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*Review Article*

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# Review Article: Skin Condition and Skin Care in Premature Infants

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**ABSTRACT**

**Background:** The majority of newborn skin care recommendations focus on concerns for healthy, full-term infants. Compared to mature infants, the skin of premature infants, those who are born at the gestational age of 37 weeks, is more vulnerable to injury, transepidermal water loss (TEWL), and transepidermal intoxication. There are no established guidelines for premature infant skin care. Discussion and review regarding this topic are needed. **Purpose:** To review the literature on skin conditions and skin care in premature infants. **Review:** The barrier function of premature skin is significantly compromised because the stratum corneum does not fully mature until late in the third trimester. Premature infants have immature skin with impaired barrier function characterized by high TEWL, increased absorption of chemicals, and increased risk of infection. Some particular issues in premature infant skin are controlling TEWL, avoiding mechanical damage, proper sterilization to control infection, awareness of percutaneous drug toxicity, appropriate bathing and umbilical cord care, and appropriate management of skin problems. **Conclusion:** Premature infant skin is more vulnerable due to immature development. Skin care for premature infants requires careful attention.

**Keywords:** skin care, infant, newborn, premature, human and disease.

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## BACKGROUND

The primary purpose of the skin is to protect, hence the immaturity of the skin adds to the vulnerability of premature infants. The primary purpose of the skin is to act as a permeability barrier, which serves as a defense against ultraviolet radiation, mechanical stress, colonization by microbes, and percutaneous absorption of exogenous xenobiotics. In addition to its barrier activities, skin plays a role in the immune, neurosensory, and thermoregulatory systems.[1,2]

The effects of skin maturity on a premature newborn depend on the timing of each cutaneous function's maturation, which in turn depends on the infants' gestational age and postnatal age. The premature newborn has thinner skin on all layers. The timeline for stratum corneum development predicts the competence of numerous skin functions as it is the primary factor in the majority of skin barrier properties.[1,2]

Skin is divided into two layers, the epidermis (ectoderm) and dermis (mesenchyme). The stratum corneum (a layer of the epidermis) begins to form at 15 weeks of gestation and continues until 34 weeks. Infants born before 30 weeks of gestation have a thin epidermis and an impaired epidermal barrier function. Most premature infant skin will properly mature in 2 to 4 weeks, or even longer in very premature infants.[1,2,3,4] Sebaceous gland secretions begin to have a role in the formation of the vernix caseos, a complex proteolipid substance, around 28 weeks during gestation. It may have involvement in regulating body temperature, permeability barriers, and innate immunity.[1]

## REVIEW

Immaturity of the epidermal lipid layer in premature infants leads to potentially life-threatening and enhances the risk of infection. In premature infants, transepidermal water loss (TEWL) is inversely proportional to gestational age. In very low birth

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weight infants needed immediately compensated by humidified incubators, plastic wraps, and topical emollients that are incompatible with life. Poor integrity of the stratum corneum puts premature infants at risk of mechanical trauma and transcutaneous infections. The extent of epidermal water loss and the risk of infections with skin colonizing microorganisms in premature infants is thus directly proportional to the infant's degree of prematurity. Table 1 shows the skin differences between term and premature infants.[5,6,7]

**Table 1.** Comparison of skin features of premature and term infants [5,6,7]

| | Premature Infants | Term Infants |
|---|---|---|
| Skin thickness | 0.9 mm | 1.2 mm |
| Epidermal surface | Vernix (gelatin) | Vernix |
| Epidermal thickness | -20-25µm | -40-50 µm |
| Stratum corneum thickness | 4-5 µm | 9-10 µm |
| | 5-6 cell layers | > 15cell layers |
| Surface pH | - | High |
| Sebum | - | - |
| Spinosum glycogen content | High | Low or none |
| Melanocytes | Large number of cells; some mature melanosomes | Cell counts similar to those of young adults; low melanin production |
| Dermal-epidermal ridge | All known adult antigens are expressed; desmosomes are fewer and smaller | Structural and antigenic features are similar to adults |
| Eccrine sweat gland | Above dermis, inactive | Above dermis, almost inactive |
| Dermal papillae | | |
| Border with reticular dermal | Present, border not clear | Present, border not clear |
| Collagen fiber bundle size | Small | Small |
| Cell density | High | High |
| Epidermal reticular | | |
| Border with subcutis | Clear | Clear |
| Collagen bundle size | Small | Small |
| Cell density | High | Moderate-high |
| Elastic fiber | Rarely; very small with immature structures | Small size and immature structure; distribution similar to adult |
| Hypodermis | Well-developed fat layer | Well-developed fat layer |
| Functional difference | | |
| Level of water absorption | - | - |
| TEWL | Very high - high (depends on gestational period) | Low |

Premature infants are at a higher risk of experiencing thermoregulation problems due to thermal evaporation and TEWL, which is represented the passive diffusion of water over a gradient of water vapor. Studies show that thermoregulation problems are due to dysfunction in the autonomic nervous system, which controls the brown adipose tissue, vasomotor tone, and sweat glands. An example of autonomic dysfunction is a poor vasomotor response to cold stress.[8]

The skin surface in an infant is larger than in adults, which makes them more susceptible to TEWL. Transepidermal water loss is measured in grams per meter squared per hour, and higher values generally reflect a less favorable skin barrier. Transepidermal water loss generally occurs through diffusion and evaporation. The rate of diffusion is largely dependent on the function of the stratum corneum, whereas the rate of evaporation varies with the humidity of the infants' environment.[3]

The association between TEWL and gestational age in premature infants is inverted. Transepidermal water loss in infants at 24 to 25 weeks of gestational age decreases during the first few days of life after birth but still increases at 28 days after birth compared to the expected degree of 5-10 g/m$^2$/hr in term infants. It can reach as high as 100g/m$^2$/h in very immature infants, which indicates that if these infants were left in a dry

environment, they might lose 20–50% of their body weight in just 24 hours. With this level of TEWL, hypernatraemia, polyglobulia, and hypothermia would happen immediately, eventually leading to periventricular hemorrhage and death. This can be avoided by increasing the surrounding humidity. Incubators for premature infants, particularly those born before 32 weeks of gestation, are now routinely humidified. For the first few days, humidity needs to be as high as 80–90% to stop heat and fluid loss. Polyethylene wraps or caps can be used right away after delivery to prevent hypothermia and TEWL.[9,10]

Based on those problems, it can be concluded that the skin of premature infants is more susceptible to skin problems, transepidermal intoxication, and thermogenesis dysfunction compared to mature infants, so special management of the skin is needed.[3,11] Some strategies include avoiding mechanical damage, proper sterilization when doing invasive procedures, umbilical cord care, appropriate skin problems management, controlling TEWL using emollients and plastic wraps, appropriate bathing procedures, and incubator usage.[3,11]

In premature infants with less than 30 weeks of gestation, excessive TEWL can be life-threatening. Infants are wrapped in polyurethane foil and placed in a humidification incubator as soon as they are born, with an initial ambient humidity of ≥ 80%. After a week, ambient humidity is often gradually lowered due to worries about an elevated risk of infection. Standard phototherapy can raise TEWL.[10]

There is a remarkable regional variation in TEWL on the skin surface; it is often higher in the abdominal skin because this is the area where the epidermal barrier matures the least. Because there is less water vapor in the air, premature infants nursing under a radiant heater evaporates at faster rates. Even when relative humidity and ambient temperature are properly regulated, it is also enhanced (by 20%) during phototherapy; this is likely due to increased cutaneous blood flow. So, during phototherapy, premature infants' maintenance fluid intake should be appropriately increased. The neonatal epidermis is easily injured (for instance, by removing plastic adhesives), which results in a quantifiable disturbance of the function of the skin barrier.[12]

Exposure to air improves postnatal barrier maturation. Most premature infants' TEWL reaches term infants' levels in 10 to 15 days. The number of lamellar bodies in stratum granulosum cells, the thickness of the stratum corneum, and the barrier lipid content of the stratum corneum all grow in parallel with this functional maturation, according to studies conducted on mice. However, this process can take a lot longer in newborns with ultra-low birthweight (23–25 weeks gestational age). Recent research has shown that even in fully mature infants, it can take up to 12 months for TEWL to normalize to levels seen in older children and adults. This process is accompanied by a steady rise in Natural Moisturizing Factor (NMF) levels in the epidermis.[12]

Premature infants, in particular, are more susceptible to heat loss in infants. During the first week of life, evaporative heat loss rather than radiative heat loss accounts for the majority of heat loss. It has been demonstrated that the occlusive wrapping of Very Low Birth Weight (VLBW) newborns can stop harmful postnatal evaporative heat loss.[12]

The gestational age affects how much sweat is produced in response to a thermal stimulus. Premature infants typically cannot sweat in reaction to heat during the first few days of life, unlike mature infants. The development of sweating, however, is accelerated postnatally similarly to their adaptation to TEWL, so that virtually all premature infants are capable of sweating at the age of 13 days, even though the heat stimulus necessary is higher and sweat output lower than in term infants.[12]

Premature infants who use incubators tend to have higher insensible water loss (IWL) as a result of their immature skin barrier and the higher temperature of the incubator. This could lead to an imbalance of electrolytes and skin temperature. A retrospective cohort study of 182 infants with very low birth weight showed that the use of a humidified incubator significantly improved control of body temperature, fluid requirements, and electrolyte balance over 28 days postnatally in premature infants without an increase in infection rates.[13]

Neonatal skin surface pH ranges from 6.2–7.5, which is generally neutral or alkaline. The pH decreases quickly in the first week in both term and premature newborns and then gradually up to the fourth week of life when it reaches a range of 5.0-5.5, which is comparable to that in older children and adults. The stratum corneum's acidity promotes the colonization of commensal bacteria and prevents the development of pathogenic bacteria and fungi.[3]

Wound healing in infant skin is different from that of children or adults, even more so in premature infants. The most striking difference is the absence of an acute inflammatory response.[4] This would become a problem for premature infants, who are more at risk of developing skin problems.[5] This ties into another problem they could have, which is transepidermal intoxication.[6,7] Thermogenesis dysfunction is also a problem in premature infants, with thermal evaporation

and transepidermal water loss (TEWL) being the main problems.[8]

Infants' skin differs from older children's in terms of wound healing, thermoregulation, and transepidermal substance penetration. The most striking difference regarding wound healing in neonates' skin is the absence of an acute inflammatory response to trauma. Fetal platelet degranulation, aggregation, and production of fibrogenic platelet-derived growth factor (PDGF) transforming growth factor (TGF) β1, and TGF β are reduced. This is caused by the low number of neutrophils attracted to the wound site, so the damaged tissue is mostly cleaned by macrophages and fibroblasts.[4] This makes them prone to skin problems, such as diaper dermatitis, which is usually caused by a fungal infection such as *Candida* infection, and transepidermal intoxication.[4–6] The immature epidermal barrier can be penetrated by substances other than water, which then can lead to another problem, transepidermal intoxication. Transepidermal intoxication can occur in newborns, especially in premature infants. Alcohol used for medical procedures such as in antiseptic can cause skin irritation, which sometimes can even lead to skin necrosis; it is also neurotoxic; topical corticosteroids can cause adrenal suppression and hyperadrenocorticism; and last but not least, povidone-iodine can also cause skin irritation, which sometimes can even lead to skin necrosis and hypothyroidism. All of those problems usually appear when the substance is used excessively. The percutaneous risk and poisoning of newborns can be seen in Table 2.[6,7]

## DISCUSSION

At birth, skin is coated with vernix caseosa, which is often wiped off immediately after delivery, but removing it is inadvisable as it has antibacterial properties that may contribute to the protection of the newborn from bacterial infections.[28]

Bathing premature infants can result in temperature instability and stress.[13] It is advisable to reduce the bathing schedule every 4 days in premature infants and it is adequate to maintain skin integrity and skin flora composition. [13,14,15] Based on the previous literature review, using soap when bathing a premature infant is not recommended for the first 2 weeks.[6,16] If soap is used, it should be mild ph-neutral soap. Shampoo is not essential for the scalp, but the risks are minimal. A bath for a newborn should not last more than 5 minutes. The temperature of the bathwater should not exceed 37 °C.[17] Bathing in a bathtub is more beneficial because it prevents temperature variability in infants.[18]

Nails should be kept short and clean. Diapers should be changed frequently at least each nursing or feeding time. The napkin area should be cleaned with sterile water. Barrier creams that are petrolatum based or contain zinc oxide may be applied to the napkin area during changes to reduce the risk of irritation.[19]

The umbilical cord is an ideal place for microorganism growth, and it is also a direct passage to the bloodstream, making it more prone to infection (even systemic infection) than other parts of the body. Umbilical cord care varies by country and region or cultural groups within a country, and various substances are used.[20] Infections that often arise from the umbilical cord are omphalitis and associated thrombophlebitis, cellulitis, and necrotizing fasciitis.[16] The paradigm for umbilical cord care has shifted toward dry umbilical cord care in high-resource countries and in-hospital birth settings. While in resource-limited countries and for infants born outside the hospital setting, unhygienic substances continue to be applied to the umbilicus, creating a milieu ideal for the development of neonatal omphalitis. Topical antiseptics such as chlorhexidine are recommended, while still considering their potential side effects.[14,15]

Premature infants are subject to invasive procedures and increased handling. Routine use of tape and adhesive dressings can cause epidermal stripping and skin breakdown. To minimize skin damage, chemical adhesive removers should be avoided and adhesive bandages should be removed by stretching the bandage horizontally along the skin surface to gently break adhesive bonds with removal. When removed, silicone-based adhesives and hydrogel adhesives cause minimal trauma, providing an alternative when secure adherence is not critical.[13]

Various emollients have been shown to improve immature epidermal barrier function in premature infants and reduce TEWL. A comparative study between tri-lipid emollients and non-emollients found reduced TEWL by approximately 68% after 5 weeks. [21] Randomized controlled trials have shown that postnatal application of topical emollients such as sunflower seed oil, coconut oil, or mineral oils (petrolatum) can reduce TEWL in VLBW premature infants, improve skin integrity, and lower the risk of bloodstream infections in premature infants. However, there are issues regarding an increased risk of nosocomial infection, systemic candidiasis, and coagulase-negative staphylococcal infection in premature newborns using emollients.[10,22] If needed emollients containing a physiological balance of epidermal lipids are optimum for barrier repair.[23]

**Table 2.** Hazardous or potentially hazardous substances that can be absorbed through the skin of premature infants[6,7]

| Compound | Toxicity | Sources |
|---|---|---|
| Alcohol (methylated spiritss) | Skin necrosis, neurotoxic | Topical antiseptic, vehicle for topical medications/products |
| Alumunium* | Neurotoxicity | Metal containers for topical ointment |
| Aniline dyes | Methemoglobinemia | Laundry marks (historical) |
| Boric acid, borax | Shock, renal failure | Antifungals, talc powders |
| Benzocaine | Methemoglobinemia | Topical analgetics; teething products |
| Benzethonium chloride* | Carcinogen | Antiseptic soap |
| Benzyl benzoate | Neurotoxicity | Scabicide |
| Bicarbonate | Metabolic alkalosis | Baking soda for diaper dermatitis |
| Camphor* | Gastrointestinal toxin, neurotoxicity | Topical antipruritic; camphorated oils (Vaporub®; Campho-Phenique®) |
| Coal tars* | Carcinogen | Topical anti-inflammatory products |
| Chlorhexidine gluconate | Skin necrosis | Topical antiseptic |
| Corticosteroid | Adrenal suppresion, hyperadrenocorticism | Topical corticosteroids |
| Diphenhydramine | Neurotoxicity | Topica analgetics (Caladryl®) |
| Epinephrine | High output failure | Topical vasoconstriction |
| Gentian violet | Possibly carcinogenic | Antimicrobial |
| Glycerin* | Hyperosmolarity | Emollients; cleanser (Aquanil®) |
| Hexachlorophene | Neurotoxicity | Antiseptic soaps (pHisoHex®) (historical) |
| Iodochlorhydroxyquin | Optic neuritis | Topical antibiotics (Vioform®) |
| Imidazoles | Drug interactions secondary tp p450 inhibitoin | Topical antifungal medications: ketoconazole, miconazole, clotrimazole (Lotrimin®) |
| Isopropyl alcohol | Skin necrosis; neurotoxicity | Topical antiseptics |
| Lactic acid* | Metabolic acidosis | Topical keratolytics (Lac-Hydrin®) |
| Lindane | Neurotoxicity | Scabicide (Kwell®) |
| Mercury | Neurotoxicity; acrodynia; nephrotic syndrome | Disinfectants; teething powder (historical) |
| Methylene blue | Methemoglobinemia | Vital stain (historical) |
| Neomycin | Ototoxicity | Topical antibiotic (Neosporin®) |
| Nystatin* | Nephrotoxicity | Topical antifungal (Mycostatin®) |
| Phenol | Cardiac and neurotoxicity | Disinfectants (e.g., Castellani's paint) |
| Propylene glycol* | Hyperosmolarity; neurotoxicity | Topical vehicles; emolients, cleansers (Cetaphile®) |
| Povidone-iodine | Skin necrosis; hypothyroidism | Topical antiseptic (Betadine ®) |
| Prilocaine | Methemoglobinemia | Topical anesthetic (EMLA®) |
| Resorcinol | Methemoglobinemia | Topical antiseptic |
| Salicylic acid | Salicylism | Topical keratolytics |
| Silver sulfadiazine | Kericterus; argyria | Topical antibiotics (Silvadene®) |
| Sulfur* | Paralysis; death | Scabicide ointment |
| Triclosan* | Neurotoxicity | Topical antiseptic |
| Urea | Elevated BUN | Topical keratolytics/emolients |

*Potentially hazardous compounds

Proper sterilization when doing invasive procedures is necessary to minimize skin problems that could appear. Venepuncture, catheter insertion, and lumbar puncture are common invasive procedures performed on premature infants. Chlorhexidine, povidone-iodine, and alcohol are common antiseptics used for this procedure, but there's a concern with transepidermal intoxication when using them.[3] A review study tries to review common antiseptic use in each procedure and concluded that chlorhexidine may be the better option when compared to povidone-iodine because povidone-iodine is associated with significant systemic absorption and hypothyroidism.[14]

Skin problems in premature infants include diaper dermatitis, which is usually caused by a fungal infection such as *Candida* infection. [4–6] Management of diaper dermatitis is based on the timing. Management for early diaper dermatitis involves reducing occlusive exposure to urine and feces. Frequent diaper changes are recommended and barrier creams or simple emollients should be used with each diaper change. When *Candida* infection is apparent, topical antifungals can be used.[24]

Percutaneous drug toxicity has been reported in newborns. The direct correlation is to a higher surface area-to-weight ratio. Other susceptible factors include an immature drug metabolism system and the immaturity of the epidermal barrier in preterm infants.[25]

In conclusion, the skin of term and premature infants differs from that of older children. Skin barrier in premature infants skin is more fragile due to their immature development and is susceptible to environmental fluctuation and infectious assault, thus in greater need of appropriate interventions.

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