What’s Unique about Baby Skin?
Anatomic and Physiologic Differences
Newborn Skin Assessment

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Disclosures
• Team leader for revision of the Neonatal Skin Care Guideline (AWHONN); due to be released in 2013
• Investigator-initiated grant to study the first bath in full term newborns, 2011 (Johnson & Johnson Consumer Products)
• Member, professional advisory panel for 3M Skin and Wound Care Division
• Will be discussing off-label use of some products

Neonatal Skin Care
First Evidence-Based Clinical Practice Guideline

2001 – Published
- AWHONN and NANN Collaboration
- US and Canadian Representation
- Review of 200 research articles, evaluated based on quality of evidence
- 51 U.S. Nurseries
- 2007 – 2nd Edition

2012 Update Includes New Information
- Newborn Skin Assessment
- Bathing
- Vernix
- Umbilical Cord Care
- Contraception Care
- Disinfectants
- Diaper Dermatitis
- Adhesives
- Emollients
- Transepidermal Water Loss in ELBW Infants
- Skin Breakdown
- Intravenous Infiltration
- Product Selection
- Microbiome of the Skin
- Atopic Dermatitis
- Parent Education

What’s Different about Neonatal Skin?
• Review of the anatomy of skin
• Differences in neonatal skin
• Differences between full term neonates and premature neonate’s skin

Skin Layers

Measuring Skin Parameters
• TEWL
  - Transepidermal Water Loss
• pH
  - acid-base balance
• SCH
  - Surface hydration
• Colorimeter
  - erythema
• Visual Inspection Scales
• Skin cultures, PCR analysis
What is Skin Barrier Function?

- Ability of skin to protect and function as barrier to toxins, pathogenic organisms
- Can be measured by the skin’s ability to hold on to water (TEWL), stay hydrated (SCH); influenced by pH
- Immaturity, alterations in pH, skin injury or disease can result in impaired barrier function

Stratum Corneum and TEWL

- 10-20 layers of stratum corneum in term infants and adults
- Far fewer layers in premature infants <30 weeks, increased fluid and heat losses
- Evaporimeter measures skin barrier function—TEWL (transepidermal water loss)
- 5-10 gms H₂O/m²/hr in adults

Premature Infants and TEWL

- 23 weeks
  - 75 gmH₂O/m²/hr
- 26 weeks
  - 45 gmH₂O/m²/hr
- 29 weeks
  - 17 gmH₂O/m²/hr
- 32-40 weeks:
  - 5-10 gmH₂O/m²/hr
- Stratum corneum becomes mature at 30-32 weeks PCA

Cohesion Between Epidermis and Dermis

- Top two layers of skin connected by fibrils
- Fewer and further apart in premature infants
- Adhesives can attach more securely to epidermis than the epidermis is attached to the dermis

Skin pH

- pH >6.0 at birth, falls to <5.0 in 4 days
- Premature infants—pH 5.5 after one week, 5.1 after one month
- Diapered areas—pH 6.0
- pH of adult skin 4.7 (24 hours after bathing)
- Acid mantle is protective—at pH 4.7:
  - resident flora grow (staph epi, micrococci, coryneforms, propionbacteria)
  - transient flora is inhibited (gram negative such as E. Coli, pseudomonas; gram positive staph, candida)
- Normal tap water increases pH for a while

Recent publications in Pediatric Dermatology and Journal of Investigative Dermatology (2008, 2010)

- Baby stratum corneum is 30% thinner than adult, epidermis is 20-30% smaller
- Keratinocyte cells smaller with higher cell turnover rate; explains better wound healing in babies
- Dermis is also different; short collagen fibers, absent reticular layer, makes skin feel softer
- Baby skin absorbs more water, and loses it faster than adult
- Baby skin contains less total lipids and less sebaceous lipids, confirming the decreased activity of glands
Increased Risk of Toxicity from Topical Agents in Newborns

- Newborn dermis is 40-60% the depth of adult dermis
- Larger surface area (compared to body weight) exposed to topical agent
- Stratum corneum maturity and integrity are factors, especially in premature infants
- pH of skin surface: more alkaline pH increases permeability
- Occlusion (ie, wearing a diaper) compromises stratum corneum, skin barrier

Misadventure in Neonatal Skin Care #1: Aniline Dye and Methemoglobinemia

- 1886, Dr. Rayner notes link between outbreak of cyanosis in normal newborns and aniline dye used to print the hospital’s name on diapers
- Found to have methemoglobinemia
- Nine further outbreaks attributed to aniline dye
- Factors include larger surface area to body weight, skin pH higher due to urine, permeability when skin is covered, occluded
- Implications for diaper dermatitis remedies in neonates

Skin Colonization: What We Thought

- After vaginal birth, skin is colonized after descent through the birth canal
- After C/S, skin thought to be sterile if intact membranes
- In utero, fetal skin colonization
  - after premature rupture of the membranes
  - penetration through amniotic membranes (candida, group B strep)
- “Under hygienic conditions, resident flora resembles that of adults after the first few weeks of life”

Do We Have the Full Story on Colonization of the Skin?

- The past decade has seen a shift in how we see the microbes and viruses in and on our bodies
- 9 in 10 of the cells in our body are microbial; especially in the gut and on the skin
- A few microbes make us sick, most are commensal (“good bacteria”)
- Imbalance of commensal bacteria may lead to disease states
- Newer studies that determine the “microbiome” of our skin and GI tract involve PCR techniques

Microbiome Aspects of Perinatal and Neonatal Health

- Using PCR technique, previously undetected microbes found in amniotic fluid with intact membranes, possible link to premature labor
- Vaginal birth infant skin colonized differently than C/S birth
- 64-82% of MRSA infection found in C/S births
- Intestinal microbiome altered in premature infants
  - antibiotics, often C/S
- Lack of protective bacteria may be involved in pathogenesis of NEC

Delivery Mode Shapes Initial Microbiota in Newborns

1. Dominquez-Bello MG et al. (2013) PNAS 110:16982-16987

1. Dominquez-Bello 2010
Diversity of the Human Skin Microbiome Early in Life


- Skin swabs from 31 infants (1-3, 4-6, 7-12 months); arm, forehead, buttocks
- Infant skin:
  - Firmicutes predominate (staph, strep, propionibacter)
- Adult skin:
  - Actinobacteria predominate (gram + organisms, mycobacteria, corynebacteria)
- Establishment of healthy skin microbiome may have role in denying access to infectious microbes, help to modulate inflammatory responses.

Skin Surface pH and Microflora

- Symbiotic relationship between skin and skin flora
- Human skin provides sebum (lipids), sweat (minerals), dead skin cells (protein) to resident flora
- Resident flora strengthens the skin’s first defence (acid mantle) by producing anti-bacterials which compete and prevent colonization with harmful bacteria

Skin and the Immunologic System

- Interplay of immune responses arise from skin
- Includes cellular and humoral components in the epidermis and dermis
- Cellular components
  - Keratinocytes
  - Monocytes and macrophages
  - Mast cells
  - Lymphocytes, primarily T cells
  - Endothelial cells

Antimicrobial Peptides and Skin

- Marchini (2002): biopsy of 4 babies with erythemum toxicum(ET), 4 without
- Human antibacterial peptide LL-37 present in skin of babies with ET, not found if no ET
- Vernix contained LL-37 and lysozymes which have antibacterial effects against pathogens (E. coli)
- Antimicrobial defense system in the skin is more than just a mechanical barrier

What is Vernix Caseosa?

- Cheesy substance composed of sebum from sebaceous glands, broken-off lanugo, desquamated cells—unique to humans
- Primarily water (80%), lipids, protein
- Production begins end of 2nd trimester, most accumulated 36-38 wks
- Vernix detaches from skin as levels of pulmonary surfactant rise
Vernix Caseosa and Neonatal Adaptation

- 60 infants enrolled
  - 30 had vernix retained (48% coverage)
  - 30 with vernix removed (26% coverage)
- Measurements (pH, SCH) at birth and 24 hours
- SCH higher at birth and at 24 hours for vernix retained infant group
- pH lower for vernix retained
  - 5.16 vs 5.97 at birth
  - 4.9 vs 5.63 at 24 hours

Should We Reconsider Antimicrobial Bathing?

- Concerns about community-acquired MRSA
- Newborns seen in emergency departments with cellulitis, skin infections due to MRSA

Misadventure in Neonatal Skin Care#2: Hexachlorophene

- Hexachlorophene was used in 1950-60 to control outbreaks of *S. aureus* infection in nurseries
- Initial bath after birth, then every 2 days
- Irreversible brain damage (vacuolar encephalopathy) in premature infants washed 4 or more times
- Extreme prematurity, low birth weight, rashes, acidosis, hyperbilirubinemia are risk factors for toxicity

Recent Studies with Chlorhexidine Baths

- Da Cunha (2008): RCT of 94 full term newborns, cleanser vs. 0.25% CHG; *S. aureus* colonization reduced at 24 hours (36.7% vs 13.6% with CHG)
- Sankar (2009): RCT of 60 premature infants 28-36 weeks; 0.25% CHG, saline, no cleansing; CHG reduced colonization by half in the axilla at 24 hours but not at 72 hours; no difference in the groin at 24 or 72 hours; skin scores not changed

Chlorhexidine Gluconate Bathing?

- Daily baths to adults in ICU reduced VRE, BSIs
- Lee (2011): Hospitalized children (12 subjects, 3 mos – 17 years), daily CHG bathing (mean daily baths 9, range 1-30), 8 subjects had samples after at least 7 days CHG exposure, low concentrations CHG, no evidence CHG accumulation
- Safety in neonates?
- Influence on normal colonization, barrier function?

International Skin Science: Topical Applications of Chlorhexidine for Prevention of Omphalitis and Neonatal Mortality in Southern Nepal

- Community-based, cluster-randomised trial
  - 4934 infants- 4% CHG
  - 5107 infants- soap and water
  - 5082 infants- dry cord care
- Severe omphalitis reduced by 75%, neonatal mortality 24% lower with CHG
- If enrolled at <24 hours of age, mortality reduced by 34%
- Questions about current WHO recommendation for dry cord care
First Bath

- Studies indicate that newborns bathed as soon as 1 hour after delivery will maintain their temperature if they have a normal temperature to begin with.
- AWHONN Guideline:
  - Vital signs, temperature stable 2-4 hours
  - Antiseptic cleaners not currently required by American Academy of Pediatrics, Center for Disease Control
  - Universal precautions until bathed
  - Not necessary to remove all vernix
- WHO: wait at least 6 hours
- Would they, or their mothers, choose to be bathed as early possible?

How to Give the First Bath?

- Sponge bath
- Under the faucet
- Small tub
- Large tub “immersion bath”
- Swaddle bath

Tub Bathing vs. Sponge Bathing

- Hennigson (1981): 232 newborns, no infection or colonization problems, better temperature, less crying with tub bathing
- Hylen (1983): 618 newborns, rectal temperatures better with tub bathing, no difference in infection
- Anderson (1995): axillary temperatures stable with tub bath, better for attachment and bonding
- Cole (1999): tub bath maintained temperature better, 70% remained drowsy or quiet alert vs 90% crying with sponge bath
- Bryanton (2004): 102 newborns randomized to tub or sponge bath. Tub bath less temperature loss, no differences in umbilical cord healing, behavior more content, mothers rated more pleasurable
- Loring (2012): 100 infants (35-36 6/7 weeks) randomized to immersion tub bathing or sponge bathing; tub bathed infants had overall higher and less variability in body temperature

Swaddled Bathing

Our “First Bath” Study (2012)

- 100 babies randomized, first bath with water alone or water with baby wash
- Babies will be immersed and swaddled in the bath
- Pre and Post-Bath Measurements include: Transepidermal water loss, pH, stratum corneum hydration, microbiome of baby and mom

Routine Bathing

Neonatal Skin Care Guideline 2007

Use mild baby wash that has been formulated for and tested on newborns and infants

Bathe every other day or less frequently, although this may be influenced by cultural factors

Avoid rubbing, use rinsing or immersion instead
What is “Soap”?

- Soap: animal or vegetable fat and lye, sometimes with added emollients; alkaline (pH > 7) if made with lye
- Mildness determined by the type of surfactants, pH
- Syndets: synthetic detergents
  - sodium lauryl sulfate is irritating
  - sodium laureth sulfate less so
  - neutral pH (5.5-7)
- Emollient bath oils, soap substitutes

Surfactants and Cleanser Mildness

Skin Physiology of the Neonate and Young Infant

- 202 healthy term neonates
- Measured pH, desquamation, SCH, texture at day 3, 4 weeks, 12 weeks
- Water bath twice weekly; moisturizers discouraged except zinc oxide
- pH decreased by 1.31 pH units between day 3 and 4 weeks
  - lower on forearm and forehead, compared to cheeks and buttocks
- SCH increased at all sites, skin desquamation increased on cheeks and forehead

Effects of Soap and Detergents on Skin pH, Stratum Corneum Hydration, Fat Content

- 40 infants age 2 weeks to 16 months old
- RCT: water, liquid detergent, compact detergent, or alkaline soap; 10 in each group
- pH, fat content, SC hydration measured before, 10 minutes after bathing
- ↑pH, ↓fat content and SC hydration in all groups, significant with soap
- “Each agent influences skin surface; increase in pH changes protective acid mantle, cutaneous microflora and enzyme activity of the epidermis.”

Water Considerations

- pH
- Hardness
- Osmolarity
- May not remove substances that are not water-soluble
- Water alone does not provide moisturization, may make skin dryer

New Evidence on Newborn Cleansing Methods: Water vs Baby Wash (Lavender, 2011)

Sample: 307 mothers and their newborns were randomized into two groups: bathing baby with water alone and bathing baby with a gentle cleanser

Measures: Primary—transepidermal water loss (TEWL) and secondary—skin hydration, skin pH, clinical observations and maternal assessment. Main outcome measures were assessed at baseline, week 2 and week 4

Key results: After 2 weeks, TEWL levels in the group bathed with the gentle baby cleanser were not worse than TEWL levels in the group bathed with water alone
Effect of Standardized Skin Regimes on Neonatal Skin Barrier Function

- 64 full term neonates randomized to treatment groups
  - Water only
  - Water + wash gel
  - Water + cream after bath
  - Water + wash gel + cream
- Measured TEWL, SCH, pH, sebumeter, neonatal skin condition score, umbilical cultures on Day 2, week 2, 4, 8
- Bathed twice weekly, no additional products
- TEWL lower (improved), SCH better with cream compared to water
- pH gradually lower over the first month of life
- No difference in umbilical cultures
- Skin care regimes do not negatively influence skin barrier adaptation

Bartels et al., Ped Derm (2010), 27:1-8

Emollients

- Can preserve, protect, and enhance the infant skin barrier
- What is their role in healthy newborn skin care?
- Considered first-line treatment for Atopic Dermatitis
- Parents taught “Soak and Seal” method
  - bathe children with AD for a few minutes, not more than 2-3 times per week, using a moisturizing non-soap cleanser
  - use an emollient after bathing to seal in hydration

What is Atopic Dermatitis?

- Allergic inflammatory skin condition-results in dry, scaly skin
- Affects about 20% of children; 60% of those by their first birthday
- AD that arises in childhood is frequently a precursor of allergic asthma and allergic rhinitis
- Cause is a combination of genetic and environmental factors
- Keeping skin barrier intact may possibly prevent disease progression by inhibiting entry of allergens and irritants
- BEEP study: Barrier Enhancement for Eczema Prevention

Skin Disinfectants

- Chlorhexidine gluconate (CHG)
- Povidone Iodine (PI)
- Isopropyl Alcohol (IA)

Evaluate
  - Toxicity
  - Skin irritation
  - Efficacy

What is Chlorhexidine?

- Topical antiseptic used since 1954
- Hand washing, skin prep, vaginal antisepsis, gingivitis, body washing
- Concentrations: 0.5%-4%, with or without isopropyl alcohol or ethanol
- Low concentrations affect membrane integrity, high concentrations cytoplasmic (cell death)
- Some pseudomonas sp, other non-fermenting gram negative organisms have high level resistance

Milstone AM et al, Healthcare Epidemiology (2008), 46:274

Chlorhexidine Gluconate

- 2% CHG aqueous
- 2% CHG in 70% isopropyl alcohol
- 0.5% CHG in 70% isopropyl alcohol
Safety of Chlorhexidine Gluconate Used for Skin Antisepsis in the Preterm Infant

- Hexachlorophene and CHG are phenol derivatives, but differ chemically, hexachlorophene is bacteriostatic, CHG is bacteriocidal.
- CHG more strongly binds to protein in the SC, withstands removal by alcohol.
- Recent survey indicates that 61% of NICUs use CHG – some restrict by weight, GA – report adverse skin reactions, no systemic toxicity.
- Skin irritation seen in preterm infants, even with aqueous CHG.
- CHG absorption also a concern, seems to increase with repeated exposures.

Toxicity from Povidone-Iodine

- Parravicini (1996): preemies with any exposure to iodine had elevated urinary iodine levels, some had abnormal thyroid levels.

Iodine-containing Antiseptics and Hypothyroidism in Preterm Infants

- Compared 2 NICUs: PI or CHG.
- TSH >30 in 13.7% with PI, 0 with CHG.
- Followed by sequential study: 24 infants PI, 22 infants CHG.
  - Area disinfection carefully controlled, PI removed.
  - T4, TSH levels weekly for 28 days, q 2 weeks until 60 days, once when 90 days.
- TSH >30 in 20.8% with PI.
- Lower T4 levels in first month in PI infants.

Is Iodine Toxicity an Issue in USA?

- Gordon (1995, ArchPedAdolescMed, 149:1336): tested premature infants (mean GA 33 weeks) once on day 7-10 of life; no abnormal thyroid levels (T4, TSH) despite elevated urine iodine levels; did dopamine, dexamethasone mask thyroid effects?
- AvRuskin (1994; J Ped Endocr, 7:205-209): 30 infants, 9 were 26-30 weeks (710-1290 g), 15 were 31-34 weeks (1210-2210 g), 6 were 34-35 weeks (1470-2440 g); significant increase in urine iodine levels, suppressed T3, T4 but only transiently.
- Are differences due to maternal, fetal and neonatal iodine sufficiency in US?

Toxicity and CHG

- Adverse reactions reportedly rare.
- Contact dermatitis.
- Corneal damage.
- Inner ear hearing loss.
- Hypersensitivity, anaphylaxis in adults.
  - CHG impregnated urinary catheter.
  - Multiple skin exposures for surgical procedures.

Effect of Chlorhexidine Gluconate on the Skin Integrity at PICC Line Sites

- 40 infants, gest age 23-39 weeks (mean 32), age at start of study 34 days (mean).
- Weekly PICC dressing changes, 2% CHG/isopropyl alcohol covered with transparent dressing.
- TEWL and visual assessment at PICC site and on contralateral arm with transparent dressing alone.
- Greater skin compromise and impaired barrier (increased TEWL) at PICC site.
Disinfectants: Skin Injury

- Povidone-iodine + isopropyl alcohol

Disinfectants: Chemical Burn

2% CHG/70% Isopropyl Alcohol

CHG Chemical Burns

- Reynolds (2005): 0.5% CHG/methanol
- Mannan (2007): 0.5% CHG/isopropyl alcohol
- Espuny (2010): 0.5% /methanol
- Anderson (2005): 2% aqueous CHG caused erythema, breakdown in 4/36 infants <1000g, <48 hours of age

Pilot Trial to Compare Tolerance of CHG to PI Antisepsis for CVC Placement in Neonates


- 47 infants >1500 grams, >2 weeks (limited by FDA)
- CHG with 70% isopropyl alcohol used for CVC placement and weekly dressing changes vs. PI
- No increase in contact dermatitis
- CHG detectable in blood in > 2/3 of the 10 infants with blood CHG levels drawn
- 2 infants showed increasing concentrations CHG over time, suggesting increased absorption or decreased metabolism or elimination

Efficacy of Disinfectants: Adults

- Chaiyakunapruk (2002): 8 studies (4143 catheters); CHG reduced risk for catheter-related blood stream infection by 49%; for every 1000 catheters, 11 infections would be prevented
- Maki (1991): randomized 668 central lines in adults; infections 2.3/100 catheters with CHG, 7.1/100 with PI, 9.3/100 with IA
- CDC strongly recommends 2% CHG/70% isopropyl alcohol used for initial skin prep, dressing changes

- Central lines in adults average 7-10 days duration

Efficacy of Disinfectants: Neonates

- Garland (1995): total of 765 peripheral IV catheters in neonates; colonization with bacteria in 4.7% with CHG, 9.3% with PI
- Linder (2004): retrospective study, PI or CHG; no differences in + blood cultures, true infections or contaminated cultures
- CDC (2011): “No recommendation can be made for the safety or efficacy of chlorhexidine in infants aged < 2 months. Unresolved issue. Antiseptics should be allowed to dry according to the manufacturer’s recommendation”

- Central lines in neonates stay in longer; hub care, sterile tubing changes may be more important to prevent infection
No Bloodstream Infection in 8 months!
(bye-bye Lariyah)

CHG Impregnated Dressings

- Garland (2001):
  - 705 VLBW infants
  - RCT: PI skin prep vs TAD vs IA skin prep, CHG foam dress
  - drsg changed weekly
  - ↓ colonization, no difference in CRBSIs or BSIs without source
  - ELBW infants: 15% developed severe contact dermatitis, pressure necrosis

- Levy (2005):
  - 145 pediatric CVS patients; RCT
  - ↓ colonization, no difference CABSI

- What about silver impregnated dressings?
  - Safe?
  - Effective?

Disinfecting Plastic Surfaces

- 70% Isopropyl alcohol or CHG on plastic surfaces
- Use sterile water or saline to remove disinfectants from skin

The Disinfectant Dilemma in the US:
“There is insufficient evidence to recommend a single product for all neonates”

Choices:
  a) 2% aqueous CHG
  b) 2% CHG/alcohol in larger neonates, PI or 2% aqueous CHG for infants<1500 grams
  c) 10% PI for all neonates, all procedures
  d) Move to Canada

Conclusions

- Goal is to protect neonatal skin and promote future skin health
- Normal skin flora are helpful in protecting skin from infection
- Preventing infection in NICU patients and neonates is imperative
- Still not sure about the best skin disinfectant for preterm and term neonates