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Original Article

Vernix Caseosa in Neonatal Adaptation

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OBJECTIVES:

To characterize vernix caseosa in newborn infants with respect to factors that influence vernix distribution on the skin surface, vernix effects on thermal stability, skin hydration, acid mantle development, and vernix antioxidant properties.

STUDY DESIGN:

Vernix distribution was determined for 430 infants. Thermal stability was assessed in parallel groups following vernix retention ($n = 66$) and removal ($n = 64$). The effects of vernix retention on skin hydration, pH, erythema, and dryness/scaling were determined. Samples were analyzed for vitamin E before and after UV exposure.

RESULTS:

Vernix distribution depended upon gestational age, delivery mode, gender, race, and meconium exposure. Retention had no effect on axillary temperatures. Skin hydration was significantly higher for vernix-retained skin. Skin pH and erythema were significantly lower with retention. Vitamin E levels were decreased by ultraviolet radiation.

CONCLUSIONS:

Vernix is a naturally occurring barrier cream with multiple salubrious effects, which support its retention on the skin surface at birth.
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INTRODUCTION

Vernix caseosa is a complex, proteolipid material synthesized in part by fetal sebaceous glands during the last trimester of pregnancy.[1–3] The strategic location of vernix on the fetal skin surface suggests participation in multiple overlapping functions required at birth, for example, barrier to water loss, temperature regulation, and innate immunity. Knowledge of the dynamic structure and function of newborn skin is important in determining optimal thermal support, providing infection control, and selecting adhesives. Such therapy begins in the delivery room and forms the foundation for the ''golden hour'' concept of newborn resuscitation.[4] Challenges faced by the newborn infant include an abrupt decrease in environmental temperature, high oxidative stress, exposure to exogenous toxins, and the rapid onset of microbial colonization.

Temperature control during the first few hours of life is a cornerstone of neonatology and is particularly important for reducing mortality and morbidity in very low birth weight preterm infants.[5] Neonates less than 28 weeks gestational age (GA) and 1000 g have an immature epidermal barrier, characterized by the absence of a competent stratum corneum (SC), and high transepidermal water loss. They also lack a protective mantle of vernix caseosa. At birth, excess amniotic fluid is typically wiped off to reduce evaporative heat loss. The hydrophobic layer of vernix is often removed. In this study, we focused on quantifying vernix distribution in older infants and hypothesized that retention of vernix on the skin surface would correlate with a diminished fall in axillary temperatures after birth, as reported years ago.[6] In contrast, it was possible that retention of a highly hydrated biological material such as vernix would impair temperature control due to increased evaporative heat loss.[7]

The identification of antimicrobial constituents in vernix[8–11] supports the intriguing hypothesis that vernix may function prenatally to protect the fetus from acute or subacute chorioamnionitis and facilitate colonization of the skin with microorganisms after birth. Newborn infants undergo a progressive adaptation immediately after birth, including a slow reduction in surface hydration, decrease in skin pH, and SC dehydration/desquamation with formation of a dry skin surface.[12] Whether this desquamatory process is secondary to removal of vernix is as yet unknown. There are no studies of the role of vernix in modulating these processes. Vernix loses its exogenous water slowly.[13] Application of vernix to adult volar forearm skin resulted in an increased capacity to bind exogenous water.[14] Vernix may also function to maintain skin hydration at birth and potentially facilitates formation of the acid mantle of the skin. An acid surface

is putatively necessary for the bacterial homeostasis/colonization of the skin.[15,16]

Finally, birth marks a time of high oxidative stress. Adult human skin possesses endogenous antioxidant capacity in the form of alpha tocopherol (vitamin E) localized in SC and in sebum.[17] Term human infants have large, hyperplastic sebaceous glands, but their role in vernix production and/or production of surface antioxidants is unclear. The presence of vitamin E in vernix was first described 40 years ago, but its functional response to oxidative stress has not previously been examined.

In this paper, we report the results of four separate studies of vernix physiology at birth: distribution on the skin surface, the effect on thermal regulation, the effect on postnatal skin surface hydration and acid mantle development, and the *in vitro* response to ultraviolet radiation. These data provide evidence for clinical decision making in the delivery room.

MATERIALS AND METHODS

Study 1. Vernix Surface Distribution at Birth

A total of 430 infants were observed at routine deliveries in three local hospitals (Christ Hospital, University Hospital, Anderson Mercy Hospital, Cincinnati, OH, USA) from August 2001 to March 2003. Table 1 shows the population demographics. Trained delivery room personnel recorded areas of vernix coverage on the front and back on standardized infant body maps (Figure 1), along with GA, delivery mode (vaginal, C-section), gender, race, presence of meconium, and other maternal factors. Instructions on the use of the vernix distribution body maps were provided and inter-rater reliability was established. An image analysis algorithm was used to calculate the area of coverage (MATLAB®, MathWorks, Natick, MA) for total body surface, front and back.

Table 1 Demographic Characteristics

Number of infants	430
Delivery Mode	
Vaginal	213
C-section	217
Gender (M/F)	
Male	233
Female	197
Race	
Caucasian	374
Black & Non-Caucasian	55
Meconium	
Present	66
Absent	367
Gestational age (weeks)	
Mean ± SD	39.1 ± 1.3
Range	33.4 to 42.3
Birth weight (g)	
Mean ± SD	3500 ± 549
Range	1921 to 5695
Apgar score (5 minutes)	
Mean ± SD	8.6 ± 0.6
Range	5.0 to 9.5
Gestational diabetes	26
Antenatal antibiotics	81
Antenatal steroids	4
Chorioamnionitis/sepsis	2

Study 2: Thermal Regulation

Totally, 130 infants of 32 to 41 weeks GA were enrolled in a randomized controlled trial in a level II birthing center (Christ Hospital, Cincinnati, OH). The Institutional Review Board of Christ Hospital approved the protocol. The IRB waived the requirement for written informed consent since the study involved minimal risk and procedures for which consent would not be required outside a research context. Infants with major congenital abnormalities or a need for resuscitation were excluded. In the delivery room, infants were randomly assigned to one of two treatment groups, irrespective of the amount of vernix on the surface and the vernix distribution was recorded. For Group A, amniotic fluid and blood were blotted with an absorbent towel, but vernix was retained on the skin surface ($n = 66$). In Group B, vernix, amniotic fluid and blood were removed by firm wiping ($n = 64$). Axillary temperatures were measured at 30 and 60-minutes after birth using a Welch Allyn Sure Temp® thermometer and vernix surface distribution was computed. Axillary temperature was selected instead of skin temperature since the latter would be confounded by the evaporative heat loss from vernix itself. During the 60-minute period, the infants were bundled and placed with the parents.

Study 3: Skin Surface Adaptation After Birth

This study was performed at a level II birthing center (Christ Hospital, Cincinnati, OH, USA). Research personnel documented vernix distribution and classified the infants into two groups, based on the amount and distribution of vernix, under the research protocol used for the thermal regulation study. Infants with major congenital abnormalities, a need for resuscitation, and questionable GA were excluded. Infants with large to moderate amounts of vernix were classified as ''vernix retained''. Surface fluids (water and blood) were removed by gentle blotting and

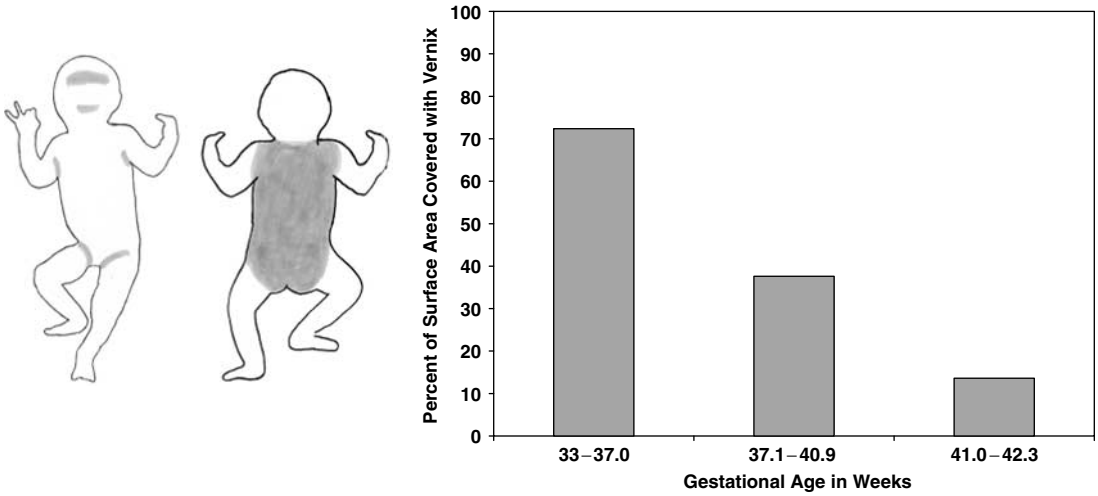

Figure 1. The data for all 430 infants were segmented into three classifications: preterm (<37.0 weeks, $n = 24$), full term (37.1 to 40.9 weeks, $n = 372$) and post-term ($\geq$41.0 weeks, $n = 34$). The percent total coverage was significantly different among the three infant subgroups ($p < 0.001$, ANCOVA) and indicates a negative relationship with GA. The error bars for the percent total coverage are too small to be visible in the graph.

vernix was left on the skin. Those with small amounts or no vernix were wiped with a cotton towel to remove vernix and classified as ''vernix removed''. All infants were then wrapped in blankets. This procedure provided a source of infants for the skin adaptation study.

Shortly after delivery and vernix classification, the parents were informed about the skin adaptation research project. The Institutional Review Board of Christ Hospital approved the research protocol. The infant's parent provided written informed consent for participation. From the total subject pool, 60 healthy newborn infants took part between November 2001 and April 2003. Skin measurements were made at sites on the infant's chest and back immediately after birth and about 4 and 24 hours later. At the time of the initial measurements, the vernix retained at birth was no longer visible on the skin surface (vernix retained group). Infants were bathed with a liquid washing product (Johnson & Johnson® Baby Bath) with nursery procedures (wet cloth, lather, wipe skin surface, rinse with wet cloth, and infant under warmer) typically after the initial measurements and about 2 hours prior to the 4-hour assessment. The SC hydration status was assessed as previously described[18,19] using a NOVA meter (NOVA Technology Corporation, Portsmouth, NH). The SC surface hydration was taken as the first reading and the moisture accumulation rate (MAT) was determined over 20 seconds. Surface pH was measured with a Skin pH Meter 900 (Courage & Khazaka, Koln, Germany) and a flat skin surface electrode calibrated daily to pH 4 and 7 buffers. The electrode was rinsed and blotted to remove bulk water prior to the measurement. A trained judge evaluated skin erythema on a 0 to 4 scale (0 none, 1 mild, 2 moderate, 3 severe, 4 bleeding) and dryness/scaling on a 0 to 3 scale (0 none, 1 mild, 2 moderate, 3 severe). Half-grade increments were used for intermediate conditions for both scales. Room temperature and relative humidity and outside conditions were recorded daily.

Study 4: Antioxidant Properties

Vernix was harvested from full-term infants born at University Hospital (Cincinnati, OH, USA), stored in sterile vials, and held at 4°C until the time of analysis. The hydrophobic components of vernix were extracted into chloroform and solvent was evaporated to dryness. The resulting residue was suspended in 95% ethanol and pelleted by low speed centrifugation. The supernatant was filtered, injected onto a C-18 HPLC column, and eluted with an isocratic gradient of 95% ethanol. Absorbance was monitored at 290 nm and vitamin E standards (Sigma Chemical Co., St. Louis, MO, USA) were used to quantify the amount of vitamin E. To evaluate the efficacy of the vitamin E in vernix, the specimens were irradiated with UVB radiation (260 to 320 nm) at a dose of 0.38 J/cm^2 for 10 minutes and analyzed for vitamin E levels by HPLC.

Statistical Analysis

Standard software (SigmaStat, SPSS and SAS®) was used for statistical analyses. Correlation coefficients were calculated using Pearson's product moment and Spearman procedures, as appropriate. General linear model regression methods (SAS®) were used to determine the influence of variables on vernix distribution. *t*-Tests were performed to compare temperatures and temperature changes for the two groups and to compare the skin parameters for the vernix retained and vernix removed groups. Paired *t*-test procedures were used to compare skin parameters at birth and 24 hours within each group. $p \leq 0.05$ was considered to be statistically significant.

RESULTS

Surface Distribution at Birth

The mean vernix surface coverage was 38±1.2 % (mean±SE) for the 430 infants, with most having a surface coverage of less than 10% or greater than 90%. The total surface distribution was significantly dependent upon GA, delivery mode (vaginal versus C-section), gender, race and the presence of meconium (Table 2). The multiple linear regression model controlled for all of the variables listed in Table 2. The vernix coverage was higher for lower GA, C-section infants, females, and Caucasian infants, and lower following meconium exposure. Vernix distribution (continuous variable) was negatively correlated with GA (correlation coefficient of -0.49, $p<0.001$). The value of R^2 was 0.29, indicating that only about one-third of the variance was explained by GA, delivery mode, gender, race, and meconium exposure. To further evaluate the effects of GA, the data for all 430 infants were segmented into three groups: preterm (<37.0 weeks, $n=24$), full term (37.1 to 40.9 weeks, $n=372$) and post-term ($\geq$41.0 weeks, $n=34$). Mean values were extracted from the analysis of covariance (ANCOVA) to adjust for the covariates in the regression model (Figure 1). The three groups were significantly different for percent total vernix coverage and indicate a negative relationship with GA. Other factors during fetal development must account for most of the variability in vernix distribution. The coverage was significantly higher on the back than the chest ($p<0.05$), indicating regional differences.

Thermal Regulation

Axillary temperatures during the first hour for the vernix retained group ($n=66$) were 98.1±0.9 and 98.1±1.0°F at 30 and 60 minutes, respectively. For the vernix removed group ($n=64$), temperatures were 98.3±1.1 and 98.1±0.9°F at 30 and 60 minutes, respectively. Vernix retention had no effect on axillary temperatures at either time point. The vernix coverage was 46±4.8% for the retained group. The distributions for the back and front were not significantly different. The preterm infants with vernix retained had significantly greater total coverage (72±7.4%) than the full-term infants with vernix retained (38±5.4%). There was no correlation between the change in temperature (30 to 60 minutes) and the percent coverage, indicating that vernix distribution did not significantly influence the thermal change. During the study, the environmental conditions of the delivery room and nursery were well controlled, thereby minimizing thermal stress due to the surroundings.

Skin Surface Adaptation After Birth

The vernix retained and vernix removed groups were not statistically different for GA, with values of 39.1±1.0 and 39.3±1.0 weeks, respectively. The gender distribution was 14 females/16 males for vernix retained and 13/17 for vernix removed. The delivery mode distribution (C-section/vaginal) was 18/12 for retained and 15/15 for removed. At birth, the total body distribution of vernix was 26±3.3% for the removed group and 48±3.3% for the retained group. The distribution was directionally higher ($p=0.07$) on the back (50±6.4%) than on the front (45±6.4%) for the retained group.

Retention of vernix on the skin following birth resulted in significantly different biophysical properties compared to infants for whom vernix was removed. The moisture accumulation rate (MAT) was significantly higher for the vernix retained group (back site) than the vernix removed group at birth (1.45±0.32 for retained, 0.55±0.20 for removed, Figure 2) and 24 hours later (0.28±0.08 for retained, 0.03±0.08 for removed, Figure 2). The baseline SC hydration was significantly higher at birth (chest and back sites) for the retained group (107.6±3.6 for chest, 128.0±10.2 for back) than for the removed group (104.2±6.9 for chest, 99.8±4.9 for back). At birth, visual erythema on both sites was significantly lower for the retained group (0.05±0.04 for chest, 0.07±0.04 for back) than for the removed cohort (0.22±0.06 for chest, 0.26±0.06 for back). Directionally lower visual dryness/scaling ($p=0.10$) was observed for vernix retention than vernix removal initially after birth. The skin surface pH was significantly lower for vernix retention than for removal, both initially (5.16±0.16 for retention, 5.97±2.8 for removal) and at 24 hours (4.90±0.19 for retention, 5.63±0.26 for removal) on the back (Figure 3).

The effect of body site was examined for each group (paired *t*-test, $p\leq0.05$). For the vernix-retained infants, MAT was significantly higher for the back (1.45±0.32) than for the chest (0.68±0.19) at birth. The skin dryness was significantly lower on the back (0.12±0.05) than on the chest (0.27±0.06). At 24 hours

Table 2 Variables Influencing Vernix Surface Distribution (Mean±SE)

	% Total surface distribution		*p*-Value*
Delivery mode	Vaginal delivery: 32.5±2.1	C-Section delivery: 42.8±2.3	0.01
Gender	Male: 33.2±2.0	Female 43.0±2.4	0.006
Race	Black & Other: 25.9±3.2	White: 39.4±1.7	0.0008
Meconium	Present: 18.8±2.4	Absent: 41.1±1.7	0.002

**p*-Value as derived from a multiple linear regression model.

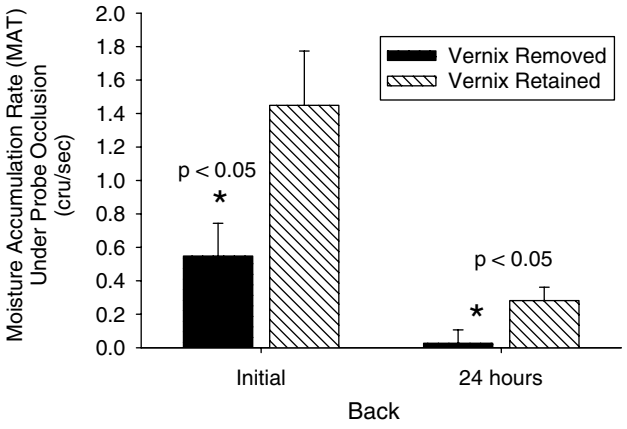

Figure 2. The moisture accumulation rate (MAT) was significantly higher for the vernix-retained skin (back site) at birth and 24 hours later (*$p<0.05$). The baseline SC hydration was significantly higher at birth (chest and back sites) for the vernix retention ($p<0.05$). Newborn skin with vernix retained was more hydrated than skin with vernix removed. Vernix retention appears to facilitate proper postnatal hydration.

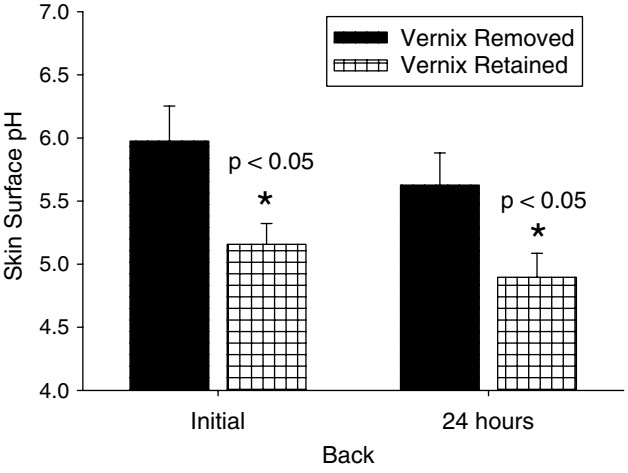

Figure 3. The skin surface pH was significantly lower with vernix retention at initially (5.16±0.16 versus 5.58±0.22) and at 24 hours (4.90±0.19 versus 5.63±0.26) for the back site (*$p<0.05$). Retention of vernix resulted in a significantly lower skin surface pH than did the removal of vernix. In the presence of vernix, the acidification of the skin surface appears to occur sooner than under conditions of removal.

post birth, MAT was significantly higher for the back (0.28±0.08) than the chest (0.12±0.04), the dryness/scaling was significantly lower for the back (0.12±0.04) than the chest (0.29±0.06), the skin surface pH was significantly lower for the back (4.90±0.19) than the chest (5.61±0.28), and the baseline hydration was significantly higher for the chest (96.1±1.3) than the back (93.3±0.6). For the vernix-removed infants, MAT was significantly lower at 24 hours for both the chest (0.02±0.05 at 24 hours, 0.56±0.24 at birth) and the back (0.03±0.08 at 24 hours, 0.55±0.20 at birth). At 24 hours, the back (0.18±0.05) was significantly less dry/scaly than the chest (0.37±0.08).

Antioxidant Properties

The mean vitamin E concentration of individual vernix specimens from eight term infants was 18.9±1.7 μg/g of vernix wet weight. In a separate experiment, recovery efficiency was found to be 58.4±8.7% (mean±SEM), indicating that the actual vitamin E levels may be higher than shown by the HPLC method. Pooled vernix specimens ($n=7$, 13.2±1.0 μg vitamin E/g wet weight) were irradiated with UVB radiation (260 to 320 nm) at a dose of 0.38 J/cm^2 for 10 minutes. Vitamin E levels had been reduced by 82% following UVB irradiation.

SIGNIFICANCE

Surface Distribution

Anecdotal reports indicate that the amount and distribution of vernix on the infant at delivery are highly variable. Akiba[20] evaluated the influence of gender, age, season, weight and parity on vernix in 643 infants. In all, 16% had vernix over the entire surface, compared to 8.6% in our group and no effects of gender or season were observed. Akiba reported coverage to be inversely related to birth weight, with a maximum for infants under 2000 g and consistent with our findings. Our findings are consistent with this observation.

Thermal Regulation

Previous work showed an effect of occlusion with water-impermeable films to reduce the fall in body temperature after birth.[21] Plastic wrap, impermeable films, kangaroo care, and oil massage were reported to be effective at controlling body temperature over the first 24 hours of life in premature infants.[21,22] There is little consensus, however, on whether vernix has an effect on body temperature regulation and on whether it should be removed or retained at birth. An association between vernix removal and the development of subnormal temperatures has been reported,[23] but vernix removal has also been linked with decreased evaporative heat loss.[7] Shulak[24] speculated that vernix could provide thermal stability, but that it was not a primary factor in thermal regulation at birth. Vernix retention had no significant effect on thermal regulation in our population. However, additional studies are required to determine the temperature effects in younger premature infants (30 to 32 weeks GA).

Skin Surface Adaptation and Acid Mantle Development

Vernix retention led to a significantly more hydrated skin surface, as evidenced by a higher moisture accumulation rate and a higher baseline hydration (Figure 3). The outcomes support our previous findings of a slow reduction in skin hydration and extend them by

suggesting that vernix retention may facilitate postnatal skin hydration. The pH decrease following birth has been attributed to maturation of the enzymes responsible for the synthesis of acidic components.[25] Fox et al.[26] suggested that the mechanism of postnatal acidification is established in early gestation and is influenced by environmental factors. Few studies have addressed the contribution of vernix caseosa to acid mantle development. Behrendt and Green[27] found no significant differences between in skin pH in contralateral sites for vernix versus a water wipe ($n = 4$) and suggested that the vernix layer (measured pH or 7.4) influenced skin acidification, as did maceration and desquamation. Puhvel et al.[28] reported the hydrolysis of the triglycerides in sebum to fatty acids by skin surface bacteria. The triglycerides in vernix could be a source of acidic fatty acids at the skin surface, provided that conditions for hydrolysis are present.[29] Sweat, sebum, topical products, washing, cleansing products, skin site, SC barrier status, pH electrode treatment, site preparation, and meter calibration can all impact skin pH measurements.[30,31] Comparisons of data across studies may reflect inherent variations in test methodology.

In this work, skin surface acidification appears to occur earlier in the presence of vernix than under conditions of vernix removal. An acidic SC is believed to provide an antimicrobial function, with inhibition of growth of pathogenic bacteria.[15,16,32] The acid mantle may facilitate colonization of the skin surface with commensal organisms.[30,33] Additional studies are warranted to assess the impact of vernix retention on the process of skin colonization.

Antioxidant Properties

Thiele et al.[17,34] have reported the presence of vitamin E in the epidermis and SC and that sebaceous secretion is a major mechanism for its delivery to the skin surface. Exposure to UVA, UVB and ozone results in reduction of vitamin E.[34,35] Gerloczy et al.[36,37] first reported vitamin E in vernix over 40 years ago at amounts from trace levels to 90 μg/g wet weight (0.21 μmole/g wet weight), comparable to levels in high vitamin E organs. We found a mean vitamin E content of 13.2 to 18.9 μg/g wet weight of vernix (0.031 to 0.044 μmole/g wet weight). When normalized to vernix lipid content, vitamin E was present at 0.15 to 0.22 μmole/g. Recent reports indicate that vitamin E levels in the SC were 0.073 and 0.10 μmole/g dry weight for the arm and face, respectively, suggesting that vernix may have higher levels of this antioxidant than normally found in adult SC.[17] The function of vitamin E in vernix is unclear. Prenatal chorioamnionitis may lead to production of oxygen radicals and a potential protective role for vitamin E in utero. After birth, the skin surface normally encounters sharp increases in oxygen levels and a pro-oxidant environment. Adult studies support an antioxidant role for vitamin E in sebum and SC. Ultraviolet light (a pro-oxidative stressor) diminishes vitamin E levels in vernix. Our results suggest that skin-based mechanisms for coping with oxidative stress may be important in the late gestation fetus and newborn.

In summary, this is the first systematic assessment of vernix function and distribution in 50 years. Many questions still remain. GA, delivery mode, race, gender, and exposure to meconium explain only one-third of the variability in vernix distribution. Amount (weight) was not quantified and may be an important factor. Additional studies are necessary to more fully understand the perinatal influences that regulate the distribution and amount of vernix.

The overall clinical implications of this research are that vernix caseosa may be left in place at birth. Parents and health-care providers can be encouraged to view vernix as a naturally occurring cream that may facilitate adaptation to a dry environment. Vernix biology is a relatively unexplored field of perinatal biology with practical implications for translational physiology, infection control, bathing practices, temperature management and surface adhesion. The effects of vernix on newborn skin raise the intriguing possibility of using vernix as a prototype for the development of new barrier creams, particularly those which could be applied to premature infant skin to facilitate the formation of an effective SC barrier.

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References

1. Hoath SB, Narendran V, Visscher M. Role and biology of vernix. Neonatal Infant Nurs Rev 2001;1:53–8.
2. Pochi P. The sebaceous gland. In: Maibach H, Berardesca E, editors. Neonatal Skin. New York: Marcel Dekker; 1982. p. 67–80.
3. Pickens W, Zhou Y, Wickett R, Visscher M, Hoath SB. Antioxidant defense mechanisms in vernix caseosa: potential role of endogenous vitamin E. Pediatr Res 2000;47(5):425A.
4. Narendran V, Hoath SB. Thermal management of the low birth weight infant: a cornerstone of neonatology. J Pediatr 1999;134(5):529–31.
5. Vohra S, Frent G, Campbell V, Abbott M, Whyte R. Effect of polyethylene occlusive skin wrapping on heat loss in very low birth weight infants at delivery: a randomized trial. J Pediatr 1999;134(5):547–51.
6. Saunders C. The vernix caseosa and subnormal temperature in premature infants. Br J Obstet Gynaecol 1948;55:442–4.
7. Riesenfeld B, Strombery B, Sedin G. The influence of vernix caseosa on water transport through semipermeable membranes and the skin of full-term infants. In: Second International Conference on Fetal and Neonatal Physiological Measurements. Butterworth Heinemann: Philadelphia; 1984. p. 3–6.

8. Yoshio H, Tollin M, Gudmundsson GH, et al. Antimicrobial polypeptides of human vernix caseosa and amniotic fluid: implications for newborn innate defense. Pediatr Res 2003;53(2):211–6.
9. Marchini G, Lindow S, Brismar H, et al. The newborn infant is protected by an innate antimicrobial barrier: peptide antibiotics are present in the skin and vernix caseosa. Br J Dermatol 2002;147(6):1127–34.
10. Narendran V, Hull W, Akinbi HT, Whitsett JA, Pickens WL, Lambers D. Vernix caseosa contains surfactant proteins: potential role in innate immune function in the fetus. Pediatr Res 2000;47:420A.
11. Akinbi HT, Narendran V, Pass AK, Markart P, Hoath SB. Host defense proteins in vernix caseosa and amniotic fluid. Am J Obstet Gynecol 2004;191(6):2090–6.
12. Visscher MS, Munson KA, Bare DE, Hoath SB. Early adaptation of human skin following birth: a biophysical assessment. Skin Res Technol 1999;5:213–20.
13. Pickens WL, Warner RR, Boissy YL, Boissy RE, Hoath SB. Characterization of vernix caseosa: water content, morphology, and elemental analysis. J Invest Dermatol 2000;115(5):875–81.
14. Bautista MI, Wickett RR, Visscher MO, Pickens WL, Hoath SB. Characterization of vernix caseosa as a natural biofilm: comparison to standard oil-based ointments. Pediatr Dermatol 2000;17(4):253–60.
15. Puhvel SM, Reisner RM, Amirian DA. Quantification of bacteria in isolated pilosebaceous follicles in normal skin. J Invest Dermatol 1975;65(6):525–31.
16. Aly R, Maibach HI, Rahman R, Shinefield HR, Mandel AD. Correlation of human in vivo and in vitro cutaneous antimicrobial factors. J Infect Dis 1975;131(5):579–83.
17. Thiele JJ, Weber SU, Packer L. Sebaceous gland secretion is a major physiologic route of vitamin E delivery to skin. J Invest Dermatol 1999;113(6):1006–10.
18. Jemec GB, Serup J. Epidermal hydration and skin mechanics. The relationship between electrical capacitance and the mechanical properties of human skin in vivo. Acta Dermatol Venereol 1990;70(3):245–7.
19. Okah FA, Wickett RR, Pickens WL, Hoath SB. Surface electrical capacitance as a noninvasive bedside measure of epidermal barrier maturation in the newborn infant. Pediatrics 1995;96(4 Part 1):688–92.
20. Akiba T. Studies on biological actions of vernix caseosa. Jpn Obstet Gynecol Soc 1955;2(4):396–411.
21. Besch NJ, Perlstein PH, Edwards NK, Keenan WJ, Sutherland JM. The transparent baby bag. A shield against heat loss. N Engl J Med 1971;284(3):121–4.
22. Johanson RB, Spencer SA, Rolfe P, Jones P, Malla DS. Effect of post-delivery care on neonatal body temperature. Acta Paediatr 1992;81(11):859–63.
23. Saunders C. The vernix caseosa and subnormal temperature in premature infants. Br J Obstet Gynaecol 1948;55:442–4.
24. Shulak B. The antibacterial action of vernix caseosa. Harper Hosp Bull 1963;21:111–7.
25. Hoeger PH, Enzmann CC. Skin physiology of the neonate and young infant: a prospective study of functional skin parameters during early infancy. Pediatr Dermatol 2002;19(3):256–62.
26. Fox C, Nelson D, Wareham J. The timing of skin acidification in very low birth weight infants. J Perinatol 1998;18(4):272–5.
27. Behrendt H, Green M. Skin pH pattern in the newborn infant. Am J Dis Child 1958;95(1 Part 1):35–41.
28. Puhvel SM, Reisner RM, Sakamoto M. Analysis of lipid composition of isolated human sebaceous gland homogenates after incubation with cutaneous bacteria. Thin-layer chromatography. J Invest Dermatol 1975;64(6):406–11.
29. Herrmann F, Behrendt H, Karp F. On the acidity of the surface of the scalp and other areas of the skin in children. J Invest Dermatol 1946;7:215.
30. Parra JL, Paye M. EEMCO guidance for the in vivo assessment of skin surface pH. Skin Pharmacol Appl Skin Physiol 2003;16(3):188–202.
31. Rippke F, Schreiner V, Schwanitz HJ. The acidic milieu of the horny layer: new findings on the physiology and pathophysiology of skin pH. Am J Clin Dermatol 2002;3(4):261–72.
32. Fluhr JW, Kao J, Jain M, Ahn SK, Feingold KR, Elias PM. Generation of free fatty acids from phospholipids regulates stratum corneum acidification and integrity. J Invest Dermatol 2001;117(1):44–51.
33. Lukacs A. In vitro control of the growth of important bacteria of the resident flora by changes in pH. In: Braun-Falco O, Korting H, editors. Skin Cleansing with Synthetic Detergents. Berlin: Springer; 1992. p. 97–105.
34. Thiele JJ, Traber MG, Polefka TG, Cross CE, Packer L. Ozone-exposure depletes vitamin E and induces lipid peroxidation in murine stratum corneum. J Invest Dermatol 1997;108(5):753–7.
35. Thiele JJ, Traber MG, Packer L. Depletion of human stratum corneum vitamin E: an early and sensitive in vivo marker of UV induced photo-oxidation. J Invest Dermatol 1998;110(5):756–61.
36. Gerloczy F, Bencze B, Ivanyi K. Demonstration of a new biologically active substance vitamin E, in the vernix caseosa. Int J vitamin Res 1961;32:1–4.
37. Gerloczy F, Bencze B, Ivanyi K. Demonstration of vitamin E, a new biologically active substrate, in the vernix caseosa. Magy Noorv Lapja 1963;26:21–2.