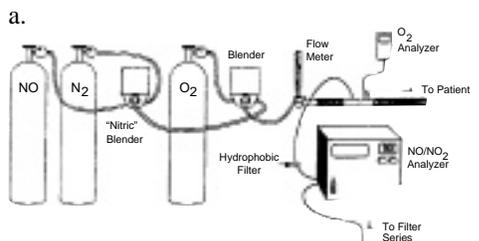
Delivery of Gas

Many systems have been designed to administer NO. (11) NO gas is stored in cylinders containing concentrations of between 500 and 2200 parts per million (ppm) diluted in nitrogen. (1, 7) Delivery of NO gas may take place with the use of pressure ventilators, volume ventilators, or high frequency jet ventilators (4) in a volume preset or time-cycled mode. (9) In neonates, a time-cycled, pressure-limited, continuous flow ventilator may be used. (15) The NO gas mixture is introduced

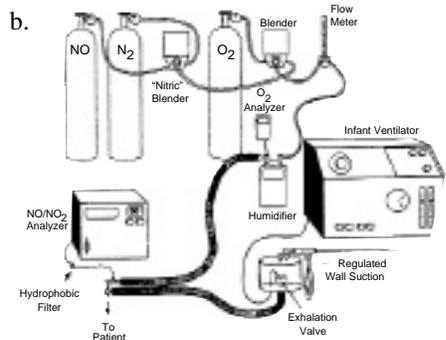
into the inspiratory limb of the ventilator circuit through a calibrated (27) flowmeter, mixing the NO gas with the constant gas flow from the ventilator. In pediatric patients, a volume or pressure controlled ventilator may be used. The NO gas mixture is introduced from the flowmeter into a nebulizer. The nebulizer injects the NO gas into the inspiratory line only within the inspiratory period. (15)

It has also been suggested that administration of inhaled NO is not in and of itself the only treatment for PPHN. Thus, a combination of NO therapy to reduce PVR and the incorporation of high frequency oscillatory ventilation (HFOV) will be most beneficial. HFOV allows for effective alveolar ventilation and recruitment while reducing the potential parenchymal and airway injury associated with large phasic pressure and lung volume changes. (22) In patients with severe PPHN and parenchymal lung disease or pulmonary hypoplasia, optimal management may include HFOV to recruit and maintain lung volume, thus promoting effective delivery of the inhalational vasodilator NO. (22)

Figure 1.



a.) The basic NO delivery system, using a double blender technique and chemiluminescence analysis.



b.) The patient requiring a time-cycled, pressure-limited infant ventilator. Currently, the use of a low flowmeter attached to the NO source tank permits the elimination of the nitrogen tank and one blender, simplifying the delivery of nitric oxide with continuous flow infant ventilators. (23)

Studies performed to determine the proper dilution and dose-response have

“Newborn” continued on page 7

"Newborn" continued from page 6

concluded that inhaled NO will reduce pulmonary artery pressure in doses from 0.1 to 100 ppm. Changes in pulmonary artery pressures in some patients have been recorded with doses as low as 0.06 ppm. (10) It is important to note that the optimum dosage is unknown. The dosage of NO should gradually be increased from a low dose to 80 ppm (in 10 ppm increments at 15 minute intervals) in order to determine the individual optimum effective level. (1) The acute physiological responses to inhaled NO may disappear at higher concentrations (= or > 80 ppm), presumably because the selective pulmonary vascular vasodilation is lost since vasodilation occurs in poorly ventilated areas of the lung. (5) The improvement in oxygenation occurs at lower doses, with maximum effects set between 8 and 10 ppm, and measurable effects as low as 0.01 ppm. In higher doses NO reverses bronchoconstriction in animals, but 20-39 ppm has been shown to increase airway resistance in humans. (10)

Studies have shown that brief (30 minutes) inhalation of NO at 80 ppm improved oxygenation in patients with PPHN, but this response was sustained in only one patient after NO was discontinued. In another report, rapid improvement in oxygenation in neonates with severe PPHN was demonstrated with the use of doses of 20 ppm NO for 4 hours, after which the dose was decreased to 6 ppm for the duration of the treatment; this strategy resulted in sustained improvement in oxygenation. In a subsequent study, this low-dose NO strategy was used in an additional nine patients with severe PPHN, including two patients with congenital diaphragmatic hernia. The management incorporated the use of HFOV to achieve optimal lung inflation during the use of NO. Eight patients had resolution of the underlying PPHN. (22) The required flow of nitric oxide mixture can be calculated using the following formula:

Nitric oxide mixture flow rate (V_{mix}) = $V / (F_{mixNO}/F_{INO}) - 1$

where: V is the flow rate of the gas stream to which the NO mixture is added (this would be the fresh gas flow on an anesthetic machine, the gas flow around the circuit on a pediatric ventilator, or the minute ventilation on an adult ventilator); F_{mixNO} is the concentration of NO in the nitric oxide/nitrogen mix; F_{INO} is the desired final inspired nitric oxide concentration. (10)

Monitoring

Oxygen saturation (SpO_2) and systemic arterial blood pressures should be monitored continuously and arterial blood gas tensions controlled at 15 minute intervals. (1) The level of methemoglobin is usually

measured after 30 minutes and then two to four hours after initiation of treatment gas and twice daily while receiving treatment gas. (5) The inspired NO and nitrogen dioxide levels should be monitored during NO administration. Continuous NO analyzers fall into three main categories: chemiluminescence analyzers, electrochemical cells, and spectrophotometric gas detectors. All NO and nitrogen dioxide analyzers need calibrating. (10)

Toxicity

There are only a few studies on the toxicity of inhaled NO. (28) Conversion of NO to nitrogen dioxide (NO_2) is a result of NO dose, FiO_2 , dwell time, and temperature. The byproduct of this process is potentially more toxic than NO and can cause epithelial injury as well as airway hyperactivity. Monitoring NO and NO_2 accurately is essential not only for the safety of the patient, but for the safety of the bedside caregivers. (4) Two concerns are the possible development of methemoglobinemia and pulmonary tissue toxicity. (22)

Pulmonary tissue toxicity is the most common toxic effect and results when NO combines with oxygen and forms the reddish brown gas nitrogen dioxide. When NO_2 is exposed to NO, dinitrogen trioxide is produced and reacts with water, forming either nitrous or nitric acid, both of which are very toxic to the alveolar epithelium. The higher the concentration of oxygen, the greater the potential for developing toxic levels of nitrogen dioxide. (11) These possible effects underscore the importance of monitoring the inhaled gas mixture. Close monitoring is essential to control the therapeutic level of NO while avoiding excessive levels of nitrogen dioxide. (11)

Methemoglobinemia develops primarily through the oxidation of NO when it comes in contact with oxyhemoglobin. Methemoglobin occurs naturally and its level is normally maintained in part by the enzyme methemoglobin reductase. This enzyme, which is found largely in red blood cells, converts methemoglobin to hemoglobin. Methemoglobinemia is the clinical condition in which more than 1% of hemoglobin in blood has been oxidized to the ferric (Fe^{+++}) form. The principle sign is cyanosis because the oxidized hemoglobin is incapable of transporting oxygen. (23) Clinical trials involving human subjects reveal that the rate of methemoglobin formation rarely exceeds the ability of the reductase to convert it, so methemoglobin levels usually stay below 2%. (28)

Discussion

Since it was discovered that endothelium derived relaxing factor is nitric oxide and that this easily diffusible gas has a potent pulmonary vasodilator effect,

numerous studies have shown the benefits of inhalation NO therapy for the treatment of persistent pulmonary hypertension of the newborn. Since PPHN is one of the most common causes of failure of conventional ventilator therapy in neonates, the use of NO therapy may be a very promising and effective alternative treatment for PPHN. One of the most beneficial and cost-effective advantages has been the avoidance of such invasive and expensive treatments as ECMO. Inhaled NO has substantial beneficial effects on pulmonary gas exchange and helps to stabilize the cardiocirculatory status of the neonate. (15) Because of the specific reaction of NO on pulmonary vascular resistance and little or no systemic effects, NO has become the preferred treatment to conventional intravenous administration of vasodilators. (19) The further study of NO therapy and FDA approval for more common use of this promising treatment will afford the respiratory therapist a unique opportunity to make great advances in this technology.

References

1. Muller W, Kachel W, Lasch P, Varnholt V, Konig SA. Inhaled nitric oxide for the avoidance of extracorporeal membrane oxygenation in the treatment of severe persistent pulmonary hypertension of the newborn. *Intensive Care Med* 1996;22:71-76.
2. Fuchs F, Hays PM, Petrie RH, eds. *Obstetrics: normal and problem pregnancies*. New York: Churchill Livingstone, 1996:663.
3. Max M, Reyle-Hahn M, Kuhlen R, Dembinski R, Rossaint E. Nitric oxide-is there a future?. *Acta Anaesthesiol Scand Suppl* 1997;111:64-68.
4. Schmidt JM. Nitric oxide therapy in neonates: adding to the arsenal. *Journal for Respiratory Care Practitioners* 1994;4:37-42.
5. Dellinger RP, Zimmerman JL, Taylor RW, et al. Effects of inhaled nitric oxide in patients with acute respiratory distress syndrome: Results of a randomized phase II trial. *Crit Care Med* 1998;26:15-23.
6. Creehan PA, Simpson KR. *Perinatal NursinR*. Philadelphia:Lippincott, 1996:358-359.
7. Zapol WM, Rimar S, Gillis N, Marletta M, Bosken CH. Nitric oxide and the lung. *Am J Respir Crit Care Med* 1994;149:1375-1380.
8. Dimas S, Kacmarek RM, Mack CW. *The Essentials of Respiratory Care*. St. Louis: Mosby, 1990:368-370
9. Atz AM, Adatia I, Jonas RA, Wessel DL. Inhaled nitric oxide in children with pulmonary hypertension and congenital mitral stenosis. *Am J Cardiol* 1996;77:316-3~9.
10. Young TD, Dyar OT. Delivery and monitoring of inhaled nitric oxide. *Intensive Care Med* 1996;22:77-85.
11. Pilbeam SP. *Mechanical Ventilation: physiological and clinical applications* St.

"Newborn" continued on page 8

"Newborn" continued from page 7

Louis: Mosby, 1998:375-376.

12. Goonasekera CD, Shah V, Rees DD, Dillon MJ. Nitric oxide activity in childhood hypertension. Arch Dis Child 1997;77:11-16.

13. Berner M, Beghetti M, Spahr-Schopfer I, Oberhansli I, Friedli B. Inhaled nitric oxide to test the vasodilator capacity of the pulmonary vascular bed in children with long-standing pulmonary hypertension and congenital heart disease. Am J Cardiol 1996;77:532-535.

14. Matthay MA, Pittet JF, Jayr C. Just say NO to inhaled nitric oxide for the acute respiratory distress syndrome. (editorial). Crit Care Med 1998;26:1-2.

15. Demirakca S, Dotsch J, Knothe C, et al. Inhaled nitric oxide in neonatal and pediatric acute respiratory distress syndrome: Dose response, prolonged inhalation, and weaning. Crit Care Med 1996;24:1913-1919.

16. Schulze-Neick I, Bultmann M, Werner H, et al. Right ventricular function in patients with inhaled nitric oxide after cardiac surgery for congenital heart disease in newborns and children. Am J Cardiol 1997;80:360-363.

17. Roberts TD, Lang P, Bigatello LM, Vlahakes GT, Zapol WM. Inhaled nitric oxide in congenital heart disease. Circulation 1993;87:447-453.

18. Beghetti M, Habre W, Friedli B, Berner M. Continuous low dose inhaled nitric oxide for treatment of severe pulmonary hypertension after cardiac surgery in paediatric patients. Br Heart J 1995;73:65-68.

19. Capellier G, Jacques T, Balvay P, et al. Inhaled nitric oxide in patients with pulmonary embolism. Intensive Care Med 1997;23:1089-1092.

20. Allman KG, Young JD, Stevens JE, Archer LN. Nitric oxide treatment for fulminant pulmonary hypertension. Archives of Disease in Childhood 1993;69:449-450.

21. Marieb EN. Human Anatomy and Physiology Redwood City: Benjamin-Cummings, 1995:657.

22. Kinsella JP, Abman SH. Recent developments in the pathophysiology and treatment of persistent pulmonary hypertension of the newborn J Pediatr 1995;126:853-861.

23. Wessel DL, Adatia I, Thompson JE, Hickey PR. Delivery and monitoring of inhaled nitric oxide in patients with pul-

monary hypertension. Crit Care Med 1994;22:930-938.

24. Wenz M, Steinau R, Gerlach H, Lange M, Kaczmarczyk G. Inhaled nitric oxide does not change transpulmonary angiotensin II formation in patients with acute respiratory distress syndrome Chest 1997;112:478-483.

25. Thomas CL., ed. Taber's Cyclopedic Medical Dictionary. Philadelphia: F.A. Davis, 1993.

26. Abman SH, Chatfield BA, Hall SL, McMurtry IF. Role of EDRF during transition of pulmonary circulation at birth. Am J Physiol 1990; 259:1921-1927.

27. Goldman AP, Tasker RC, Hosiasson S, Henrichsen T, Macrae DJ. Early response to inhaled nitric oxide and its relationship to outcome in children with severe hypoxemic respiratory failure. Chest 1997;112:752-758.

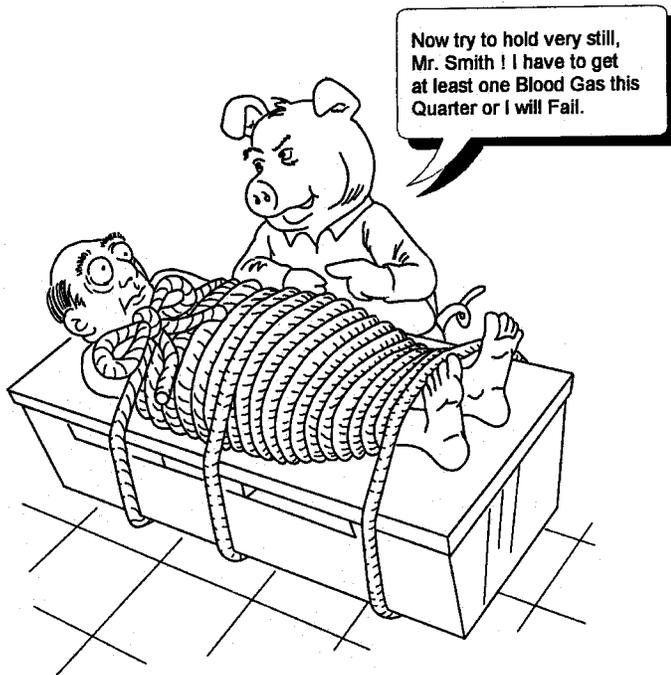
28. Wessel DL, Adatia I, Gigilia TM, et al. Inhaled nitric oxide and acetylcholine in the evaluation of pulmonary hypertension and endothelial function after cardiopulmonary bypass. Circulation 1993;88A:2128. ■

Hot List Topics: AARC Times Wants Your Input

AARC Times is looking for clinical topics to feature during 1999 and is asking the members of our section to help come up with a "hot list." What are the key issues that we would like to see fea-

tured in the magazine over the coming year? Please take a minute to jot down the topics you would most like to read about in '99 and e-mail them to AARC Times Editor Marsha Cathcart at cath-

cart@aacr.org. If you would like to write on one of those topics, please let Marsha know and she'll get back to you with the details regarding article submission. ■



Summer 1998

This cartoon is reprinted with permission from the Summer 1998 issue of *The Airway*, the official newsletter of the Alabama Society for Respiratory Care.

7th International Conference

Noninvasive Ventilation Across the Spectrum from Critical Care to Home Care

March 14 - 17, 1999
Orlando, Florida

Comprehensive Program Features:

- Spectacular Educational Exhibits
- International Faculty
- Presentations on key aspects of noninvasive ventilation

For registration information call American College of Chest Physicians at 800-343-2227 or visit www.chestnet.org/education/courses/noninvasive. Registration Deadline is March 1.

Sponsored by AARC & ACCP