



eNeonatal Review

supported by an unrestricted educational grant from Forest Pharmaceuticals, Inc.

COURSE DIRECTORS

Edward E. Lawson, M.D.

Professor
Department of Pediatrics – Neonatology
The Johns Hopkins University School of Medicine

Lawrence M. Noguee, M.D.

Associate Professor
Department of Pediatrics – Neonatology
The Johns Hopkins University School of Medicine

Christoph U. Lehmann, M.D.

Assistant Professor
Department of Pediatrics – Neonatology
The Johns Hopkins University School of Medicine

Lorraine A. Harbold, R.N., M.S.

The Johns Hopkins Hospital;
NICU Education Coordinator

PROGRAM INFORMATION

CE Info

[Accreditation](#)

[Credit Designation](#)

[Target Audience](#)

[Learning Objectives](#)

[Faculty Disclosure](#)

[Disclaimers](#)

LENGTH OF ACTIVITY

0.5 hours

EXPIRATION DATE

February 16, 2005

NEXT ISSUE

March 16, 2004

[Recommend to a Colleague](#)

[Post-Test](#)

In this issue... Volume 1, Number 6

This month's topic is persistent pulmonary hypertension of the newborn (PPHN).

PPHN is the name given to a clinical state in the newborn characterized by failure to initiate, or to sustain, the pulmonary vascular relaxation that normally occurs after birth.

PPHN can be associated with a variety of neonatal diseases, including perinatal asphyxia, meconium aspiration syndrome (MAS), Group B Streptococcal (GBS) sepsis, and pulmonary hypoplasia. Many cases are characterized as "idiopathic", although the majority of these are thought to be due either to chronic intrauterine hypoxia or antenatal constriction of the ductus arteriosus.

PPHN leads to impaired oxygenation of varying degrees. In the most severe cases, neonates remain dangerously hypoxemic on maximal ventilatory supports, including high frequency ventilation. Extracorporeal membrane oxygenation (ECMO) was developed for these neonates with severe PPHN, but is expensive, highly invasive, and depending on the underlying disease, unsuccessful in more than 20% of cases.

While a variety of therapies, most of which have not been subjected to randomized controlled trials, have been employed for this disorder, optimal management remains controversial. Although inhaled nitric oxide (iNO) has recently been approved for treatment of PPHN, there have been concerns about the safety of this highly reactive gas. However, recent follow-up studies have reassured us that iNO does not appear to be associated with adverse long-term outcome (1,2). Unfortunately, iNO is unsuccessful in as many as 40% of infants with severe PPHN; thus, therapeutic alternatives, as reviewed here, are actively being investigated.

Reviews

Peter F. Resnick, MD

Guest Editors of the Month

Commentary

James J. Cummings, MD

- [Commentary](#)
Our guest editor opinion
- [GBS-INDUCED PPHN](#)
- [GBS-INDUCED PPHN: NEW INSIGHTS](#)
- [SUPEROXIDE DISMUTASE](#)
- [STERIODS AND MAS](#)
- [ALVEOLAR CAPILLARY DYSPLASIA](#)
- [NSAID EXPOSURE IN UTERO](#)
- [REFERENCES AND ADDITIONAL SOURCES OF INFORMATION](#)

James J. Cummings, MD
Professor of Pediatrics and
Physiology
Brody School of Medicine at East
Carolina University
Greenville, North Carolina



Peter F. Resnick, MD
Fellow in Neonatal-Perinatal
Medicine
Brody School of Medicine at East
Carolina University
Greenville, North Carolina



Guest Faculty Disclosures

James J. Cummings, MD

Faculty Disclosure: No relationship with commercial supporters

Peter F. Resnick, MD

Faculty Disclosure: No relationship with commercial supporters

Unlabelled/Unapproved Uses

Dr. Cummings and Dr. Resnick both have reported that they discuss the unlabeled use of Recombinant human superoxide dismutase in this activity.

COMMENTARY

Since this forum is intended for those involved in the day-to-day care of critically ill neonates, we have chosen for review some recent studies in newborn infants and animal models which have implications for the management of PPHN. At the same time, these studies also provide much valuable insight into both the pathophysiology of the disorder, and the physiology of the neonatal pulmonary circulation in general. One point strongly underscored is that PPHN is not a singular pathophysiologic response to a variety of physiologic insults, but instead represents a set of biologic responses that vary according to the underlying disease. While these responses are only partly understood, they do share a final common pathway, namely insufficient alveolar capillary perfusion.

Three of the articles (Kelly, Ambalavanan, and Steinhorn) highlight the fact that pulmonary vascular resistance, and hence pulmonary blood flow and capillary perfusion, is controlled by a complex network of mediators — some acting in concert, others in opposition, and still others in a parallel (though independent) fashion. While the endogenous nitric oxide/cyclic GMP (cGMP) pathway clearly plays a role in PPHN, other, non cGMP-mediated pathways appear to be equally — and perhaps even more — important in certain disease states.

For example, in their piglet model, Ambalavanan et al found that while both endogenous nitric oxide and endothelin-A modulated hypoxia-induced PPHN, neither decreased nitric oxide production nor increased endothelin-A activity could explain GBS-induced pulmonary vascular resistance. In fact, ET-A blockade with BQ 610 actually worsened GBS-induced PPHN.

In addition, the report by da Costa et al of dexamethasone treatment of infants with MAS and severe PPHN (without resorting to nitric oxide or ECMO) reminds us that PPHN is usually a secondary complication, not a primary disease, and that attention to the underlying disease may be as important as therapies aimed at improving pulmonary perfusion.

Although we are accustomed to treating PPHN as a perinatally acquired disorder, there are clearly

cases of fetal origin, either due to maldevelopment of the pulmonary vasculature or vascular remodeling due to either chronic hypoxia or ductal constriction in utero. The articles on alveolar capillary dysplasia (Tibballs & Chow), and on non-steroidal anti-inflammatory drugs in meconium (Alano) suggest that fetal origins of PPHN may be much more common than previously thought, and have clear implications for clinical practice.

Specifically:

- In cases of pulmonary vascular maldevelopment such as alveolar capillary dysplasia (or underdevelopment such as pulmonary hypoplasia), PPHN may be irreversible. Consequently, since PPHN is a disorder which can expend more resources on a daily basis than any other neonatal disease or condition, we must find ways to promptly identify those situations in which our efforts will likely prove to be futile.
- In cases of pulmonary vascular remodeling due to ductal constriction in utero, while PPHN may be reversible, it may take weeks to months to resolve. In these circumstances, we must find alternatives to iNO that are less expensive and less potentially toxic, so that they may be administered safely and cost-effectively over a prolonged period of time.

The diversity of underlying causes of PPHN and our expanding knowledge about the various ways in which pulmonary vascular resistance can be modulated have resulted in a plethora of anecdotal, unproven therapies. Reflecting on the success of iNO in treating many infants with PPHN, it is clear that future advances in treating this difficult disorder can only be achieved if we couple our clinical and laboratory observations with well-designed, prospective, randomized trials. Further, as we continue to unravel the intricacies of neonatal pulmonary vascular regulation, we must remind ourselves that each case of PPHN represents a unique clinical challenge, and that for our therapy to be successful, it must be tailored not only to improving alveolar perfusion, but also to treating the underlying disease as well.

INHALED PROSTACYCLIN

Kelly LK, Porta NFM, Goodman DM, Carroll CL, Steinhorn, RH. Inhaled prostacyclin for term infants with persistent pulmonary hypertension refractory to inhaled nitric oxide. *The Journal of Pediatrics* 2002; 141:830-32.

Four infants with severe PPHN unresponsive to inhaled nitric oxide show improvement with inhaled prostacyclin.

Investigators from Northwestern University Medical School in Chicago present four term infants transferred to their NICU for consideration of ECMO due to severe, refractory PPHN. Three infants were diagnosed with meconium aspiration syndrome (MAS) and one had idiopathic PPHN. ECMO was felt to be contraindicated in two of the four infants; one because of probable irreversible lung injury due to prolonged mechanical ventilation and the other because of a subdural hematoma. Therapy at their referral center included high-frequency ventilation, initiation or continuation of inhaled nitric oxide (iNO), and medical inotropic support; all three patients with MAS also received surfactant. Despite aggressive therapy, all four infants had persistent hypoxemia with a mean oxygenation index (OI) of 29 ± 5 (range, 24 to 36).

The intravenous form of prostacyclin (PGI_2) was aerosolized in an alkaline solution and delivered by continuous nebulization through the respiratory circuit. Age at initiation of PGI_2 ranged from 1 day old to 16 days old and was preceded with iNO for at least 3 hours (range 3hr to 14 days). Within 1 hour of initiation of PGI_2 , mean PaO_2 increased from 57 to 100 ($p = 0.06$) and within 2 hours, mean OI decreased from 29 to 19 ($p < 0.05$). The one infant with idiopathic PPHN had only transient improvement in oxygenation and died 6 days later; this infant was subsequently diagnosed with alveolar capillary dysplasia. The three remaining infants continued to improve, were extubated within 3 weeks of initiating PGI_2 , and were discharged on room air.

It is generally agreed that the mechanism of action of iNO is induction of soluble guanylate cyclase in pulmonary vascular smooth muscle. This promotes the synthesis of cyclic GMP (cGMP) which causes local smooth muscle relaxation and thus pulmonary vasodilation.

Prostacyclin, in contrast, acts by way of a cAMP pathway. Although PGI_2 has been shown by others to improve oxygenation and reduce pulmonary vasoconstriction in neonates with PPHN, it had not

yet been studied in infants refractory to iNO. The authors note that the beneficial effects of PGI₂ may have been enhanced by the concomitant use of milrinone in some of their infants. A potent inotrope, milrinone is known to act as a specific type 3 phosphodiesterase inhibitor, and therefore would attenuate the normal conversion of cAMP by phosphodiesterase.

The authors propose that infants unresponsive to iNO may have impaired cGMP-mediated pulmonary vasodilation, and that by treatment through a non-cGMP mediated pathway PGI₂ may be of benefit in infants with PPHN who fail to respond to iNO.

(For non-journal subscribers, an additional fee may apply for full text article)



[view journal abstract](#)



[view full article](#)

[↑ back to top](#)

GBS-INDUCED PPHN

Ambalavanan N, Philips JB III, Bulger A, Oparil S, Chen Y-F. Endothelin-A receptor blockage in porcine pulmonary hypertension. *Pediatric Research* 2002; 52:913-921.

In this animal model, pulmonary hypertension induced by hypoxia was responsive to ETA-blockers while pulmonary hypertension induced by GBS was unresponsive.

Endothelin-1 (ET-1) causes vasoconstriction in the pulmonary arteries by activation of Endothelin-A (ET_A) receptors. ET-1 has been found to be elevated in neonates with pulmonary hypertension and is considered a marker of disease severity. ET-1 is felt to play a role in the pathogenesis of PPHN caused by hypoxia or meconium aspiration, while thromboxane appears to mediate pulmonary hypertension caused by Group B Streptococcal (GBS) sepsis. In this study, the authors compared the effects of ET_A receptor blockade in piglets with either hypoxia-induced or GBS-induced pulmonary hypertension.

Pulmonary hypertension was induced by one of two methods: in one group animals were intubated and made hypoxic by breathing a 10% oxygen/nitrogen mixture; in the second group animals were given an infusion of heat-killed GBS bacteria. Within each group, half the animals received the ET_A blocker EMD 122946 and the other half received the ET_A blocker BQ 610, both intravenously. Once PPHN was induced, both groups were then treated with inhaled nitric oxide (iNO).

In piglets with hypoxia-induced pulmonary hypertension, pulmonary artery pressure and pulmonary vascular resistance dropped significantly in response to both ET_A blockers. By contrast, those with GBS-induced pulmonary hypertension showed no significant decrease in pulmonary artery pressure or pulmonary vascular resistance in response to either ET_A blocker; in fact, the pulmonary vascular resistance increased significantly when BQ 610 was given to the GBS-infused piglets. There were no changes in either systemic blood pressure or peripheral vascular resistance in any of the four subgroups.

A separate group of animals were pre-treated with the NO synthase blocker L-NAME, to induce pulmonary hypertension by blocking endogenous NO production. Subsequent treatment with GBS, but not hypoxia, worsened measures of PPHN, suggesting that GBS caused PPHN by means other than reduction in endogenous nitric oxide.

(For non-journal subscribers, an additional fee may apply for full text article)



[view journal abstract](#)



[view full article](#)

[↑ back to top](#)

SUPEROXIDE DISMUTASE

Steinhorn RH, Albert G, Swartz DD, Russell JA, Levine CR, David JM. Recombinant human superoxide dismutase enhances the effect of inhaled nitric oxide in persistent pulmonary hypertension. *American Journal of Respiratory and Critical Care Medicine* 2001; 164:834-839.

In this animal model of PPHN, SOD was given with iNO and resulted in significantly lower pulmonary artery pressures and pulmonary vascular resistance than with iNO alone.

The use of inhaled nitric oxide (iNO) in a high oxygen environment (such as in the treatment of PPHN) generates potentially harmful free radicals, including oxygen radicals such as superoxide and NO radicals such as peroxynitrite (ONOO⁻). Superoxide dismutase (SOD) is a superoxide scavenger. It has been shown that pretreatment with recombinant human superoxide dismutase (rhSOD) reduces inflammatory changes and lung injury caused by prolonged exposure to high concentrations of iNO and oxygen.

Using a well-described animal model of pulmonary hypertension, fetal lambs had surgical closure of the ductus arteriosus nine days prior to preterm operative delivery.

In the *in vitro* portion of the study, several lambs were sacrificed immediately at delivery, and fifth generation pulmonary arteries were isolated from their lungs. Some vessels were then exposed to the NO donor S-nitrosyl-acetylpenicillamine (SNAP) while others were first pre-treated with rhSOD. In the group pretreated with SOD, the relaxation induced by SNAP was found to be significantly greater than with SNAP alone. Pre-treatment with catalase, to inhibit hydrogen peroxide production, did not alter these findings - suggesting that the effect of rhSOD on enhancing pulmonary vasodilatation was not mediated by hydrogen peroxide.

In an *in vivo* part of the study, several fetuses were delivered with the placental circulation intact to allow for placement of an endotracheal tube and catheters for hemodynamic measurement prior spontaneous breathing. The umbilical cord was then ligated and the lambs were placed on mechanical ventilation with 95% oxygen. Three groups were studied: one pre-treated with rhSOD (by intratracheal bolus) alone, a second receiving iNO (5 ppm and 80 ppm) alone, and the third receiving both rhSOD with iNO. Interestingly, rhSOD alone significantly reduced pulmonary artery pressures versus those who received no treatment at all. While iNO at 5 ppm alone significantly reduced pulmonary artery pressure and pulmonary vascular resistance, pre-treatment with rhSOD significantly enhanced these responses.

The authors postulate that by scavenging superoxide and decreasing the formation of peroxynitrite, SOD may enhance the bioavailability of both endogenous and exogenous NO. In the clinical setting, SOD may improve the safety of iNO when given with high inspired oxygen concentrations, as in neonates with severe PPHN.

(For non-journal subscribers, an additional fee may apply for full text article)



[view journal abstract](#)



[view full article](#)

[↑ back to top](#)

STERIODS AND MAS

Da Costa DE, Nair AK, Pai MG, Al Khusaiby SM. Steroids in full term infants with respiratory failure and pulmonary hypertension due to meconium aspiration syndrome. *European Journal of Pediatrics* 2001; 160:150-153.

In a center with no access to inhaled nitric oxide or ECMO, 14 patients with MAS and severe PPHN not responding to conventional therapy were treated with dexamethasone and most showed prompt improvement

Although extracorporeal membrane oxygenation (ECMO) and inhaled nitric oxide (iNO) have been shown to be beneficial in patients with PPHN, these techniques are very expensive and not readily available in all tertiary centers. The authors report on their 3-year experience treating meconium aspiration syndrome (MAS) with dexamethasone at the Royal Hospital in the Sultanate of Oman, where ECMO and iNO are not available. The rationale is that meconium aspiration is known to cause an intense pulmonary inflammatory response in part mediated by cytokines, and that steroids not only suppress the production of some of these cytokines but also suppress the formation of potent pulmonary vasoconstrictors such as thromboxane and PGF₂.

Term infants with MAS and PPHN were included in the study, while infants with suspected or proven infection were excluded. Of 14 eligible infants, all had an oxygenation index (OI) of >25. Adjunctive therapies included surfactant (10), high frequency ventilation (4) and magnesium sulfate (2). Infants were given a nine-day tapered course of dexamethasone intravenously starting with 0.5 mg/kg/day between 48-96 hours of age.

The average OI (determined every 8 hours) in their study population decreased significantly, from

27 to less than 20 by eight hours post-dexamethasone and continued to drop during the subsequent thirty-two hours. One infant developed septicemia and one developed bacterial pneumonia. Thirteen of the 14 infants recovered and only 1 died.

The authors noted that in the two years preceding this study, of 19 infants at their center with severe PPHN and OI >25, 10 went on to an OI > 35 and 8 of these infants died.

(For non-journal subscribers, an additional fee may apply for full text article)



[view journal abstract](#)



[view full article](#)

[↑ back to top](#)

ALVEOLAR CAPILLARY DYSPLASIA

Tibballs J & Chow CW. Incidence of alveolar capillary dysplasia in severe idiopathic persistent pulmonary hypertension of the newborn. *Journal of Pediatrics and Child Health* 2002; 38:397-400.

An 18-year record review in Australia shows that six of the seven infants who died with severe idiopathic PPHN were diagnosed with ACD post-mortem.

Alveolar capillary dysplasia (ACD) is a congenital condition characterized clinically by severe idiopathic PPHN, and histologically by misalignment of pulmonary vessels, absence of capillaries in contact with alveolar epithelium, thickened medial muscle in small pulmonary arteries, muscularization of the smallest intraacinar arterioles, and thickened alveolar walls. The diagnosis is generally made at autopsy, although (less reliably) lung biopsy can also identify these patients while alive. Infants with this condition rapidly succumb to progressive, unremitting hypoxemic respiratory failure.

Until recently, ACD was felt to be an extremely rare disorder, but increasing numbers of cases have been reported in the literature. The authors sought to determine the incidence of ACD in infants treated at their institution for severe, idiopathic PPHN.

By way of record review from 1982 to 2000, all newborns with the diagnosis of PPHN at Royal Children's Hospital in Victoria, Australia, were identified. Diagnosis was made based on clinical and echocardiographic findings. Patients with a presumed cause for their PPHN were excluded; these causes included those with perinatal asphyxia, congenital heart disease, meconium aspiration, congenital diaphragmatic hernia, pulmonary hypoplasia, hyaline membrane disease, GBS or other sepsis, and ductal closure secondary to maternal drug therapy.

During that 18-year record review period, the investigators identified 13 infants with severe, idiopathic PPHN. Of these, six died in the neonatal period and seven survived. All six infants with idiopathic PPHN who died during the neonatal period were found to have ACD at autopsy. In addition, one infant died at 3 months of age of a pulmonary hypertensive crisis; however, autopsy did not reveal ACD.

The authors conclude that, when faced with an infant with severe idiopathic PPHN who is recalcitrant to medical therapy, the diagnosis of ACD should be seriously entertained and that an open lung biopsy should be considered.

(For non-journal subscribers, an additional fee may apply for full text article)



[view journal abstract](#)



[view full article](#)

[↑ back to top](#)

NSAID EXPOSURE IN UTERO

Alano MA, Ngougma E, Ostrea EM Jr., Konduri GG. Analysis of nonsteroidal antiinflammatory drugs in meconium and its relation to persistent pulmonary hypertension of the newborn. *Pediatrics* 2001; 107:519-523.

By way of meconium analysis, investigators: a) show that NSAID use during pregnancy is significantly underreported, and b) identify which NSAIDs are associated with the development of PPHN.

The use of nonsteroidal antiinflammatory drugs (NSAIDs) during pregnancy has been shown to be associated with the development of persistent pulmonary hypertension of the newborn

(PPHN). Prostaglandins and thromboxane are involved in pulmonary vascular regulation and in maintaining ductal patency. NSAIDs are cyclooxygenase inhibitors that block the synthesis of prostaglandins and thromboxane. Antenatal exposure to NSAIDs has been shown in animal studies to produce ductal constriction, and to increase both pulmonary artery smooth muscle thickness and pulmonary artery hypertension.

Meconium was collected from infants cared for at 2 hospitals in Michigan during a 20-month period and analyzed with gas chromatography and mass spectrometry. The study included 40 newborns with clinical and echocardiographic evidence of PPHN. Twenty-five percent of the cases of PPHN were idiopathic, 35% were associated with meconium aspiration, 20% with respiratory distress syndrome (RDS), and 7.5% with Group B streptococcal sepsis or pneumonia. A control group consisted of 61 randomly selected infants with an uncomplicated neonatal course.

While the authors found that 50% of all the samples (both control and PPHN groups) were positive for any NSAID, these findings were in sharp contrast to the reported maternal history. Specifically:

MECONIUM FINDINGS POSITIVE FOR:	%	MATERNAL HISTORY REPORTED USE:	%
ASPIRIN	44%	ASPIRIN	1%
IBUPROFEN	23%	IBUPROFEN	13%
NAPROXEN	19%	NAPROXEN	12%
INDOMETHACIN	8%	INDOMETHACIN	2%

In infants with PPHN, 88% showed at least one NSAID in the meconium versus 25% in the control group ($p=0.001$). The authors concluded that maternal reporting grossly underestimates the true fetal exposure to NSAIDs, which in turn may be a much more common cause of idiopathic PPHN than previously thought.

(For non-journal subscribers, an additional fee may apply for full text article)

 [view journal abstract](#)

 [view full article](#)

[↑ back to top](#)

REFERENCES AND ADDITIONAL SOURCES OF INFORMATION:

References:

1. Lipkin PH, Davidson D, Spivak L, et al. Neurodevelopmental and medical outcomes of persistent pulmonary hypertension in term newborns treated with nitric oxide. *J Pediatr* 2002; 140:306-10.

(For non-journal subscribers, an additional fee may apply for full text article)

 [view journal abstract](#)

 [view full article](#)

[↑ back to top](#)

2. Clark RH, Huckaby JL, Kueser TJ, et al. Low-dose nitric oxide therapy for persistent pulmonary hypertension: 1-year follow-up. *J Perinatol* 2003; 23: 300-3.

(For non-journal subscribers, an additional fee may apply for full text article)

 [view journal abstract](#)

 [view full article](#)

[↑ back to top](#)

Additional Reading:

1. Walsh MC and Stork EK. Persistent pulmonary hypertension of the newborn: rational therapy based on pathophysiology. Clin Perinatol 2001; 28(3):609-27.

(For non-journal subscribers, an additional fee may apply for full text article)

 [view journal abstract](#)

[↑ back to top](#)

2. Weinberger B, Weiss K, Heck DE, et al. Pharmacologic therapy of persistent pulmonary hypertension of the newborn. Pharm Ther 2001; 89:67-79.

(For non-journal subscribers, an additional fee may apply for full text article)

 [view journal abstract](#)

 [view full article](#)

[↑ back to top](#)

3. Rosenberg AA. Outcome in term infants treated with inhaled nitric oxide. J Pediatr 2002; 140:284-7.

(For non-journal subscribers, an additional fee may apply for full text article)

 [view journal abstract](#)

 [view full article](#)

[↑ back to top](#)

4. Rabinovitch M. Developmental biology of the pulmonary vasculature. In Fetal and Neonatal Physiology (Polin RA, Fox WW, and Abman SH, eds.), 3rd edition, Saunders, Philadelphia, 2004, p 690-701.

 [link to publisher](#)

[↑ back to top](#)

[Click here to go to the Post-Test and receive CE credit](#)

[Recommend eNeonatal Review to a colleague](#)

Accreditation [back to top](#)

Physicians

The Johns Hopkins University School of Medicine is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Nurses

The Institute for Johns Hopkins Nursing is accredited as a provider of continuing education in nursing by the American Nurses Credentialing Center's Commission on Accreditation.

Credit Designations [back to top](#)

Physicians

The Johns Hopkins University School of Medicine designates this educational activity for a maximum of 0.5 category 1 credits toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

Nurses

The Institute for Johns Hopkins Nursing designates this activity for a maximum of 0.5 contact hours for this eNewsletter.

Respiratory Therapists

Contact your state licensing board to confirm that AMA PRA category 1 credits are accepted toward fulfillment of RT requirements.

Target Audience [back to top](#)

This activity has been developed for Neonatologists, NICU Nurses and Respiratory Therapists working with Neonatal patients. There are no fees or prerequisites for this activity.

Learning Objectives [back to top](#)

The Johns Hopkins University School of Medicine and The Institute for Johns Hopkins Nursing take responsibility for the content, quality, and scientific integrity of this CE activity. At the conclusion of this activity, participants should be able to:

- Develop a more complete understanding of the diverse pathophysiology of PPHN.
- Understand the rationale behind some potential treatments for PPHN and the varying effectiveness of each modality.
- Appreciate the importance of accurate diagnosis and appropriate management of the disease process(es) underlying PPHN.

Faculty Disclosure Policy Affecting CE Activities [back to top](#)

As providers accredited by the Accreditation Council for Continuing Medical Education and American Nursing Credentialing Center, it is the policy of The Johns Hopkins University School of Medicine and The Institute of Johns Hopkins Nursing to require the disclosure of the existence of any significant financial interest or any other relationship a faculty member or a sponsor has with the manufacturer(s) of any commercial product(s) discussed an education presentation. The presenting faculty reported the following:

- Dr. Noguee has indicated a financial relationship of grant/research support with Forest Laboratories and has received

an honorarium from Forest Laboratories.

- Dr. Lawson has indicated a financial relationship of grant/research support from the NIH. He also receives financial/material support from Nature Publishing Group as the Editor of the Journal of Perinatology.

All other faculty have indicated that they have not received financial support for consultation, research, or evaluation, nor have financial interests relevant to this e-Newsletter.

Unlabelled/Unapproved Uses [back to top](#)

In accordance with the ACCME and ANCC Standards for Commercial Support, the audience is advised that one or more presentations in this continuing education activity may contain reference(s) to unlabeled or unapproved uses of drugs or devices.

No faculty member has indicated that their presentation will include information on off label products.

Disclaimers [back to top](#)

The opinions and recommendations expressed by faculty and other experts whose input is included in this program are their own. This enduring material is produced for educational purposes only. Use of The Johns Hopkins University name implies review of education format design and approach. Please review the complete prescribing information of specific drugs or combination of drugs, including indications, contraindications, warnings, and adverse effects before administering pharmacologic therapy to patients.

Internet CE Policy [back to top](#)

The Offices of Continuing Education (CE) at The Johns Hopkins University School of Medicine and The Institute for Johns Hopkins Nursing are committed to protect the privacy of its members and customers. The Johns Hopkins University maintains its Internet site as an information resource and service for physicians, other health professionals and the public.

The Johns Hopkins University School of Medicine and The Institute For Johns Hopkins Nursing will keep your personal and credit information confidential when you participate in a CE Internet based program. Your information will never be given to anyone outside The Johns Hopkins University program. CE collects only the information necessary to provide you with the service you request.

Copyright

© JHUSOM, IJHN, and eNeonatal Review
