



# 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

Christoph U. Lehmann, M.D.  
Assistant 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

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](#)

[Recommend to a Colleague](#)

### LENGTH OF ACTIVITY

0.5 hours

### EXPIRATION DATE

December 15, 2006

### NEXT ISSUE

January 15, 2005

[Post-Test](#)

## In this issue... Volume 2, Number 4

The skin is the largest and most accessible organ of the body. From the moment of birth, the skin must perform multiple simultaneous functions, including acting as a barrier to water and heat loss, as a surface for infection control, and as a dynamic interface for sensory interactions with parents and caregivers. In the NICU environment, the skin is also a platform for adhesives and monitoring devices, and thus is susceptible to trauma from various care interventions. The epidermal barrier of the very low birth weight (VLBW) infant is particularly vulnerable compared to the term infant.

Despite the overwhelming importance of an intact integumental system, there is a relative lack of consensus on basic descriptors of neonatal skin condition. Likewise, there is a disconcerting lack of standardization across institutions and cultures in the methods of skin care practice. The skin is a key biological surface for the discussion of environmental and hygienic conditions that impact newborn health. Recent work on the biology of the fetal skin surface and the development of natural multifunctional barrier creams such as vernix caseosa dovetail neatly with clinical studies designed to prevent infectious complications in the neonate.

In this month's issue, we focus on the implementation and optimization of novel skin care practices that, from a global perspective on neonatal morbidity and mortality, may be employed as feasible and fiscally practical approaches to decreasing neonatal mortality world-wide. The implication of these care practices for the high risk VLBW preterm infant is also addressed.

## Commentary by

Steven B. Hoath, MD

## Reviews by:

Valencia P. Walker, MD

→ [Commentary](#)

Our guest editor opinion

→ [INTERVENTIONS TO REDUCE NEONATAL MORTALITY](#)

→ [NEONATAL SKIN CARE STANDARDS](#)

→ [UNDERSTANDING SKIN BIOLOGY](#)

→ [NOVEL SKIN CARE PRACTICES FOR REDUCING NEONATAL MORTALITY AND MORBIDITY](#)

## Guest Editors of the Month

### Steven B. Hoath, M.D.

Professor of Pediatrics,  
Division of Neonatology  
Medical Director,  
Skin Sciences Institute  
Cincinnati Children's Hospital  
Medical Center  
Cincinnati, OH



### Valencia P. Walker, MD

Neonatology Fellow  
Cincinnati Children's Hospital  
Cincinnati, OH



## Guest Faculty Disclosure

*Steven B. Hoath, MD*

Faculty Disclosure: No relationship with commercial supporters

*Valencia P. Walker, MD*

Faculty Disclosure: No relationship with commercial supporters

## Unlabelled/Unapproved Uses

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

# COMMENTARY

The period from the onset of labor to 72 hours after birth is arguably the most dangerous time in the life span of an individual and carries the highest mortality rate of any comparable period. Understanding the structural and functional changes associated with human birth and instituting care strategies to reduce neonatal morbidity and mortality at this time are top priorities in neonatology. Despite improvements in childhood mortality, as the Darmstadt and Osrin articles point out, mortality rates in the newborn period remain unacceptably high with an estimated 4 million neonatal deaths per year worldwide. Infection remains a leading cause of infant mortality in developing countries and, in the United States, infection continues to play a significant role, particularly in very low birth weight premature infants. In this review, we consider various skin care interventions to reduce neonatal mortality, which at the international level must include considerations of financial feasibility and access to health care.

Given the clinical importance and the multiple functions performed by the skin at birth, it is surprising that so little attention has been given to the standardization of skin care practices. Recently Lund, et al have worked to establish scoring systems for evaluating neonatal skin condition and have incorporated such scores into clinical practice guidelines aimed at the development of cross institutional standards. It is often overlooked that skin assessment also figures prominently in the Apgar score, the Neonatal Infant Pain Scale (NIPS) scoring system, and in multiple behavioral assessment scales. The skin also participates directly in multiple care practices in neonatology with variable degrees of evidentiary support: e.g., kangaroo care, infant massage, developmental care, therapeutic touch, etc.

Recent advances in understanding prenatal skin development have opened the door to new concepts and therapies. Vernix caseosa, for example, is the natural barrier cream which coats the fetal skin during the last trimester. The Yoshio and Moraille articles demonstrate that vernix contains multiple innate immune molecules and acts as a functional skin cleanser after birth.

These findings support the hypothesis that vernix is a multi-functional skin cream with multiple properties ranging from infection control, anti-oxidant activity, skin cleansing and moisturization/water-proofing. Current recommendations from the World Health Organization recommend retention of vernix on the skin surface and delay in bathing for six hours following birth.

A series of recent clinical studies have investigated the utility of topically applied skin barrier creams to protect the preterm infant and reduce the incidence of nosocomial infection. The use of petrolatum - a mixture of non-physiological lipids as a protective barrier in the VLBW infant - has produced conflicting evidence, with the largest multi-institutional study showing an increase in nosocomial infections in the smallest preterm infants. In contrast, the study by Darmstadt et al using sunflower seed oil massage in preterm infants showed a reduction in nosocomial infections. The advantage of the latter treatment regimen includes low cost, ease of application, clinical efficacy, use of a natural material, and cultural integration into existing skin care practices. Focus on such treatment modalities may not only impact neonatal morbidity and mortality at an international level, but also may have a broader impact in terms of facilitating the cross-cultural appreciation of newborn skin as a rich, multifunctional, and largely unexplored physiological interface critical for the health and well being of the infant.

## **INTERVENTIONS TO REDUCE NEONATAL MORTALITY**

**Darmstadt GL, Lan JE, Costello A. Advancing the state of the world's newborns. Bull World Health Organ 2003;81:224-5. Epub 2003 May 16**

**Osrin D, Vergnano S, Costello A. Serious bacterial infections in newborn infants in developing countries. Curr Opin Infect Dis 2004;17:217-24**

*Presenting an international epidemiological perspective.*

In the latter half of the 20th century, the initiation of global health incentives to reduce mortality rates in infants and children under five years of age led to an approximately 50% reduction in mortality rates for this group. Most of this success, however, occurred in children outside of the neonatal period (first 28 days of life). Unfortunately, as stated in the Darmstadt paper, neonatal mortality has remained relatively static with an estimated four million neonatal deaths per year.

Numerous causes can be cited for this alarming and disheartening statistic. During the lifespan of the human organism, the period from the onset of labor to 72 hours after birth has the highest mortality rate of any comparable period of life. In developing countries, moreover, births often occur at home with limited access to formal health care services. As such, for many neonatal deaths there is little opportunity for diagnosis or intervention. Based on epidemiological studies, the majority of these deaths are attributable to infection. Osrin et al reviewed serious bacterial infections among neonates in developing countries and concluded that infections were a major cause of morbidity and mortality in the neonatal population. In the United States, infection also contributes significantly to neonatal mortality, particularly in the most vulnerable population - VLBW premature infants.

Other causes that contribute to the high neonatal mortality rate include birth asphyxia, birth injuries, and complications of prematurity. Low birth weight is a common finding associated with poor neonatal outcome and is often cited as a marker of poor maternal health. Poor hygiene, lactation failure, and cultural differences may also contribute to adverse outcomes. In particular, the persistent belief must be countered that the high mortality rate of the newborn period is socially acceptable or an inevitable accompaniment of birth.

Thus, there is a multiplicity of biological, environmental, and cultural factors that contribute to the estimated four million neonatal deaths per year. There is a need to develop affordable and effective plans to decrease this number. One of the most disturbing perceptions is the idea that interventions for the neonate require exorbitant amounts of money and technology. On the contrary, the Osrin paper identifies neonatal skin care as one area of research that could potentially impact the high morbidity and mortality associated with serious bacterial infections. Research on the biology of fetal and neonatal skin adaptation and innate immune function support such approaches. Of interest, skin care interventions modeled on biologically-based barrier creams show promise for being embraced, not only for the VLBW preterm infant but also

in societies with vastly different cultural practices surrounding the birth of an infant.

**Darmstadt GL, Lan JE, Costello A. Advancing the state of the world's newborns. Bull World Health Organ 2003;81:224-5. Epub 2003 May 16**

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

 [view full article](#)

[↑ back to top](#)

**Osrin D, Vergnano S, Costello A. Serious bacterial infections in newborn infants in developing countries. Curr Opin Infect Dis 2004;17:217-24**

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

 [view journal abstract](#)

 [view full article](#)

[↑ back to top](#)

## NEONATAL SKIN CARE STANDARDS

**Lund CH, Osborne JW, Kuller J, Lane AT, Lott JW, Raines DA. Neonatal skin care: clinical outcomes of the AWHONN/NANN evidence-based clinical practice guideline. Association of Women's Health, Obstetric and Neonatal Nurses and the National Association of Neonatal Nurses. J Obstet Gynecol Neonatal Nurs 2001;30:41-51**

**Lund CH, Osborne JW. Validity and reliability of the neonatal skin condition score. J Obstet Gynecol Neonatal Nurs 2004;33:320-7**

### *Reporting on the drive to reform clinical practices.*

The implementation and comparison of global skin care practices in the newborn would be facilitated by reliable, valid ways of communicating and quantifying skin condition prior to and after clinical interventions. Traditionally, the assessment of skin integrity has been a job relegated to the nursing staff. Without formal training in skin assessment or standardized guidelines to follow, these descriptions are understandably subjective and not based on objective evidence.

Lund et al have worked for several years to develop a Neonatal Skin Condition Score (NSCS) to evaluate basic skin characteristics. The NSCS evaluates dryness, erythema and breakdown/excoriation. The score is done on a scale of 3 to 9. Three is a perfect score with nine being the worst possible score obtainable. The utility of the NSCS lies in its simplicity, reliability and validity. Focus on standardizing skin scores brings into sharp relief the role of the skin and its appearance in multiple other scoring systems including the Apgar score, the Neonatal Facial Coding System (NFCS), the Neonatal Infant Pain Scale (NIPS) and multiple behavioral scores. Given the dual role of the skin as a perceptual interface and an environmental interface, the participation of the skin in these diverse clinical scoring systems is understandable though not always clearly delineated in clinical practice.

Facilitated by the use of the NSCS - which unlike the other scoring systems is solely focused on measurable skin properties - information on skin integrity and the interaction with the environment was obtained. For example, the most common location for skin breakdown in the NICU tended to be the extremities. The anterior and posterior trunk, face and diaper also tended to exhibit deleterious effects of environmental interactions. This trend held up in the well-baby population as well. On the contrary, the cause of skin integrity disruption varied between the two groups. In the NICU population, adhesives were the most common culprit for skin breakdown followed by diaper rash, friction, thermal burns, infection, birth injury, and chemical burns due to intravenous infiltrates. In the well-baby population, the most common cause of skin breakdown was diaper rash rather than adhesives and friction.

More importantly, the NSCS allowed Lund et al to advocate for evidence-based skin care practices in the nursery. The bathing frequency, use of isopropyl alcohol and use of adhesives decreased in response to the results of the NSCS, and the guidelines established for skin care. Overall, the

study authors were able to demonstrate an improvement in skin integrity.

However, all systems have flaws. One of the main limitations with Lund's system is that it relies heavily on visual assessment. The score also cannot factor out the effects of gestational age with younger infants having a higher score due to the immaturity of the stratum corneum. Lastly, several other skin assessment scores do exist, and there has not yet been a general consensus to adopt any one score as a standard of care in Neonatology.

**Lund CH, Osborne JW, Kuller J, Lane AT, Lott JW, Raines DA. Neonatal skin care: clinical outcomes of the AWHONN/NANN evidence-based clinical practice guideline. Association of Women's Health, Obstetric and Neonatal Nurses and the National Association of Neonatal Nurses. J Obstet Gynecol Neonatal Nurs 2001;30:41-51**

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

 [view journal abstract](#)

 [view full article](#)

[↑ back to top](#)

**Lund CH, Osborne JW. Validity and reliability of the neonatal skin condition score. J Obstet Gynecol Neonatal Nurs 2004;33:320-7**

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

 [view journal abstract](#)

 [view full article](#)

[↑ back to top](#)

## UNDERSTANDING SKIN BIOLOGY

**Yoshio H, Tollin M, Gudmundsson GH, Lagercrantz H, Jornvall H, Marchini G, Agerberth B. Antimicrobial polypeptides of human vernix caseosa and amniotic fluid: implications for newborn innate defense. Pediatr Res 2003;53:211-6.**

**Moraille R, Pickens WL, Visscher MO, Hoath SB. A novel role for vernix caseosa as a skin cleanser. Biol Neonate. 2004 Aug 27;87(1):8-14**

### *Reports on the utility of augmenting skin function.*

Vernix caseosa is a substance identified only in humans that is structurally similar to the outermost layer of the epidermis, the stratum corneum. Studies have revealed anti-infective, antioxidant, water-proofing and moisturization properties of this uniquely human skin product. In the delivery room, many caregivers perceive this natural skin cream as a soil which warrants immediate removal after birth. In several recent articles, Yoshio et al and Moraille et al have demonstrated potential efficacious properties of vernix in the form of multiple antimicrobial peptides and the ability of vernix to act as a skin cleanser. In the Moraille article, the investigators compared the efficacy of vernix to two commercially available cleansers, wherein vernix was equally robust as a cleanser with potential advantages for cleaning of deep furrows and pores associated with the pilosebaceous apparatus. The two articles argue in favor of leaving vernix intact on infant skin after birth given its multiple salubrious properties. This rationale concurs with the WHO recommendation that residual vernix be left intact after the initial drying process after birth. It also lends support to the WHO recommendation that the first bath be delayed at least 6 hours.

All of these suggestions emphasize the need to minimize disruption of skin integrity, particularly in the neonate with an impaired adaptive immune system. The literature is consistent with the presence of a fully functional innate immune system in term and near term infants as demonstrated by the presence of anti-microbial peptides in vernix. Not surprisingly, given its structural similarity to vernix, there is evidence to suggest that the stratum corneum has anti-microbial peptides as well. To date, there is little information on the relative immaturity of cutaneous innate immunity in preterm versus term infants or the assessment of current skin practices such as adhesive use and bathing to disrupt innate immune function after birth. This

remains an interesting area of research to pursue with implications for understanding bacterial colonization after birth and mechanisms of endogenous infection control.

**Yoshio H, Tollin M, Gudmundsson GH, Lagercrantz H, Jornvall H, Marchini G, Agerberth B. Antimicrobial polypeptides of human vernix caseosa and amniotic fluid: implications for newborn innate defense. *Pediatr Res* 2003;53:211-6.**

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

 [view journal abstract](#)

 [view full article](#)

[↑ back to top](#)

**Moraille R, Pickens WL, Visscher MO, Hoath SB. A novel role for vernix caseosa as a skin cleanser. *Biol Neonate*. 2004 Aug 27;87(1):8-14**

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

 [view journal abstract](#)

 [view full article](#)

[↑ back to top](#)

## **NOVEL SKIN CARE PRACTICES FOR REDUCING NEONATAL MORTALITY AND MORBIDITY**

**Conner JM, Soll RF, Edwards WH. Topical ointment for preventing infection in preterm infants. *Cochrane Database Syst Rev* 2004:CD001150**

**Edwards, WH, Conner, JM, Soll, RF; Vermont Oxford Network Skin Care Study Group. The effect of prophylactic ointment therapy on nosocomial sepsis rates and skin integrity in infants with birth weights of 501 to 1000g. *Pediatrics* 2004; 113:1195-203.**

**Darmstadt GL, Badrawi N, Law PA, Ahmed S, Bashir M, Iskander I, Al Said D, El Kholy A, Husein MH, Alam A, Winch PJ, Gipson R, Santosham M. Topically applied sunflower seed oil prevents invasive bacterial infections in preterm infants in Egypt: a randomized, controlled clinical trial. *Pediatr Infect Dis J* 2004;23:719-25**

### ***Examining interventions in a high-risk population of preterm infants.***

The preterm infant population has a well-demonstrated increased susceptibility to infection associated with increased morbidity and mortality. Presumably, the lack of vernix, the relative stratum corneum immaturity, and the overall compromised function of the skin coupled with multiple procedural interventions all contribute to this clinical problem. To further complicate the issue, malnutrition of infants (as often seen in developing countries) can further compromise skin barrier function. As mentioned previously, the implementation of neonatal skin practices which can improve barrier function have been identified as an area of research where potential interventions can be made inexpensively and with cultural sensitivity and acceptance.

The Connor paper is a Cochrane systematic review of prophylactic ointment therapy in preterm infants. It is heavily weighted by a randomized control trial done by the same group of authors examining the effect of a prophylactic, petrolatum-based, ointment therapy (Aquaphor™) on nosocomial sepsis rates and skin integrity in infants less than 1000g. The major finding of this review was the increased risk of nosocomial infection with coagulase negative staphylococci among VLBW infants receiving prophylactic topical therapy.

The Darmstadt paper also examines the use of prophylactic topical therapy in preterm infants. Rather than use a topical emollient/petrolatum ointment, sterile sunflower seed oil was applied to the skin. Interestingly, countries in Africa and elsewhere including Bangladesh, China, Egypt, India and Nepal all practice routine oil massage for infants. The results of the Darmstadt study indicated a 54% reduction in the rates of nosocomial infection among treated infants versus the control group. The authors did not find a significant difference in mortality rates between groups in this small study.

Questions arise regarding the difference in conclusions between the two papers. The Cochrane paper reflects the results obtained with a group of smaller, more premature infants who also received considerable mechanical manipulation, such as central lines. The use of indwelling catheters has long been an independent and associated increased risk for infection. The use of the emollient may act synergistically with this known complication. In the Darmstadt paper, the authors speculate that other factors including the decreased use of indwelling catheters in their study population minimized the potential for the negative outcomes seen by Connor et al. They also hypothesize that sunflower seed oil works, in part, by accelerating skin barrier ontogenesis, decreasing inflammation, and forming a physical barrier over the skin of the premature infant. Regardless, the use of sunflower seed oil as a natural barrier, along with delayed removal of vernix and delayed bathing, demonstrate viable and inexpensive areas of neonatal skin care practices which have the potential to reduce infection rates in the neonatal period.

**Edwards, WH, Conner, JM, Soll, RF; Vermont Oxford Network Skin Care Study Group. The effect of prophylactic ointment therapy on nosocomial sepsis rates and skin integrity in infants with birth weights of 501 to 1000g.**

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



[view journal abstract](#)



[view full article](#)

[↑ back to top](#)

**Darmstadt GL, Badrawi N, Law PA, Ahmed S, Bashir M, Iskander I, Al Said D, El Kholy A, Husein MH, Alam A, Winch PJ, Gipson R, Santosham M. Topically applied sunflower seed oil prevents invasive bacterial infections in preterm infants in Egypt: a randomized, controlled clinical trial. *Pediatr Infect Dis J* 2004;23:719-25**

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



[view journal abstract](#)



[view full article](#)

[↑ back to top](#)

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

[Recommend eNeonatal Review to a colleague](#)

[View this newsletter as a downloadable PDF](#)

#### **Accreditation [back to top](#)**

##### **Physicians**

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of The Johns Hopkins University School of Medicine and The Institute for Johns Hopkins Nursing. The Johns Hopkins University School of Medicine is accredited by the ACCME 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:

- Recognize the potential to reduce global neonatal mortality by improving the care of neonatal skin;
- Discuss the advantages and disadvantages of using a neonatal skin condition score to guide clinical practices;
- Implement simple, inexpensive and novel skin care practices that can potentially improve outcomes in at-risk neonatal populations in your clinical practice.

**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 provider has with the manufacturer(s) of any commercial product(s) discussed in 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 educational 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