Expert Forum
NEONATAL SKIN HEALTH AND SKIN CARE SYMPOSIUM
Making Education Easy

About the Reviewers

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Ms. Kuller has a 30-year career in neonatal care and is currently a neonatal clinical nurse specialist at Children's Hospital and Research Center in Oakland, California. She has written numerous articles and book chapters on neonatal skin care and has been involved in several clinical research projects assessing the barrier function of the neonate's skin. Her special areas of research include the effects of adhesives, phototherapy, and the first bath on neonatal skin. Ms. Kuller has been a member of the AWHONN Neonatal Skin Care Evidence-Based Guideline development team for all three editions.

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Prof. Michael Cork is Head of Academic Dermatology at the University of Sheffield, School of Medicine and Biomedical Sciences, and an Honorary Consultant Dermatologist to Sheffield Children's Hospital and Sheffield Teaching Hospitals NHS Foundation Trust. His research is aimed at identifying gene-environment interactions leading to skin barrier breakdown in the development of atopic dermatitis and understanding how topical agents interact with the skin barrier, using this information to enhance the treatment of atopic dermatitis. In addition, he is closely involved in developing new treatments for psoriasis, such as the vitamin A metabolic pathway inhibitors. Prof. Cork was a member of the guideline development group for treatment of atopic eczema in children for NICE.

Welcome

to this review of the Australian College of Neonatal Nurses (ACNN) Conference Symposium on Neonatal Skin Health and Skin Care, held in Sydney on 12th September 2015. The forum featured presentations from international and local experts including Professor Michael Cork from the University of Sheffield, UK and Neonatal Clinical Nurse Specialist Joanne Kuller, USA. This review is a summary of the presentations at the symposium.

SKIN ASSESSMENT AND PRESSURE INJURY TOOLS AND TREATMENT

Ms Joanne Kuller, Neonatal Clinical Nurse Specialist, Children's Hospital and Research Center, Oakland, USA

Protecting the newborn's delicate skin and promoting an intact and healthy skin barrier is challenging but is important in the neonatal period, especially for infants in NICU. Routine assessment of skin is necessary; it allows for assessment of skin integrity breakdown risk and for early identification and treatment of skin problems. Skin breakdown can lead to systemic infection, increased morbidity, and increased cost of care.

What is skin barrier function?

The skin has the ability function as barrier against toxins and pathogenic organisms. Skin barrier function can be measured by the skin's ability to hold on to water (i.e. reduce transepidermal water loss [TEWL]), stay hydrated, and regulate pH. Immaturity, alterations in pH, skin injury or disease can all result in impaired barrier function. Skin barrier function is also influenced by the microorganisms colonized on the surface.

Figure 1 shows a cross section of the layers of the skin. The upper most layer of the skin is called the epidermis. The epidermis is comprised of two parts – the stratum corneum and the basal layer of the epidermis.

The stratum corneum is a non-living layer of skin comprised of fat and protein, often described as arranged like the bricks and mortar of a wall. The stratum corneum provides the barrier functions of the skin, protecting against toxins and microorganisms and retaining heat and fluid. The basal layer of the epidermis contains cells called keratinocytes, which create the stratum corneum. Beneath the epidermis is the dermis.

The dermis contains collagen and elastic fibers in a gel continuum and this provides the elasticity of skin over joints, as well as cushioning the body. Hair follicles, nerve cells, sweat glands and sebaceous glands originate in the dermis. Beneath the dermis is the subcutaneous layer, which is a layer of fat that is deposited largely in the third trimester of pregnancy. Many premature infants do not have a subcutaneous layer if they are born very early.

Infants have a defective skin barrier

Thinner stratum corneum

The stratum corneum contains 10 to 20 layers in adult skin. It does not function as well as adult skin throughout the first year of life and is about 30% thinner than that of adult skin.[1] There are only about two or three layers of stratum corneum in a baby born at < 30 weeks gestation,[2] while babies born at 23–24 weeks gestation have virtually no stratum corneum and therefore a negligible barrier function,[3] and high TEWL and heat loss.[4] Directly beneath the stratum corneum is the basal layer of the epidermis, and this is about 20% thinner than that of the adult.[5] Keratinocyte cells in this layer have a higher turnover rate, which may account for the faster wound healing that has been observed in neonates.[5]

Decreased cohesion between epidermis and dermis

The dermis in the newborn is thinner and not as well developed as the adult dermis. Collagen fibers are shorter and less dense, and the reticular layer of the dermis is absent, which makes the skin feel soft.[5] Between the epidermis and dermis are fibrils that connect these two layers of the skin. In premature infants, the fibrils are fewer in number than in full-term or adult epidermis, with wide spaces between connecting points.[2] The decreased cohesion between the epidermis and dermis places the premature newborn at risk for skin injury when medical adhesives attached to the skin are removed. The bond between the adhesive and the epidermis may be stronger than that between the epidermis and dermis, resulting in stripping of the epidermal layer and decreased skin barrier function.[6]

Skin pH

Skin consists of an 'acid mantle' which inhibits the growth of pathogenic microorganisms and gives immunologic properties to the skin.[7] Full-term newborns are born with an alkaline skin surface (pH > 6.0) but within 4 days the pH typically falls to < 5.0.[8] The skin pH in premature infants has been reported to be more than 6 on the first day of life, decreasing to 5.5 by the end of the first week, and then to 5.1 by the end of the first month.[9] Bathing in normal tap water and other topical treatments transiently affect skin pH,[10] and skin covered by nappies has a higher pH because of the combined effects of urine and occlusion.[11]

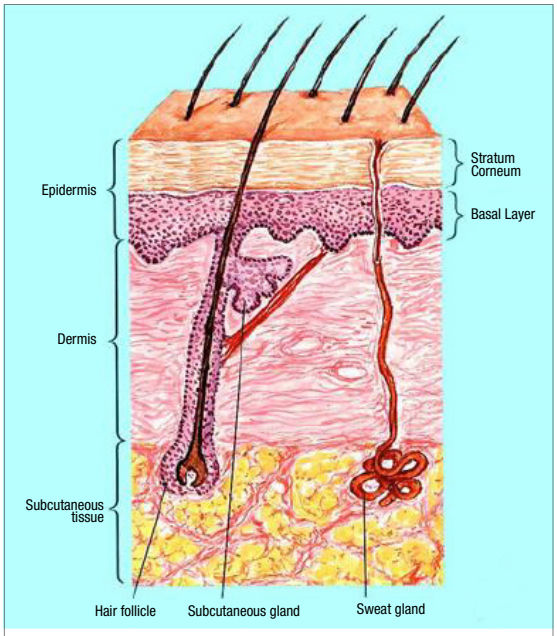


Figure 1. Cross-section of the skin

Skin and risk assessment tools

While there are a number of tools for assessing risk for skin injury, Ms Kuller cautioned that **risk assessment is not the same as skin assessment** and actually just looking at a baby's skin to determine whether it has broken down. One of the challenges in skin risk assessment is that the term "pressure Injury" can encompass multiple categories of iatrogenic tissue damage to the skin.

Braden Q risk assessment tool

The Braden Q risk assessment tool is difficult to use in NICU infants because it measures factors such as mobility, activity and ability to respond to verbal commands (absent in all NICU infants) and moisture (present in all NICU infants). Furthermore, no studies to date suggest that risk assessment tools reduce the development of new pressure ulcers. Therefore, the Braden Q is not a worthwhile tool in Ms Kuller's opinion.

Neonatal Infant Pressure Injury Risk and Assessment tool

Deanne August and colleagues from Townsville Hospital reviewed 247 patients with mean gestational age of 28 weeks and published a cohort study on the prevalence of pressure injuries and identified contributing factors (Neonatal Infant Pressure Injury Risk and Assessment [NIPIRA] tool).[12] Skin injury was identified in 31% of babies. Causes of injuries included indwelling vascular catheters (22.5%), noninvasive CPAP delivery devices (14.0%), and oxygen saturation and temperature probes (18%). Interestingly, they found that 32% of injuries could not be associated with a specific risk factor. The NIPIRA tool is being further developed and validated.

Neonatal Skin Condition Score

Because pressure ulcers from devices are the most common pressure-related injuries in the neonatal period, it is necessary to be aware of which devices are often involved (such as nasal CPAP), and to assess skin condition frequently. Consider using a valid and reliable assessment tool to provide an objective measurement of skin condition. One such tool is the Neonatal Skin Condition Score (NSCS). The NSCS is not a risk assessment tool but rather evaluates overall skin condition on a nine-point scale according to three categories: erythema, breakdown, and dryness. It was used in the original AWHONN Neonatal Skin Project (2,820 neonates) and has been validated for all gestational ages for detection of pathologic skin conditions – although is not specific for pressure ulcers.

Risk factors and causes of skin injury

Risk factors for skin injury in neonates include the following:

- Gestational age < 32 weeks
- Oedema
- Poor nutritional status
- Immobility
- Use of vasopressors
- Surgical wound
- Ostomies
- Nasal CPAP
- Use of endotracheal tubes, nasogastric or orogastric tubes, vascular access devices, monitors, electrodes, probes
- High-frequency ventilators
- Extracorporeal membrane oxygenation
- Prolonged EEG monitoring

Potential causes of skin injuries in neonates include adhesive removal, burn/thermal injury, abrasion/friction, nappy dermatitis, pressure ulcers, infection, and use of a cooling blanket.

Pressure ulcers

Pressure ulcers are one of the most common causes of skin injury in premature infants. Pressure ulcers are defined as localized areas of tissue destruction that develop when soft tissue is compressed between a bony prominence and an external surface for an extended period of time. This compression causes tissue ischaemia and buildup of metabolic wastes at the site, leading to the development of a pressure ulcer.[13]

Pressure ulcer scoring is shown in Figure 2. It is important that stage I is identified early so that immediate intervention can occur before the ulcer progresses to stage II.

Pressure ulcers can be prevented by vigilant inspection, use of gel pillows, special beds and surfaces, frequent turning, good nutrition and oxygenation, maintaining a table skin temperature and use of a barrier ointment.

Nappy dermatitis

Prolonged contact of skin with urine and faeces is a primary cause of nappy dermatitis. This is because some of the bacteria in faeces contain enzymes that release ammonia from urine, contributing to raising skin pH which in turn activates proteases and disrupts the epidermis. Nappy use also increases skin surface pH and skin wetness, with wet skin known to increase the susceptibility of skin to damage from friction.[14] Risk factors for nappy dermatitis include malabsorption, foecal incontinence, atopic dermatitis, oral antibiotics, and simply wearing nappies.

Preventing nappy dermatitis

Skin care practices such as bathing and emollient use can greatly influence the ability of the skin to function as a barrier against environmental stresses such as those causing nappy dermatitis.[15]

Frequent nappy changes and use of absorbent nappies helps decrease skin wetness and contact with faecal enzymes, thereby maintaining skin pH. Super absorbent disposable nappies have been associated with a reduced incidence and decreased severity of irritant nappy dermatitis when compared with washable cloth nappies.[14]

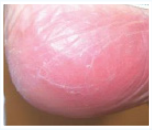
Water alone is not an effective cleanser

Water and cotton, mild soap and water, or baby wipes are adequate for cleansing the nappy area.[16] Water alone may be insufficient to remove faeces and fats.[17] Some studies show that water and mild cleansers have similar effects on skin pH and hydration, while others show that water alone may be more drying.[18] A baby wash containing emollients may offer further protective effects.[19] Excessive scrubbing and washing may promote irritation and further damage skin barrier properties, therefore gentle cleansing, rinsing and patting dry is recommended.[20]

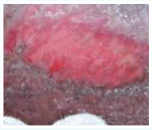
Wipes may be better than water

A lot of parents do not want to use baby wipes at all. While wipes containing alcohol are not advisable, not all wipes are bad. Studies have shown that wipes may be a better cleanser than water because they have a lower pH and therefore do not disrupt the baby's acid mantle.

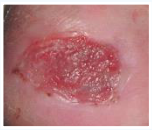
Baby wipes with a pH buffering capacity have been shown to be well tolerated and more comfortable among infants aged 3–24 months with atopic dermatitis when compared to the use of water only and a wash cloth.[21] A randomised, controlled trial of 280 full-term infants showed the use of wipes to be similar to the use of cotton wool and water when measuring TEWL, pH, redness, and skin colonization at 48 hours and 4 weeks.[22] Mothers of infants in the water group reported more nappy rash. A randomised, controlled trial of 130 NICU infants comparing two types of wipes to cloth and water only found improved nappy area skin condition and barrier function when using wipes made from a soft, nonwoven material with water and emollient cleansers.[23]



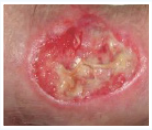
Stage: I
Nonblanchable Erythema
Intact skin with non-blanchable redness of a localized area usually over a bony prominence. Darkly pigmented skin may not have visible blanching; its colour may differ from the surrounding area.



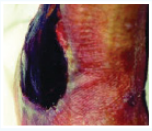
Stage II:
Partial Thickness Skin Loss
Partial thickness loss of dermis presenting as a shallow open ulcer with a red pink wound bed, without slough. May also present as an intact or open/ruptured serum-filled blister.



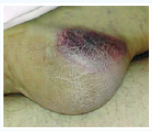
Stage III:
Full Thickness Skin Loss
Full thickness tissue loss. Subcutaneous fat may be visible but bone, tendon or muscle are not exposed. Slough may be present but does not obscure the depth of tissue loss. May include undermining and tunneling.



Stage IV:
Full Thickness Tissue Loss
Full thickness tissue loss with exposed bone, tendon or muscle. Slough or eschar may be present on some parts of the wound bed. Often include undermining and tunneling.



Suspected Deep Tissue Injury: Depth Unknown
Purple or maroon localized area of discoloured intact skin or blood-filled blister due to damage of underlying soft tissue from pressure and/or shear. The area may be preceded by tissue that is painful, firm, mushy, boggy, warmer or cooler as compared to adjacent tissue.



Unstageable: Depth Unknown
Full thickness tissue loss in which the base of the ulcer is covered by slough (yellow, tan, gray, green or brown) and/or eschar (tan, brown or black) in the wound bed.

Figure 2. Pressure ulcer staging

Preventing nappy dermatitis

- Maintain an optimal skin environment in the perineal area
  - change nappies every 1–3 hours during the first month
  - consider using superabsorbent disposable nappies
  - consider nappy holidays
  - some wipes are better than plain water
- Implement strategies to reduce the risk and severity of nappy rash
  - perform skin assessment
  - use petrolatum- or zinc oxide-based ointment
  - avoid rubbing skin barrier product off during cleansing
  - avoid alcohol-containing products
- Treat skin excoriation from nappy dermatitis
  - protect injured skin with thick application of barrier cream
  - consider cholestyramine agents
- Treat nappy dermatitis complicated by *Candida albicans* with barrier cream and antifungal agents
- Talcum powder, topical antibiotics and topical corticosteroids are not recommended

Principles of wound healing

Ongoing wound assessment is important to monitor healing and documentation should be considered. Record the colour of tissue in the wound base; slough is moist stringy yellow or grey loose tissue, while eschar is tough and leathery and most often black or dark in colour. Note the location and size of the wound and depth from skin surface to the deepest part of the wound bed. Record the amount, colour, and odor of exudate and the condition of surrounding skin. Finally, consider using photographs to monitor healing.

Principles of wound healing include the following:

- Gentle cleansing
  - never put anything on a wound that you wouldn't put in your eye
  - avoid use of disinfectants
  - irrigation provides gentle debridement
- Moist wounds heal faster than dry wounds
  - as much as 3–5 times faster
- Grease is good for prevention of skin surface breakdown
- Attention to nutrition, oxygenation and fluid balance can enhance healing
- Culture and treat if infected
- Provide ongoing wound assessment

Suitable wound healing products include gauze (primarily for closed wounds), hydrocolloids (gentle, moldable wafers), polyurethane films (transparent), hydrogels (promote epithelialization), foams (sponge-like and very absorptive), wound stabilizers (nonadherent but protective), barrier creams and pastes, and silicone.

TAKE HOME MESSAGES

- Neonates and infants are all at risk for skin injury while in the hospital
- Causes include IV extravasations, nappy dermatitis, ischaemic pressure injuries, device related pressure injuries and medical adhesives
- Risk assessment along with implementation of targeted prevention and treatment strategies can reduce skin injury
- Prolonged contact of skin with urine and faeces is a primary risk factor for nappy dermatitis
- Bathing and emollient use can improve the ability of the skin barrier to protect against nappy dermatitis
- Baby wipes and a mild baby wash may be more effective than water alone at cleansing the nappy area

DEVELOPMENT OF THE NEONATAL SKIN MICROBIOME

Ms Joanne Kuller, Neonatal Clinical Nurse Specialist, Children's Hospital and Research Center, Oakland, USA

In addition to the growing body of evidence about the uniqueness of neonatal skin, recent advances have enabled clinicians to understand the processes involved in colonization of skin with microorganisms. The term microbiome describes the collective genomes and gene products of the microbes living within and on humans.

As a result of the NIH-sponsored Human Microbiome Project, bacteria are now identified through DNA analysis.[24] Most of these bacteria are healthy or commensal bacteria and some are pathogens. New research suggests that a disease state may not simply be the presence of pathogens but the absence of commensal bacteria. Beneficial bacteria aid in development and stimulation of the gut mucosa, development of immunity, protection from diverse pathogens, and vitamin production.

Vaginal vs Caesarean delivery

In the newborn period and in infancy, the skin and gut microbiome are influenced by the mode of delivery.[25] As shown in Figure 3, the microbiome of babies born vaginally matches the mother's vaginal bacteria, whereas the microbiome of babies born by Caesarean section (C-section) match the mother's skin bacteria. During vaginal birth, contact with the mother's vaginal and intestinal flora colonizes the skin and gut. During C-section delivery, contact of the newborn's mouth with vaginal and intestinal microbiota is missing: more non-maternally derived bacteria is seen; less diverse flora is seen; there is delayed intestinal colonization; and the skin surface is dominated by *S.aureus*. The relevance of the influence of delivery mode on the skin microbiome is not yet clearly understood, but this information may generate a better understanding of how some skin and gut disorders develop.

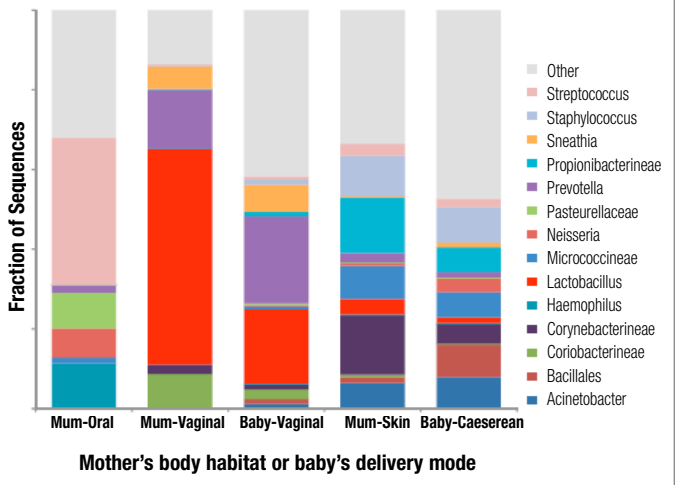


Figure 3. Microbiome transmission from mother to baby at birth correlates with region of first maternal contact[25]

Factors promoting a healthy microbiome

Current research shows that a baby's gut is colonized from four sources: placenta during pregnancy, birth canal during vaginal birth, mother's skin from skin-to-skin contact, and breastfeeding. Intestinal bacteria promote development of the gut's immune system, stimulate the production of antibodies, help reduce an over-reactive immune response and aid in food digestion. Of note, the incidence of inflammatory conditions in childhood, such as atopic dermatitis, asthma and food allergies are rising. Therefore, proper and early establishment of a healthy skin microbiome may affect the development of skin immune function and the development of the systemic immune system.

Commensal bacteria are transferred to the baby during and immediately after birth via the birth canal, immediate skin-to-skin contact, and breastfeeding. Full term birth, avoidance of antibiotics and exposure to a variety of microorganisms also promote a healthy microbiome. In babies born by C-section, skin-to-skin contact is associated with enhanced breastfeeding, less cold stress, decreased crying and longer periods of alertness, as well as transfer of commensal bacterial from the mother.

Microbiome seeding

In babies born by C-section, there is a growing practice of swabbing newborns with healthy bacteria from the mother's vagina. Dr Dominguez-Bello, a microbiologist at New York University School of Medicine, is at the forefront of research about seeding. She recently studied 21 babies and found that swab seeding positively affected the microbiome in C-section newborns. According to Dr Sandy Dietert from Microbirth, a documentary revealing the microscopic events taking place during childbirth, "The single most important thing we can do for a healthy baby across a life-course is to ensure that microbial seeding occurs completely at birth through vaginal delivery when possible, that skin-to-skin contact occurs and that the microbes are supported through breastfeeding of significant duration."

Considerations for the first bath

At birth, the skin of newborns enters a process of change. It is recommended that the first bath be given once the infant has achieved thermal and cardiorespiratory stability. It is ideal to wait at least 2 hours, but up to 4 hours is recommended for late preterm infants. Keep the duration of the bath as short as possible (5–10 minutes) to limit changes in the infant's physiological parameters. Warm tap water should be used with a minimal amount of pH-neutral or slightly acidic cleanser to assist with removal of blood and amniotic fluid. Vernix assists in development of the acid mantle of the skin and protects against bacterial and fungal organisms so should not be removed during the first bath.[14]

Antibiotic use alters the microbiome

Maternal antibiotic use alters the oral and intestinal microbiota composition. Adult studies show that antibiotics reduce microbial diversity within days and may upset the GI tract for several years. C-section mothers are routinely given antibiotics, which raises the question of whether antibiotics are a factor in the different gut microbiome of the C-section delivered infant and influence higher asthma and allergy rates.

In infants given antibiotics, an overall reduction in the diversity of microbial community is seen. An increased incidence of necrotizing enterocolitis (NEC) and diarrhoea may be related to the use of antibiotics in very low birthweight infants, as well C-section deliveries. Faecal samples from NEC patients have a microbial analysis distinct from non-NEC patients.

Should we reconsider antimicrobial bathing?

Newborns are at increased risk of toxicity from topical agents. Their skin has a larger surface area compared to body weight, resulting in greater exposure to topical agents. The stratum corneum maturity and integrity are factors, especially in premature infants. The more alkaline pH of skin surface increases permeability, and occlusion (i.e., wearing a nappy) compromises the stratum corneum and skin barrier function. Furthermore, newborns have an immature renal and hepatic function, reducing excretion of absorbed agents. A randomised controlled trial of 94 full term newborns showed that chlorhexidine gluconate (CHG) significantly reduced *S. aureus* prevalence in the armpit at 24 hours compared to neutral soap (13.6% vs 36.7%, respectively).[26] However, a randomised controlled trial of 60 premature infants born at 28–36 weeks showed that compared to no cleansing, CHG reduced *S. aureus* prevalence by 62% in the armpit at 24 hours, but not at 72 hours.[27] There was no significant reduction

compared to saline cleansing. In the groin, there was no significant difference among the three groups at 24 or 72 hours. All of these factors have led clinicians to question whether we should reconsider routine antimicrobial bathing of NICU neonates.

The US FDA has issued a labelling change for antiseptics containing CHG, warning that CHG-containing skin antiseptics should be used with caution in premature infants or infants less than 2 months of age, as they may cause chemical burns. At the same time, case reports of CHG/alcohol skin disinfectants and dressings causing skin injuries are becoming more frequent; therefore, the selection of skin disinfectants for extremely premature infants remains a dilemma for clinicians.

TAKE HOME MESSAGES

- Goal is to protect neonatal skin and promote future skin health
- Normal skin flora are helpful in protecting skin from infection
- Care practices should promote presence of commensal bacteria
- Bathing with water alone may not be better than using gentle baby wash
- Skin disinfection vs maintenance and promotion of commensal bacteria is a complicated issue

Ms Kuller: overall conclusions

Protecting newborn's skin and maintaining a normal skin barrier is crucial in the neonatal period, particularly for infants in NICU. Normal skin flora is helpful in protecting the skin from infection and as such, care practices should promote the presence of beneficial bacteria. Routine assessment of infant skin enables early identification and treatment of skin injury, of which nappy dermatitis is a common cause. Bathing with a mild baby wash, and use of wipes and emollients can improve the ability of the skin barrier to protect against nappy dermatitis, and may be more effective than water alone.

PREVENTING ATOPIC DERMATITIS BY CHANGING THE WAY WE TREAT A NEWBORN'S SKIN FROM BIRTH

Professor Michael Cork, Head of Academic Dermatology, University of Sheffield Medical School, UK

Maintaining the skin barrier is key to healthy skin. The normal skin barrier protects the body from the penetration of irritants and allergens. In an infant the skin barrier has not matured and as a result is much less protective against the environment than in an older child and an adult. This is why the infant is vulnerable to diseases which are caused by a defective skin barrier. The presence of a normal skin barrier is important in the maintenance of the normal microbiome.

What is at stake if baby skin is not cared for appropriately?

A baby with the genetic predisposition to develop atopic dermatitis can develop it if we don't care for their skin appropriately. Atopic dermatitis can be mild, or much more severe with devastating effects on the child and their parents at a crucial time in their development. The prevalence of atopic dermatitis among babies and children has risen from around 5% in the 1940s to up to 25% today. Clearly over this period genetics haven't changed, but our environment has, particularly the way we treat babies' skin.

In 1991, Duff made the point that current medicine only treats clinical disease. He identified the treatment of genetic susceptibility and preclinical disease as the future of medicine for all diseases. If we could treat a baby with a genetic predisposition for any disease we might be able to prevent it from developing. In Figure 4, a baby is shown with the genetic susceptibility to develop atopic dermatitis. The baby has a breakdown in the skin barrier, leading to subclinical inflammation; but the baby's skin still looks totally normal. Eventually the baby develops atopic dermatitis and is treated. The future of atopic dermatitis treatment lies in proactively preventing it from developing in the first place.

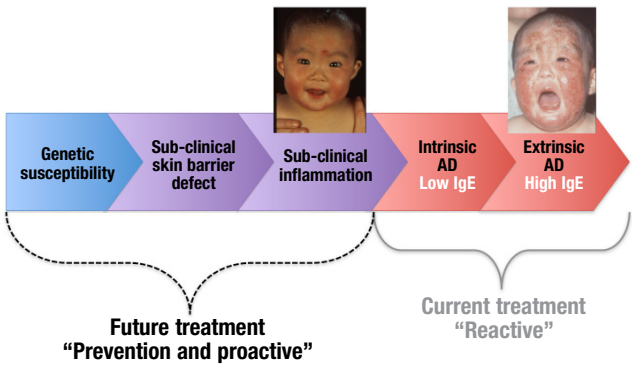


Figure 4. The future of atopic dermatitis treatment

Preventing the 'atopic march'

Atopic dermatitis is caused by skin barrier disruption, as a result of a complex interaction between genes and negative environmental factors such as harsh soaps and detergents that break down the skin barrier. Allergens can then enter the skin and atopic dermatitis develops. Atopic dermatitis may lead on to other diseases such as food allergies, asthma, and hay fever; this process is known as the 'atopic march'. But it can be prevented by changing the environment a new born baby is exposed to from negative to positive. Importantly, a window of opportunity exists in the first few months after birth to change the environment to prevent the development of atopic dermatitis. By changing the way we treat a baby's skin from birth, we can prevent the development of atopic dermatitis. Everything we put on a baby's skin from birth, including emollients, wash products and wipes, should be designed to enhance the skin barrier rather than damage it.

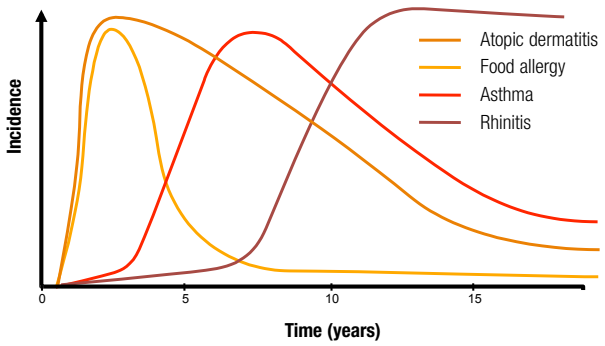
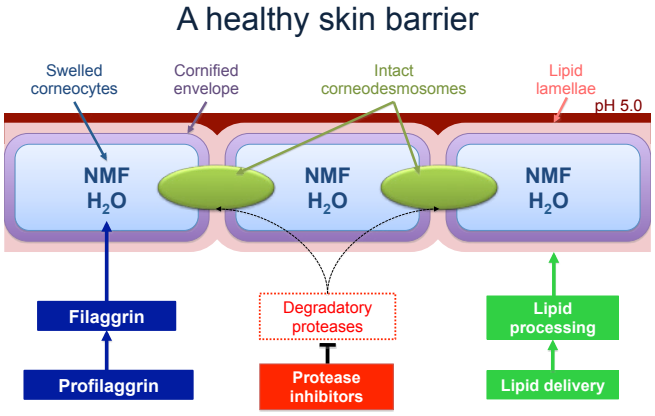


Figure 5. Atopic dermatitis: part of the atopic march

The importance of low pH for maintaining normal skin

Figure 6 shows a normal skin barrier compared with a defective skin barrier. Within the skin are the skin cells (corneocytes) which act like bricks in a brick wall. The lipid lamellae act like mortar in a brick wall. Corneodesmosomes are like iron rods, linking the skin cells together, giving a normal skin barrier tensile strength. Within the corneocytes is a substance termed natural moisturising factor (NMF), which is generated by the breakdown of filaggrin. NMF has two main roles: 1) it attracts water, making skin cells swell to close gaps between them; and 2) it contains acids which are absolutely pivotal to normal skin barrier function. These acids keep the pH of normal skin to around 5–5.5. Skin cells are shed from the surface of the skin by the



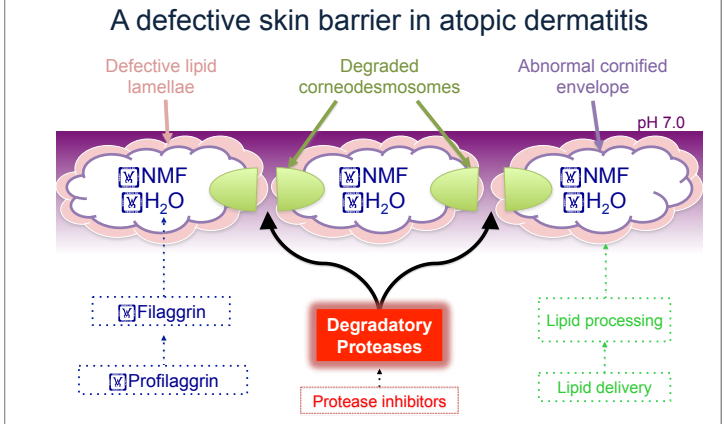


Figure 6. A normal vs defective skin barrier

breakdown of corneodesmosomes by protease enzymes. It is very important that the proteases are kept in check because otherwise corneodesmosomes would break down all the way through the skin barrier allowing allergens to enter. Proteases are held in check in normal skin by protease inhibitors, but perhaps even more important is low pH. Low pH switches off proteases, which is why low pH is important for maintaining normal skin. Low pH also switches on lipid lamellae ('mortar') production.

When an infant is genetically predisposed to atopic dermatitis, there is a defect in the filaggrin gene,[28] leading to less NMF, and therefore less acids; the pH of the skin rises to 7.0. High pH switches on proteases which breakdown the corneodesmosomes. High pH also switches off the lipid processing enzyme so the lipid lamellae start to breakdown. The result is a defective skin barrier, leaving the infant more vulnerable to the effects of the environment. When the stratum corneum is impaired, e.g. by hard water, soap and detergents elevating skin pH from 5.5 to 7, 8, or even 9, the skin barrier can no longer prevent allergens and infections from reaching the dermis, leading to inflammation characteristic in atopic dermatitis and the development of allergies. The skin barrier may be restored by avoiding negative environmental influences, and protected through skincare regimes that involve products of optimal pH that repair/respect the skin barrier. By protecting the skin barrier, the atopic march of atopic dermatitis, asthma, food allergies and hay fever may be prevented in some babies.

Development of peanut allergy in childhood

In 2003 Lack and colleagues showed that the main route of sensitization to peanuts was not by eating them but through the skin.[29] At that time, peanut oil was used in multiple products from emollients to barrier creams. The group have since shown that feeding peanuts to non-allergic children can actually induce tolerance. This shows that the way food allergens enter the immune system and the time at which they enter during newborn development is very important.

Assessing the effect of topical products on the skin barrier

We cannot use clinical measures to assess the effects of topical products on the skin barrier, because babies do not have clinical atopic dermatitis at birth. What we can do is look inside the skin and determine whether the barrier is breaking down. Assays have been developed to measure the effect of wash products, wipes and emollients on the skin barrier by measuring protease activity, antimicrobial peptides, NMF components, cytokines and pH (Figure 7). These assays are much more sensitive than clinical scoring. A protease assay by Cork and colleagues showed the clinical relevance of the effect of skin pH. Protease activity in normal skin (pH 5.0) was turned off, but was switched on in skin with current atopic dermatitis (pH 5.7) – without the addition of any topical products. With the addition of products such as soap or detergent, pH was raised even more (8.5), leading to acute atopic dermatitis.

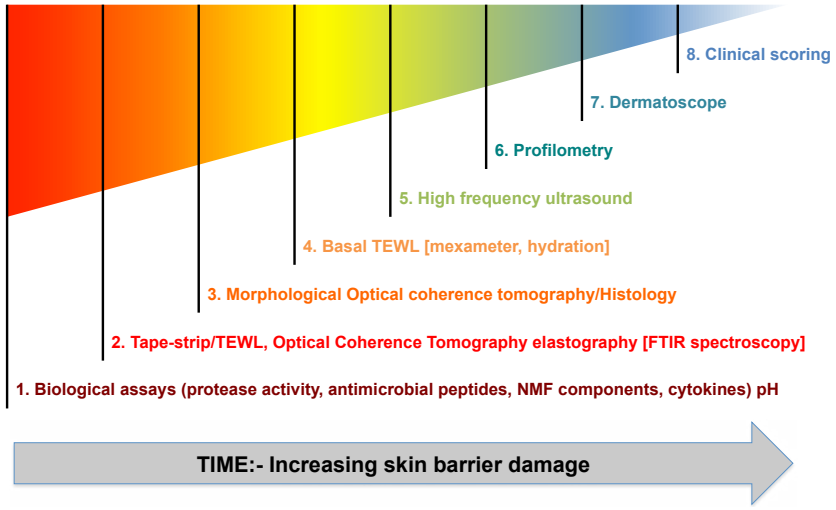


Figure 7. Measuring the effects of wash products on skin: sensitivity of assessments

Myths about baby skin care: water is good

Is water good? How safe is water? What is water? The pH of water alone is 7.2, but water hardness and harsh soap raises pH **even more**. Water pH can be lowered to an optimal 5.5 using appropriate cleansers. Water is irritant because of the calcium carbonate content, and hard water has been shown to increase the prevalence of atopic dermatitis.[30] However, a randomised controlled trial of water softeners showed no benefit for atopic dermatitis,[31] because water softeners substitute sodium for calcium, which has a slightly higher pH. So the challenge is to lower the pH of water by using a wash product that soaks up calcium, known as a 'chelator'.

Myths about baby skin care: all wash products are bad

Water alone is not an effective cleanser because it is unable to remove protein, fats, urine and faeces. Detergents are able to remove these impurities without the need for excessive friction. But there are many types of detergent; some have a high pH and can disrupt the skin barrier, such those containing sodium lauryl sulfate (SLS), while at the other end of the enormous spectrum are very, very mild detergents with low pH (Figure 8).

Professor Cork and colleagues conducted a study comparing the effects of ivory soap versus a wash product formulated for newborns (Top To Toe) on skin surface pH and protease activity. [Danby and Cork, unpublished] A 2-minute wash in bath water containing ivory soap raised skin pH to 6.8 at 15 minutes and maintained it at around that level for 4 hours. In contrast, Top To Toe wash raised skin pH to about 5.7 at 15 minutes, and maintained it at slightly lower than that level for 4 hours. These results were reflected in measurements of

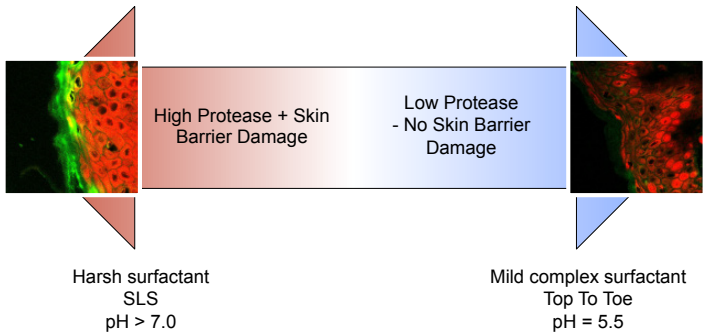


Figure 8. Spectrum of surfactant wash products: effects on protease activity in the skin barrier

protease activity over 4 hours; ivory soap increased protease activity substantially whereas Top To Toe wash did not increase protease activity.

A randomised controlled trial of 370 healthy full term infants showed that bathing with Top to Toe wash was no worse than bathing with water alone in terms of skin water loss, pH alterations, and clinical observations of dry skin.[32]

Professor Cork and colleagues then evaluated the effects of three different cleansers on newborn skin. [Danby and Cork, unpublished]. At weeks 2 and 4, an organic baby soap (Earth Mamma Angel Baby) increased pH, TEWL and protease activity substantially compared to two liquid cleansers (Top To Toe and Neutrogena). When adult women used these products on their skin for 4 weeks, the organic soap altered the microbiome but the two liquid cleansers did not. Professor Cork concluded that not only did the soap product damage the skin barrier but it also damaged the microbiome. So it really matters which type of product we use on the skin because harsh products can have a profound effect on the development of atopic dermatitis.

TAKE HOME MESSAGES

- Gene-environment interactions drive atopic dermatitis progression
- Negative environmental factors such as harsh soaps and detergents can break down the skin barrier
- Genetically-predisposed infants are at risk for atopic dermatitis if their skin is not cared for appropriately
- Atopic dermatitis and the atopic march can be prevented by changing the environment skin is exposed to from birth
- Low pH is important for maintaining normal skin
- Water alone is not an effective cleanser:
  - cannot dissolve impurities
  - high pH
- The high pH of water can be lowered using an optimal wash formulation
- Detergents containing SLS have a high pH and can disrupt the skin barrier
- Optimal wash products, wipes and emollients with very mild detergent maintain a normal skin barrier and normal skin microbiome and can prevent the development of atopic dermatitis

EMOLLIENT THERAPY: TREATMENT AND PREVENTION OF ATOPIC DERMATITIS

Professor Michael Cork, Head of Academic Dermatology, University of Sheffield Medical School, UK

Not all emollient formulations are the same

Repair of the skin barrier is the first step in both the treatment and prevention of atopic dermatitis. This involves removing all negative environmental factors and replacing them by positive interventions. Emollients formulated with ingredients that restore lipid levels, improve hydration, replenish depleted levels of NMF, and which offer significant buffering capacity, such that skin pH is normalised and the microbiome minimally affected, may offer clinically protective benefits. However emollients which are not correctly formulated can damage the skin barrier rather than repair it. When selecting an emollient it is essential to know its formulation and the effect of the formulation on the skin barrier.

In a pilot trial of infants genetically predisposed to develop atopic dermatitis, emollient use from birth reduced the prevalence of atopic dermatitis by 50% at 6 months compared to no treatment (Figure 9).[33] Emollients used in the trial were sunflower seed oil with a high ratio of linoleic/oleic acid, Doublebase Gel, liquid paraffin 50% in white soft paraffin, Cetaphil Cream, or Aquaphor Healing Ointment. None of the emollients contained SLS.

Simple occlusive emollients containing oil such as paraffin or petrolatum are useful in infants with a very defective skin barrier, but are not very cosmetically acceptable and need to be applied very frequently (every 30–60 minutes to have optimal effect). Furthermore, such ointments only produce a partial repair of the skin barrier – the underlying defect is not repaired.

Repair of the skin barrier can be achieved by humectants, which lower pH and retain water in the skin barrier. Examples include urocanic acid, pyrrolidone carboxylic acid, lactate citrate, urea and glycerol. When humectants are combined with occlusive emollients, the skin barrier can be partially repaired at the surface as well as within.

Lipids can be returned to the skin barrier by incorporating physiological lipids such as ceramides, cholesterol, linoleic acid, and palmitic acid into emollients. Natural lipids may help to restore normal barrier function; however, this is an area of ongoing research.

Buffers can also be added to emollients to reduce pH. Importantly, pH buffered products need to keep skin pH lowered for several hours, not just a few minutes, in order to repair the skin barrier and microbiome.

Aqueous cream should never be used in atopic dermatitis

Would you use a cream produced in 1958 on a baby's skin? Aqueous cream first appeared in the British National Formulary in 1958. Its formulation containing 1% SLS remains largely unchanged today. SLS is one of the harshest surfactants and can cause significant damage to the skin barrier.

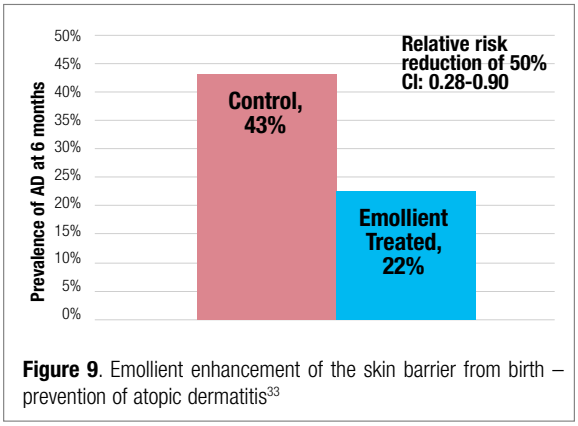


Figure 9. Emollient enhancement of the skin barrier from birth – prevention of atopic dermatitis[33]

Aqueous cream was shown in an audit of infants and children with atopic dermatitis to cause irritation (sometimes very severe) in 55% of them.[34] Consequently, further studies of the effects of aqueous cream were conducted and it was shown to cause severe damage to the skin barrier in adults with a previous history of atopic dermatitis,[35] and 20% thinning of the skin barrier in normal adult skin.[36] In a study in healthy volunteers, aqueous cream raised skin TEWL, whereas yellow soft paraffin reduced TEWL.[Danby and Cork, unpublished] Importantly, NICE guidelines have recommended that aqueous cream should never be used as a leave-on emollient in infants and children with atopic dermatitis.[37]

Myths about baby skin care: olive oil is good

Olive oil contains oleic acid which can disrupt skin barrier function.[38] Topical application of olive oil has been shown to compromise the integrity of the adult stratum corneum and induce mild skin irritation.[39] In contrast, the same study showed that sunflower seed oil, which

contains linoleic acid, preserved stratum corneum integrity, did not cause irritation, and improved hydration. Of note, some sunflower oils are genetically modified in order to taste like olive oil and as such contain high levels of oleic acid and low levels of linoleic acid.

Colloidal oatmeal repairs the skin barrier

Colloidal oatmeal, a natural product derived from oat grains, induces the skin to repair itself by producing more fatty acids to make ceramides. A paper from 1953 demonstrated that colloidal oatmeal reduced the skin pH of elderly people with atopic dermatitis for three hours.[40] A randomised controlled clinical trial in 30 adults with dry skin showed significant benefits of a moisturizing lotion containing colloidal oatmeal (Aveeno) versus its vehicle control for scaling, skin dryness and hydration at 21 and 28 days.[41] Another study compared the effects of Aveeno, aqueous cream and Epaderm cream (0.5% SLS at the time of study; now contains no SLS) on skin pH.[Danby and Cork, unpublished] Aqueous cream and Epaderm cream raised pH for 6 hours but Aveeno lowered pH for 3 hours.

TAKE HOME MESSAGES

- Not all emollient formulations are the same
- When selecting an emollient it is essential to know its formulation and its effect on the skin barrier
- Emollients which are not correctly formulated can damage the skin barrier rather than repair it
- Aqueous cream contains 1% SLS which can cause significant damage to the skin barrier
- NICE guidelines recommend that aqueous cream should never be used as a leave-on emollient in infants and children with atopic dermatitis
- Olive oil can damage the skin barrier
- Colloidal oatmeal can repair the skin barrier
- The correct emollient formulations can treat existing atopic dermatitis, prevent flares and prevent atopic dermatitis developing

Professor Cork: overall conclusions

In conclusion, a normal infant has a defective skin barrier. If this skin is not cared for appropriately, an infant with the genetic predisposition to develop atopic dermatitis is at high risk of developing it, because gene-environment interactions drive the progression of the disease. The skin barrier may be restored by avoiding negative environmental influences, and protected through skincare regimes that involve products that repair/respect the skin barrier. Such regimes include washing with mild cleansers that maintain normal protease activity and washing with water that is not hard. Emollients formulated with ingredients that normalise skin pH and minimally affect the microbiome may offer clinically protective benefits. Enhancing skin barrier function, through the avoidance of negative environmental influences such as harsh detergents and harsh emollients, in babies at risk of atopic dermatitis could prevent the development of the disease in some of them.

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