Neonatal Skin Science 2012
Anatomic and Physiologic Differences
New Adhesives, Diaper Dermatitis and IV Infiltrates

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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

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 – Transdermal 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
Skin Science, NCANN 2012
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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 gms H₂O/m²/hr
- 26 weeks
  - 45 gms H₂O/m²/hr
- 29 weeks
  - 17 gms H₂O/m²/hr
- 32-40 weeks:
  - 5-10 gms H₂O/m²/hr
  - Stratum corneum becomes mature at 30-32 weeks PCA

Development of Skin Barrier Function in Premature Infants

- 10 infants, 23-32 weeks gestational age, <7 days of age
- Measured barrier function using two methods: TEWL (evaporimeter) and impedance spectroscopy
- Barrier matures at 200-230 days (30-32 weeks)

Phototherapy and TEWL

- Halogen phototherapy lights increase TEWL by 10% in premature infants <1500 grams; fluorescent phototherapy lights do not increase TEWL (SPR 2003: Lund, Nonato, Kuller, Durand)
- LED phototherapy lights do not increase TEWL in neonates (AAP 2005; Lund, Kuller, Durand)

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

Disruption of Barrier Function Associated With Adhesive Removal

- 30 infants, 26-40 weeks, <7 days of age
- Significant alteration in TEWL, color, visual assessment after removal of plastic tape and pectin barrier
- Changes seen in bigger as well as smaller babies
- Hydrogel fell off in 7 infants before 24 hours
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 Assessment: Which Scale?

- Braden Q, Starkid Skin Scale
  - Assess risk for pressure sores, skin breakdown in pediatric patients
  - Number of neonates in each study not indicated, no premature infants included
- Neonatal Skin Condition Score (NSCS)
  - Used in original Neonatal Skin Project
    - Sample 2,820 neonates
    - Validity, reliability demonstrated using data set from project (Lund & Osborne 2004)
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 (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”)
- Inbalance of commensal bacteria may lead to disease states
- Newer studies that determine the “microbiome” of our skin and GI tract involve PCR techniques

Neonatal Skin Condition Scale

- **Dryness:**
  - 1 = Normal, no signs dryness
  - 2 = Dry skin, visible scaling
  - 3 = Very dry skin, cracking/fissures
- **Erythema:**
  - 1 = No evidence erythema
  - 2 = Visible erythema, <50% body surface
  - 3 = Visible erythema, >50% body surface
- **Breakdown:**
  - 1 = None evident
  - 2 = Small, localized areas
  - 3 = Extensive
  - **Perfect score = 3**
  - **Worst score = 9**

Skin Assessment

- Neonatal Skin Condition Score (NSCS) recommended in 2007 guideline:
  - Objective scale quantifies overall skin condition
  - Does not replace head-to-toe assessment
  - May be linked to actions: consult with skin team/CNS, emollient use, skin culture, etc
  - Need to identify infants at high risk for pressure sores: HFV, hypotension/hyoperfusion, ECMO, NCPAP

Starkid Skin Scale

Pressure Sores in Neonates
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 (Dominquez-Bello 2010); 64-82% of MRSA infection found in C/S births (Malloy, Peds 2008: 122-245)
- Intestinal microbiome altered in premature infants
  - antibiotics, often C/S
- Lack of protective bacteria may be involved in pathogenesis of NEC

Diversity of the Human Skin Microbiome Early in Life

- PCR microbiome: skin swabs from 31 infants (1-3, 4-6, 7-12 months); arm, forehead, buttocks
- Infant skin: Firmicutes predominate (staph, strep, propionbacter)
- 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.

Our “First Bath” Study

- 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, and microbiome of baby and Mom.

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
• Humoral components
  – Antimicrobial peptides
  – Complement proteins
  – Immunoglobulins
  – Cytokines
  – Prostaglandins

Antimicrobial Peptides and Skin

• Marchini (2002): biopsy of 4 babies with erythema 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

Should We Reconsider Antimicrobial Bathing?

• Concerns about community-acquired MRSA
• Newborns seen in emergency departments with cellulitis, skin infections due to MRSA
• Would initial bath with antimicrobial cleansers decrease infection?

What’s Wrong with this Picture?

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 (vacular 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; staph 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
- Clinical trial in pediatric patients
- Safety in neonates?
- Influence on normal colonization, barrier function?

Blood Concentration of CHG in Hospitalized Children Undergoing Daily CHG Bathing

- Lee et al (2011) Inf control and Hosp Epidemiol 32:395-397
- 12 subjects, 3 months – 17 years
- 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

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

Adhesives: New Technologies

Diaper Dermatitis

IV Infiltrates: Prevention and Immediate Treatment

Adhesives in the NICU

- Widely used in premature and full term infants
- Attach life support devices such as ETTs, intravenous and arterial catheters, chest tubes, and monitoring sensors, electrodes
- Adhesive removal was primary cause of skin breakdown in AWHONN neonatal skin care project

Other Adhesive Products

- Hydrocolloids, pectin barriers
- Hydrogels
- Transparent adhesive dressings
- Silicone adhesives
Types of Adhesive Skin Damage
- Skin stripping
- Tearing
- Maceration
- Tension blisters
- Chemical irritation
- Sensitization
- Folliculitis

Concerns with Adhesive Removers
- Solvents contain hydrocarbon derivatives or petroleum distillates
- Toxicity can result from absorption through the skin
- Case report of skin injury and hemorrhage in premature infant after exposure to Detachol

Tips for Safer Adhesive Removal
- Peel adhesive back parallel to skin surface instead of straight up
- Hold skin surface next to adhesive.
- Use water soaked cotton balls.
- Use mineral oil, petrolatum ointment if no need to reattach appliance.
- Transparent dressings: stretch to release adherence

Bonding Agents
- Tincture of Benzoin, Mastisol
- Increase adhesive strength
- Used to enhance adhesion of wound closure tapes
- Not recommended in newborns, can increase epidermal stripping

What to Do With Benzoin
- Plastic polymers sprayed or wiped on skin to protect from trauma
- Alcohol-free products less irritating to skin
- Cavilon is FDA approved in infants >30 days as diaper dermatitis treatment
- Other manufacturers haven’t approached FDA

Barrier Films
New Technology: Silicone Adhesives

Silicone Tape in High Humidity

Redesigning Adhesive Products

Diaper Dermatitis

- Irritant contact diaper dermatitis (IDD)
- Candida (fungal) diaper dermatitis
- Combination
Pathogenesis IDD

- Wetness
  - Maceration of stratum corneum, impaired skin barrier function
- Friction
  - Mechanical trauma from skin-to-diaper contact
- Urine and feces
  - Ureases in stool release ammonia
  - Increase in skin pH
  - ↑ pH activates proteases and lipases, disrupts epidermal barrier

Risk Factors for IDD

- Malabsorption
  - Short bowel syndrome
  - Infectious diarrhea
  - Opiate withdrawal
- Fecal incontinence
  - Hirschsprung’s disease
  - Ano-genital malformations
- Atopic dermatitis (altered barrier function)
- Wearing diapers!

Diapers

- Frequent changes
  - Every 3-4 hours, more frequently in neonates
- Super-absorbent diapers bind fluid with a gel matrix
- Breathable covering
  - Permeable to air and vapor, impenetrable to leaks
- ? Petrolatum liners
- Diaper wipes: +/-
  - Wide range of brands, chemicals in formulations
  - Fragrance, preservative free are best
  - Some reported to cause allergic contact hand dermatitis in mothers

Skin Care in the NICU Patient: Effect of wipes vs. Cloth and Water on Stratum Corneum Integrity

- 130 NICU infants, 23-41 weeks, 30-51 weeks when studied
- RCT: wipe A, wipe B or cloth/water
- Measured TEWL, erythema, pH, SCH, skin condition every day
- TEWL, erythema ↓ with wipes
- pH lower with wipe B (acidity as preservative)

Premie Diapers?

Contact Irritant Diaper Dermatitis: Create a Barrier “frosting-on-a-cake”
Ingredients in Diaper Dermatitis Treatments

- Zinc oxide
- Petrolatum
- Pectin
- Dimethicone (silicone)
- Plastic polymers
- Lanolin
- Glycerin
- Cholestyramine

Barrier Films

- Plastic polymers sprayed or wiped on skin to protect from trauma
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- Cavilon is FDA approved in infants >30 days as diaper dermatitis treatment, peri-ostomy skin protection
- Other manufacturers haven’t approached FDA

Candida Diaper Rash

- Fiery red, satellite lesions
- Distributed on thigh, perineum
- Treat with antifungal ointment (not powder)

Fungal Diaper Dermatitis Products

Combination Diaper Rash

- Dust with antifungal powder
- Seal powder on with skin protectant
- Apply thick layer of barrier

Treat the Underlying Cause!

- Diarrhea from malabsorption, opiate withdrawal, infection
- May need change in formula to reduce frequency of stooling
Diaper Dermatitis

- Contact irritant or candida?
- Primary irritant is fecal enzymes
- Use protective coating: zinc oxide, pectin paste, plastic polymer to protect skin from re-injury
- Candida diaper dermatitis: antifungal ointment
- Avoid products with multiple chemicals

Preventing IV Infiltrates

- Insertion site clearly visible
- Check every hour
- Keep IV site out of swaddling blankets
- Tape at joint: knee for foot, elbow for hand
  - OR no arm- or foot-board at all!
- Avoid tape or wraps that constrict venous return

Preventing IV Infiltrates: Other Issues

- Avoid calcium-containing infusions whenever possible
- If calcium in IV fluids, consider placing two IVs and “rotating” sites for infusion
- Are intermittent boluses of calcium less irritating to veins compared to continuous infusion?
- Consider PICC line if: vasopressors, calcium infusions, irritating meds (Vancomycin, Amphotericin, Nafcillin/Methicillin/Penicillin, Acyclovir)

IV Infiltrate Requiring Intervention

- Swelling
- Pain at site
- Blanching or coolness of skin
- Leakage at site
- Erythema
- Severe cases: blisters, ischemia

Characteristics of Infiltrates Requiring Intervention

Hyaluronidase and Phentolamine

- Vitrase: www.istavision.com
- Amphadase: www.amphastar.com
- Doses 15-20 units, 1 cc volume injected at 5 sites around periphery
- Do not use for vasopressors; phentolamine (Regitine) is antidote
IV Infiltrates: Multiple Puncture Technique

- Disinfect skin
- Analgesia
- Puncture at 5-10 sites with 22-24 gauge needle
- Apply saline soaked gauze
- Compress to release more fluid

Hyaluronidase + Puncture + Gel/Bag

- Vitrase (hyaluronidase)
  - 20 units
- Deliver 0.2 ml in 5 sites around periphery of infiltrate
- No need to change needles

Approach to IV Infiltrates (CHO)

- Use combination of hyaluronidase and multiple puncture technique
- No time frame, although earlier is best
- Be aggressive to allow extravasated fluids to leak out; several “rounds” may be needed
- Use bag/boot method with hydrogel immediately after punctures, hyaluronidase

History of the Neonatal Skin Care Guideline

- Collaboration between two national nursing organizations in the US (AWHONN and NANN)
  - Included Canadian representation
  - Reviewed over 200 research articles about neonatal skin and skin care
- First evidence-based, clinical practice guideline (2001) evaluated in 51 US nurseries
- Revision of guideline December 2007.
- Revision planned for 2012
2007 Neonatal Skin Care Guideline

- Newborn skin assessment
- Bathing
- Vernix
- Umbilical cord care
- Circumcision care
- Disinfectants
- Diaper dermatitis
- Adhesives
- Emollients
- Transepidermal water loss in ELBW infants
- Skin breakdown
- Intravenous infiltration

2012 Neonatal Skin Care Guideline

- Will include New Information on:
  - Product Selection
  - Microbiome of the Skin
  - Atopic Dermatitis
  - Parent Education