

# Update on the Use of Topical Agents in Neonates

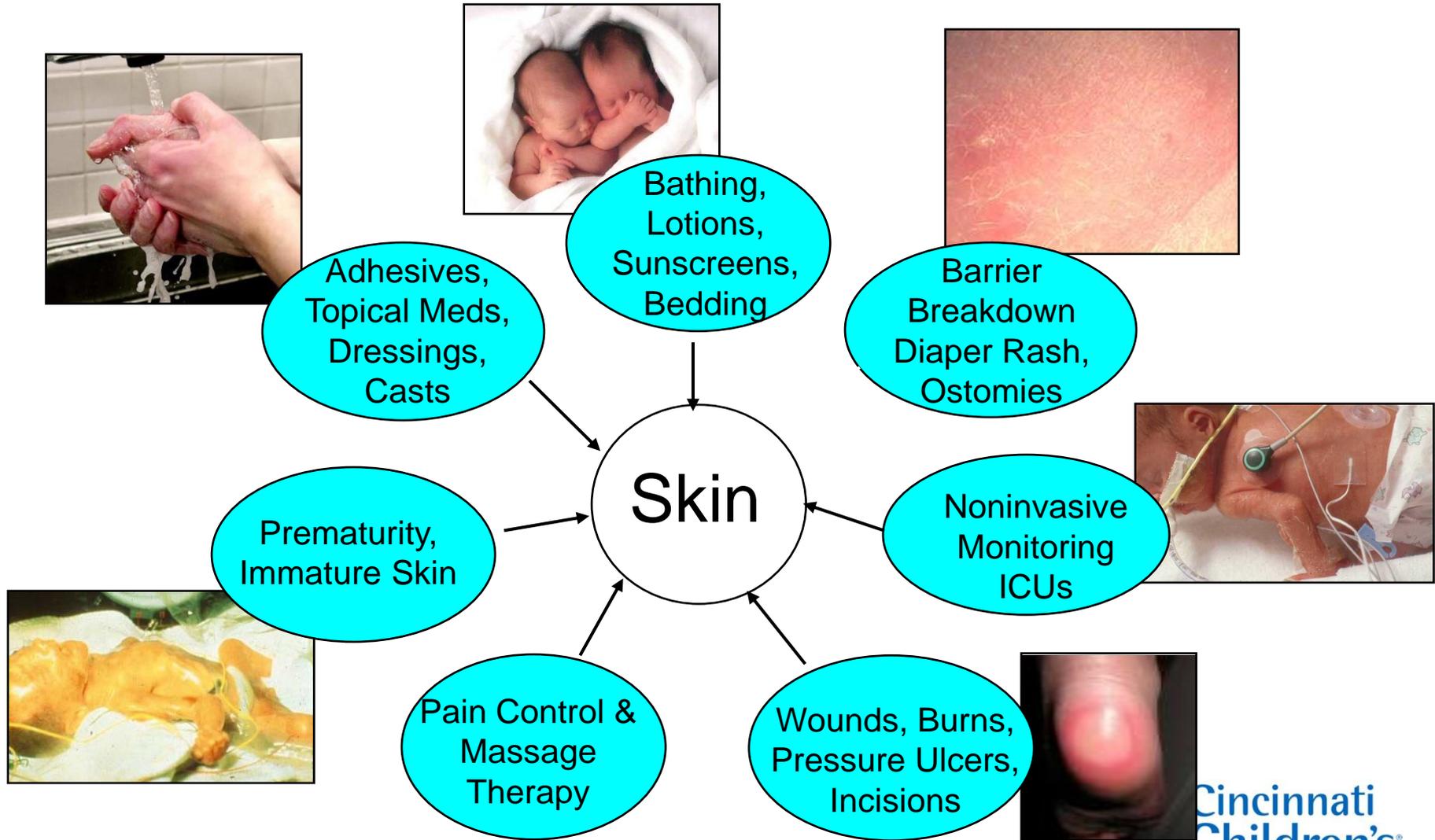
*Marty Visscher, PhD, Skin Sciences Program  
Cincinnati Children's Hospital Medical Center*

May 2011



*Change the Outcome<sup>®</sup>*

# Skin: A Primary Care Interface



# Objectives

1. Describe skin structure and function in general and for premature and full term neonates
2. Explain how common “topical agents”, encountered in the care of neonates, influence neonatal skin health and describe the potential effects of their use
3. Develop and implement a strategy for decision making regarding the use of specific topical agents on neonates

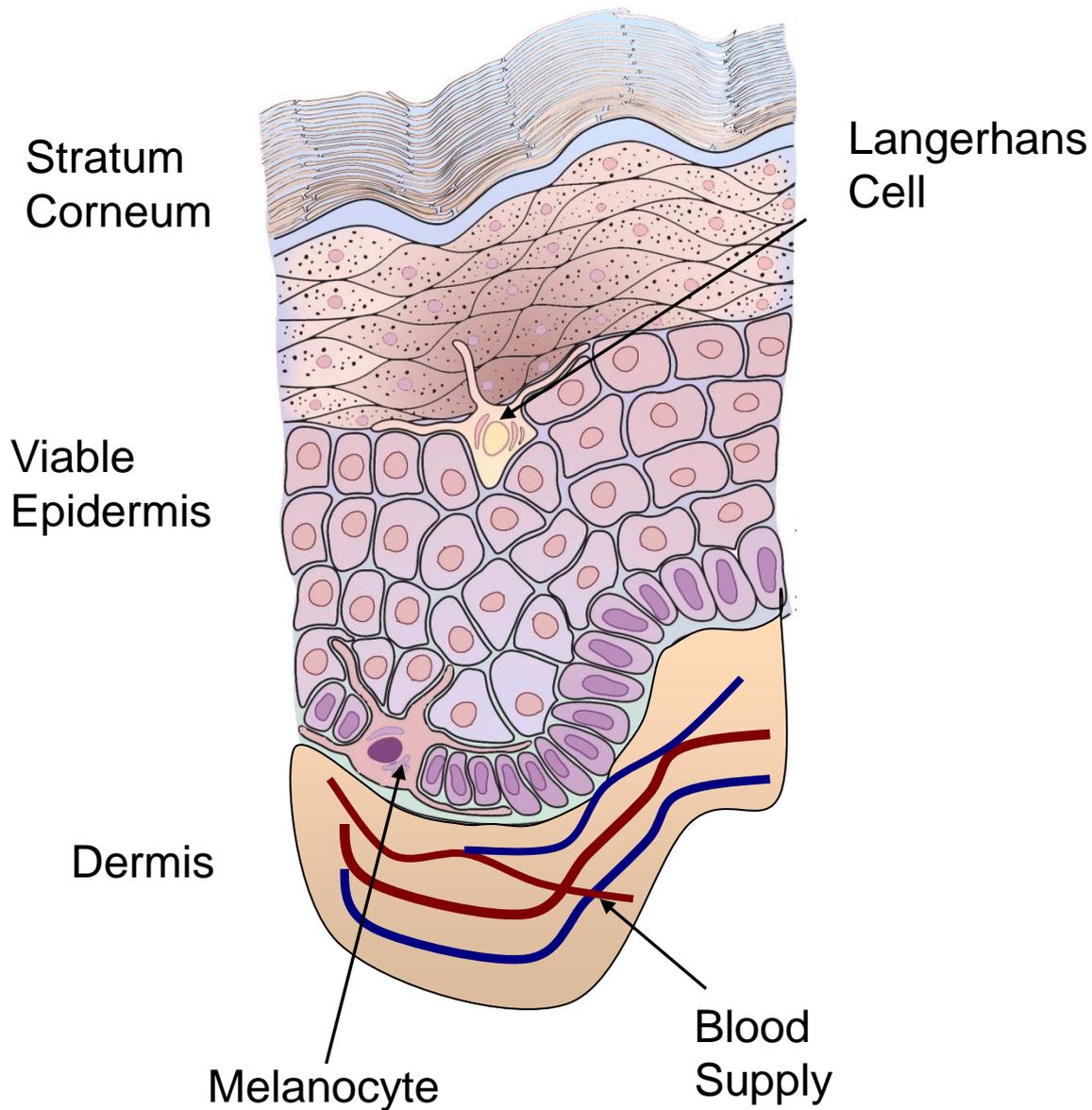
# Perspective: Touch

- Touch is the first sense to develop.
- Touch is a central component of the infant-mother co-regulatory system.
- Therefore, the skin is important in how the infant perceives and reacts to the environment of care and, consequently, in neurodevelopment.

*Tronick E. Touch in mother-infant interaction, in Touch in early development, T. Field, Editor 1995, 53-95.*

# Roles of the Skin at Birth

1. Protection - barrier to water loss, light and irritants
2. Infection control and immunosurveillance
3. Resilience to mechanical trauma
4. Sensation and tactile discrimination
5. Thermal regulation
6. Acid mantle formation



**Stratum Corneum:**  
 Physical barrier to irritants  
 Tactile discrimination  
 Acid mantle formation

**Viable Epidermis:**  
 Physical barrier  
 Tactile discrimination  
 Sensation  
 Acid mantle formation

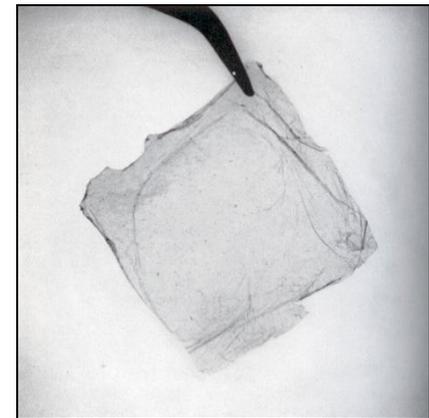
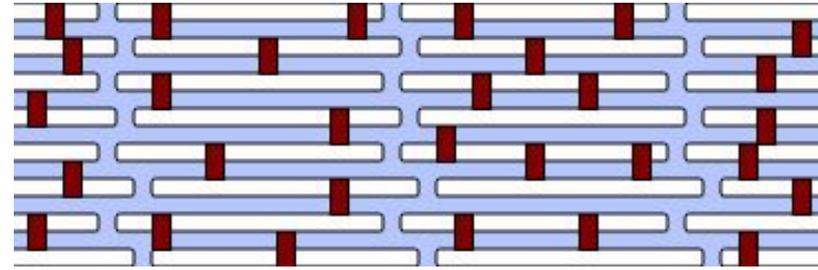
**Dermis:**  
 Resilient foundation  
 Thermal regulation  
 Sensation  
 Blood supply

**Melanocyte:**  
 Protection – light  
 Color

**Langerhans Cell:**  
 Barrier – Immunological

# Stratum Corneum

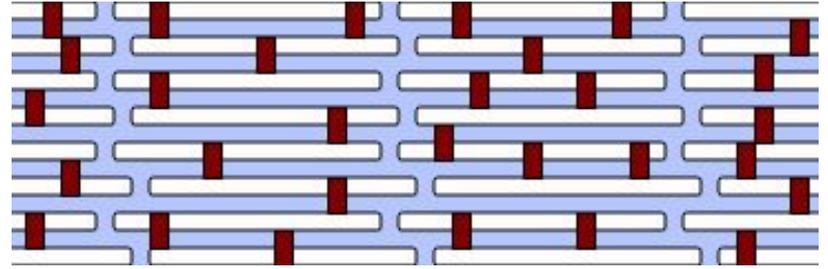
- Has ~ 16 cell layers
- Thickness 10–40 microns, about 1/5 as thick as paper
- Variable thickness depending on body site
- Mechanically tough, difficult to penetrate
- Contains antimicrobials
  - lysozyme, lactoferrin, etc.



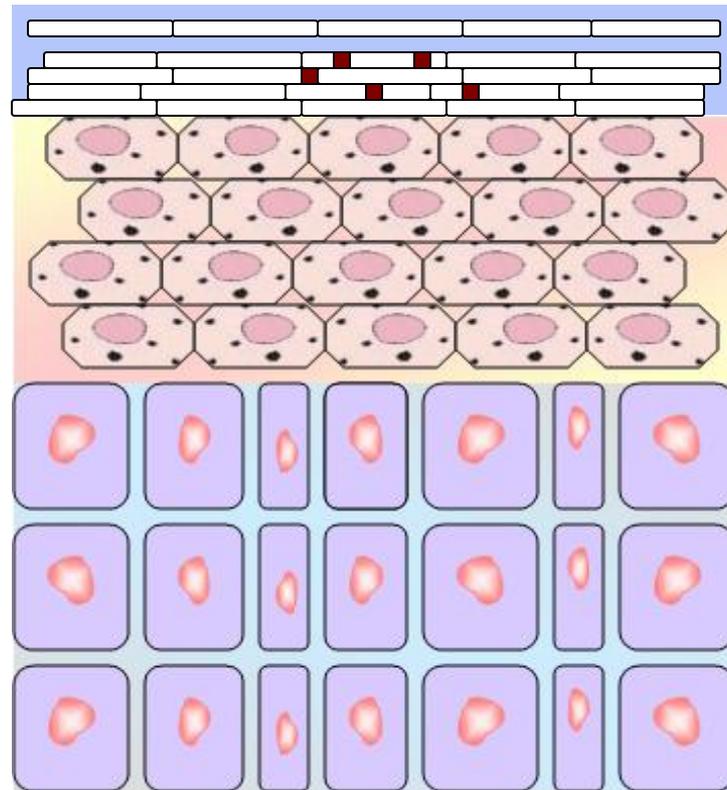
From: The Epidermis, ed. W. Montagna, W.C. Lobitz

# Stratum Corneum

- Cells – corneocytes
- Lipid bilayers
- Cells connected by desmosomes, molecular “rivets”
- Formed by the viable epidermis
- “Replaced” every 14 days

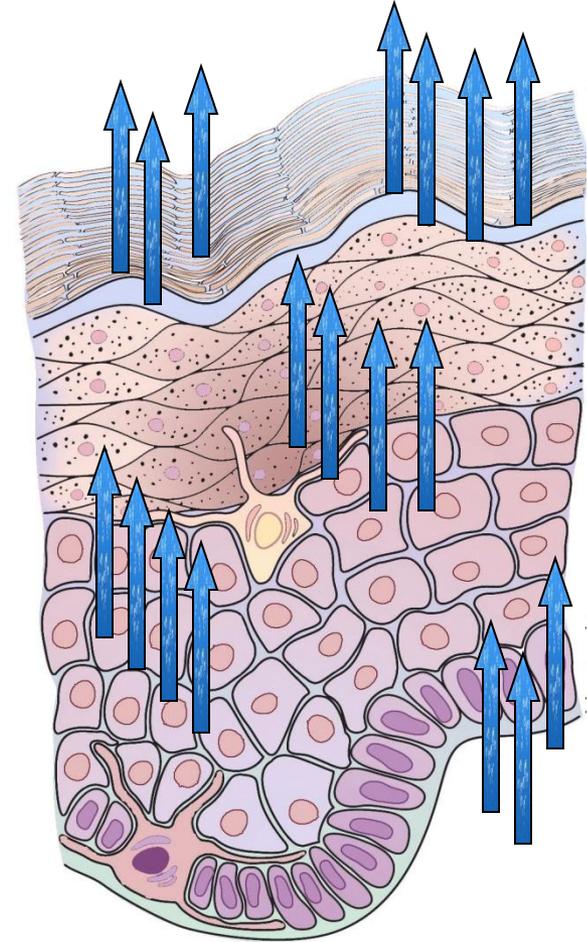


# Stratum Corneum Formation



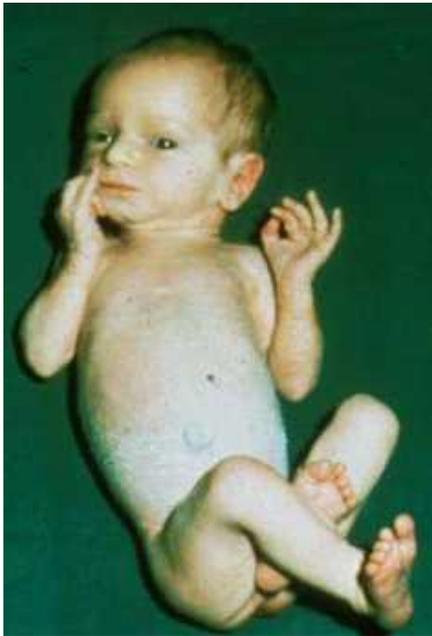
# Transepidermal Water Loss (TEWL)

- Water of respiration normally moves through the stratum corneum from below.
- The rate of transepidermal water loss (TEWL,  $\text{g}/\text{m}^2/\text{hr}$ ) is a measure of skin barrier integrity
- TEWL is higher (faster) when the barrier is damaged.

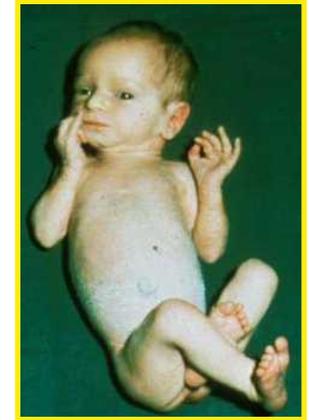


# Clinical Relevance

- How do we achieve optimum adaptation to a dry environment at birth?
- How do we facilitate barrier development in the premature infant?

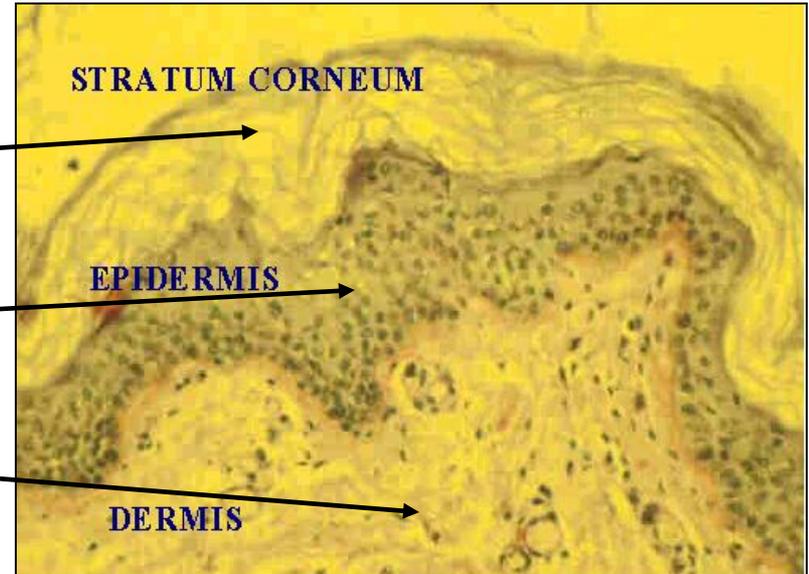


# Full Term Infant Skin



## *Healthy infants*

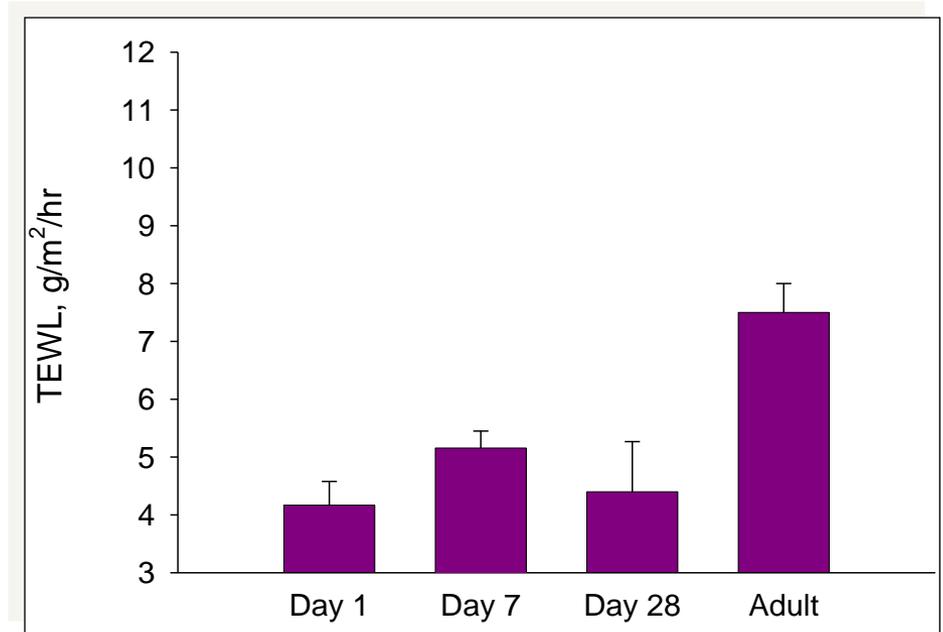
- Well-formed stratum corneum.....note multiple layers
- Thick epidermis
- Structural proteins present in the dermis



# Full-Term Newborn SC Barrier

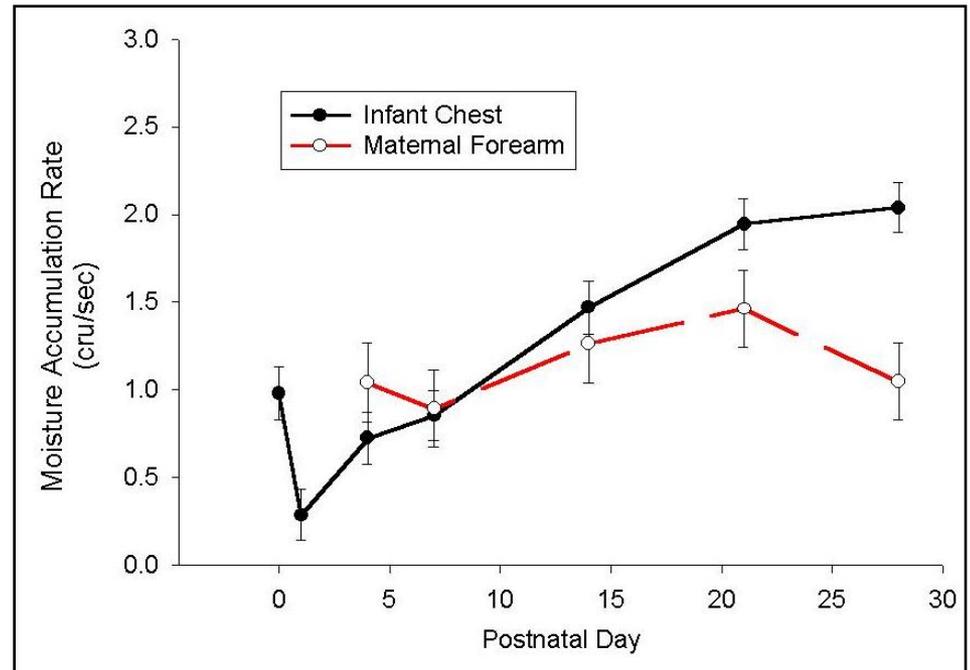
## *TEWL*

- very low at birth
- 4-6 g/m<sup>2</sup>/hr
- remains low over month 1
- lower than adult values of 6-8 g/m<sup>2</sup>/hr



# Full-Term Skin Adaptation

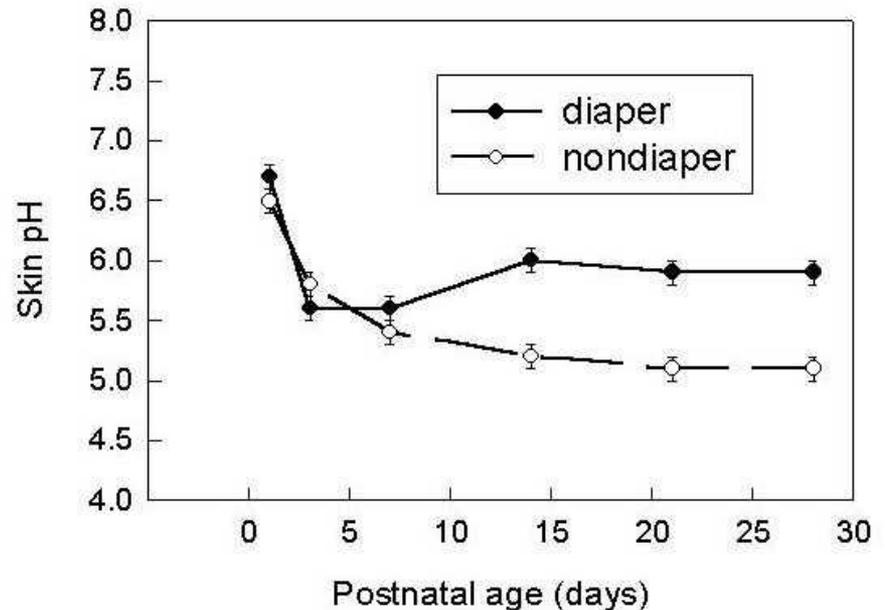
- The SC undergoes a rapid transition at birth.
- The water handling behavior changes significantly over the first month.
- By one month, the moisture accumulation rate is significantly higher for the infant vs. mother.



Visscher, Hoath, et al., *Pediatr Dermatol*, 2000; 17(1):45-51.

# Newborn Skin Adaptation: pH

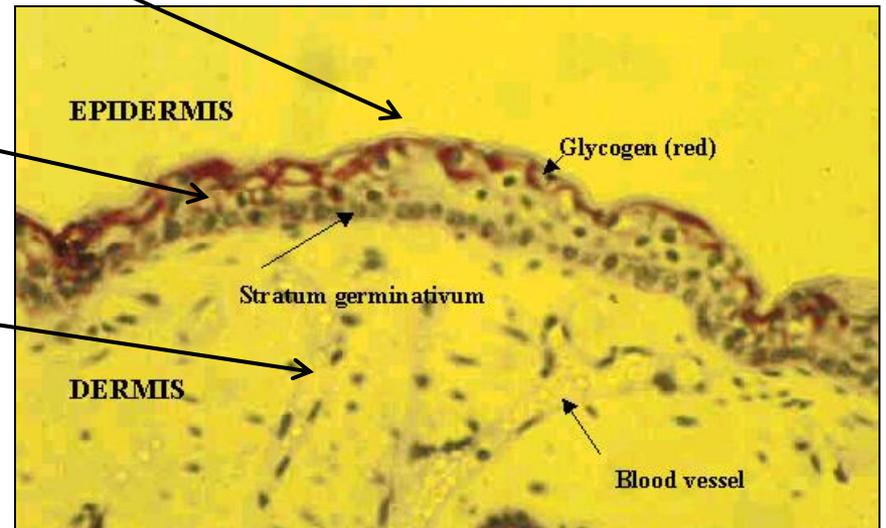
- Skin pH nearly neutral at birth.
- Rapid decrease during first 4 days.
- Regional differentiation with lower pH for nondiaper site.



*Visscher, Hoath, et al., Pediatr Dermatol, 2000; 17(1):45-51.*

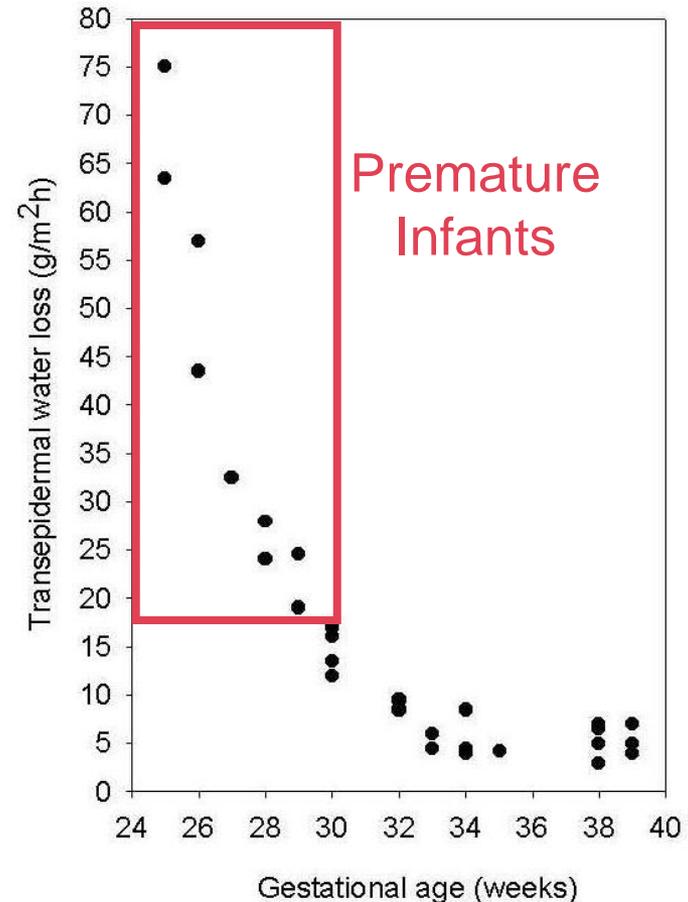
# Premature Infant Skin

- Stratum corneum poorly developed or absent
- Thin epidermis
- Dermis not fully formed and deficient of structural proteins



# Premature SC Barrier

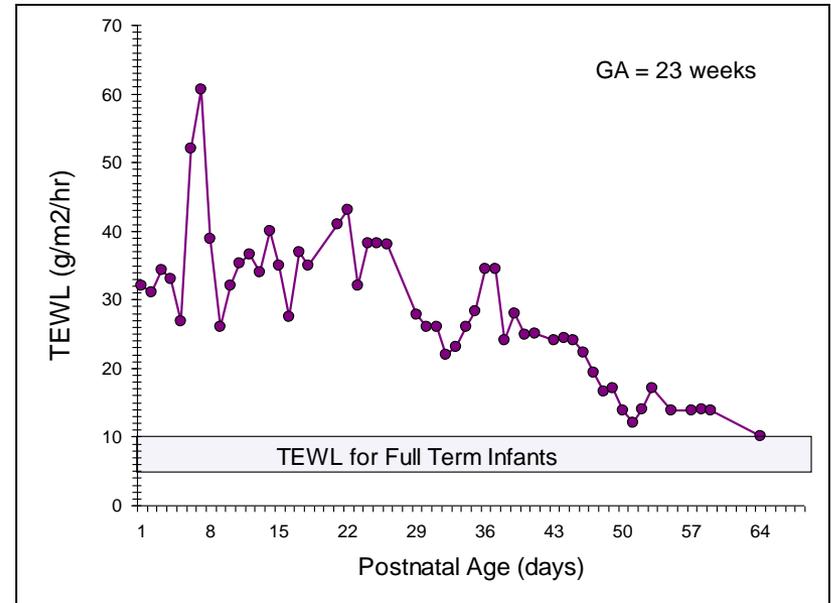
- Premature infant skin barrier integrity varies greatly with gestational age.
- TEWL for 24 – 25 wks gestation is very high, comparable to epidermis without a SC barrier.



*Sedin et al., Acta Paediatr Scand Suppl, 1983, 305: 27-31.*

# Premature Barrier Maturation

- Case study report on 10 infants aged 23-24 wks at birth
- TEWL decreased and conductance increased over time.
- Proposed a maturation time of 9 weeks



*Kalia et al., J Invest Dermatol, 1998, 111:320-326.*

# Premature Skin Adaptation: pH

- Skin pH profile for the mature infant varies with gestational age.
- Initial pH drop was observed in both groups.
- Smaller babies have a higher pH for a longer time.



*Fox, et al, J Perinatology, 1998, 18(4): 272-275.*

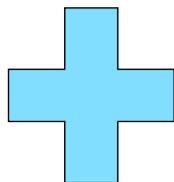
# Topical Treatments for Infants

## Products

### *Working Definition:*

Anything that touches the skin surface, including

- environment (e.g., humidity)
- creams, lotions, oils
- diapers, bedding, cloths, wipes
- cleansers, water
- tapes, adhesives
- devices (masks, PICC lines)

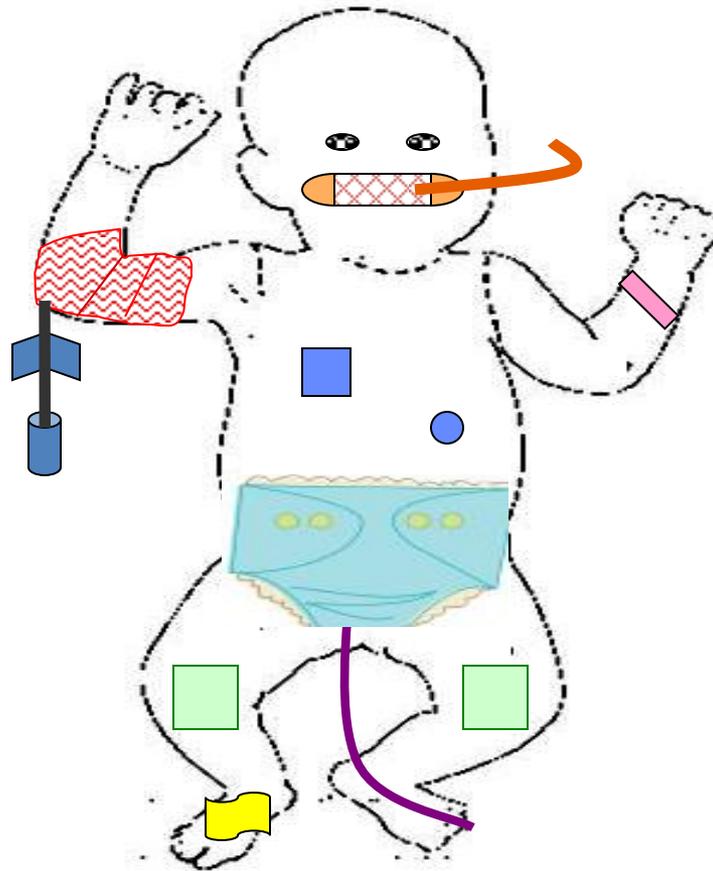


OR



???

# “Dressing” the NICU Patient



# Significance

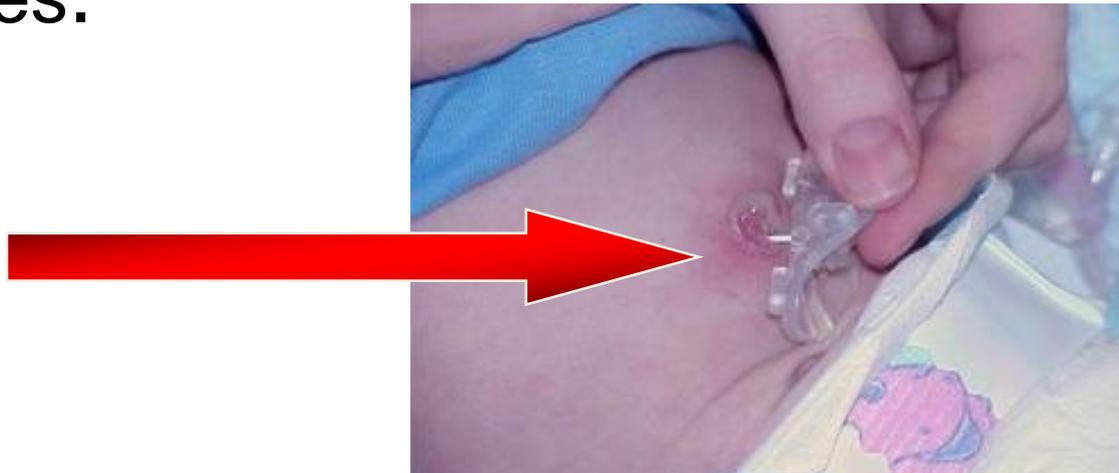
1. NICU patients at risk for skin breakdown
  - Prematurity, irritants (e.g., feces), stress
2. Epidermis is less well developed in premature versus full term neonates
3. Skin breakdown can result in
  - Infection, fluid loss, discomfort, stress, delay in start of oral feeding, anxiety for caregivers and families

# Skin Breakdown: Examples

- Erythema, inflammation, irritant dermatitis, diaper irritation
- Dryness/scaling
- Tape stripping
- Occlusion induced irritation
- Allergic contact dermatitis
- Pressure ulcers

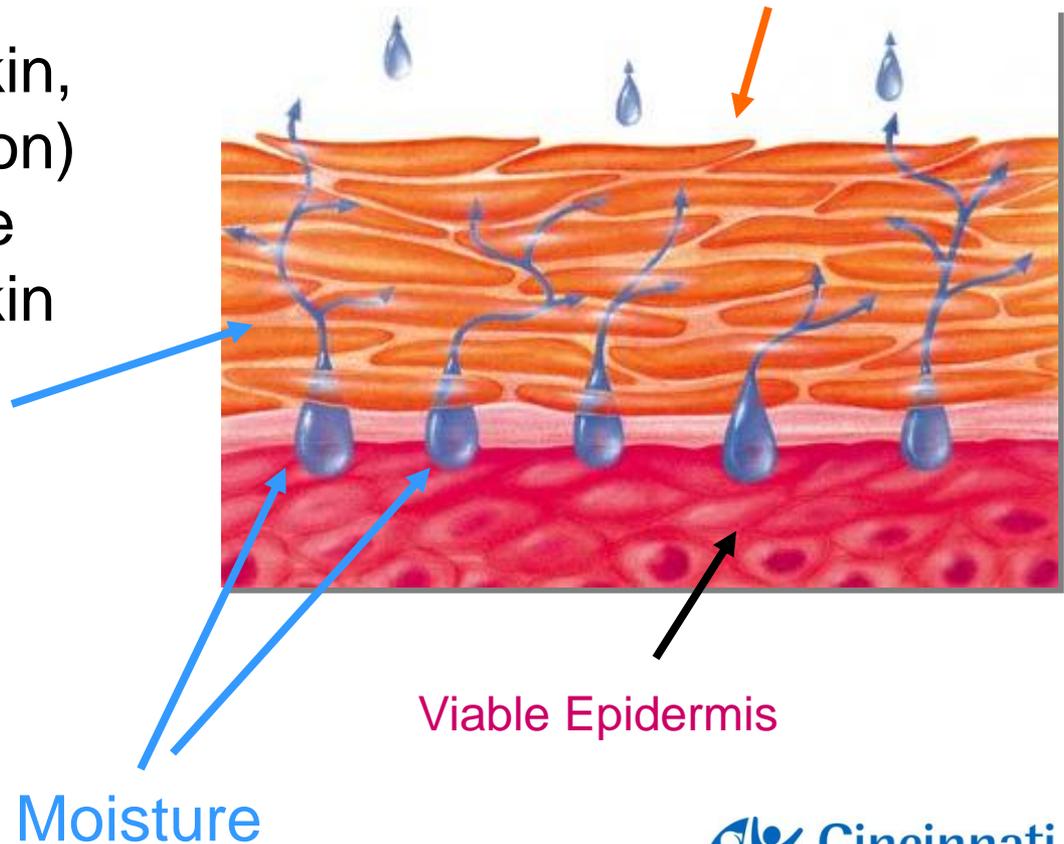
# G-tubes, Trachs: Irritant Dermatitis

- Secretions from G-tube sites, moisture under covers and friction (between skin and cover) can cause irritant dermatitis.
- Similarly, skin irritation can occur at trach sites.



# “Normal” Skin Moisture

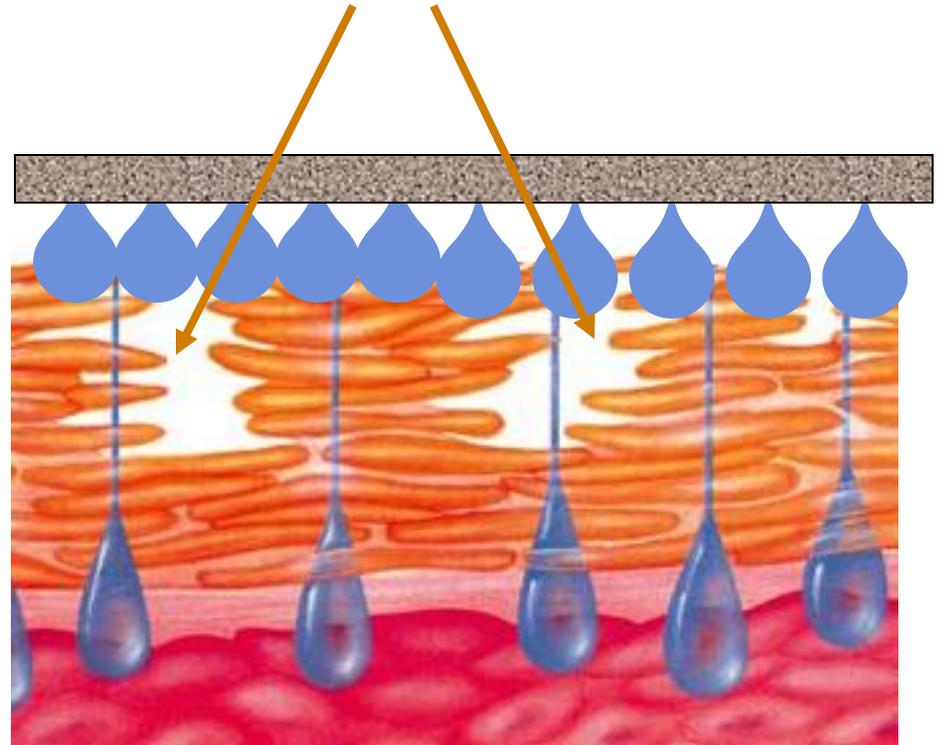
- In normal, healthy skin, water (from respiration) is lost from the viable tissue through the skin barrier.



# Occlusion

- Occlusive (non-breathable) items prevent normal water loss
- Water accumulates and compromises the barrier
- Increased permeability
- Risk of
  - **Irritation**
  - **infection**

## Compromised Skin Barrier



# Occlusion: Irritation

- Occlusion of normal skin with a tape barrier can cause transient water to build up under the film.
- Over time, the barrier becomes less permeable and more occlusive
- As a result, the skin becomes overhydrated, is more permeable and begins to breakdown.



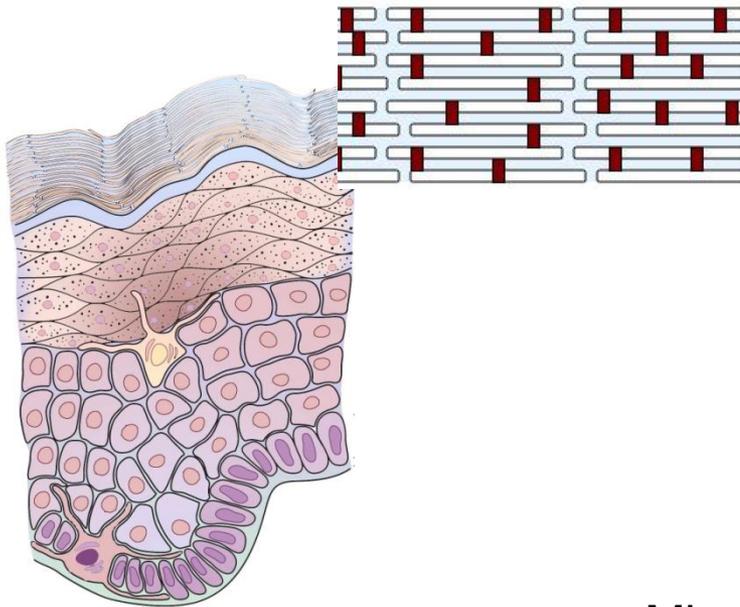
Irritation from  
film on face

# Tapes: Removal

- Removal of dressings and tapes can cause stripping of some of the outer layers of skin, creating a superficial wound.
- As a result, the skin is more permeable to irritants and susceptible to infection.



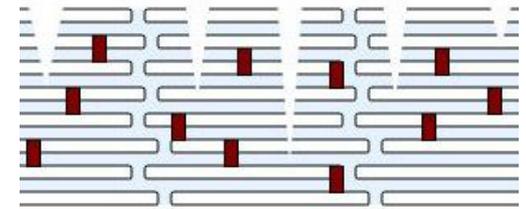
# Skin Compromise



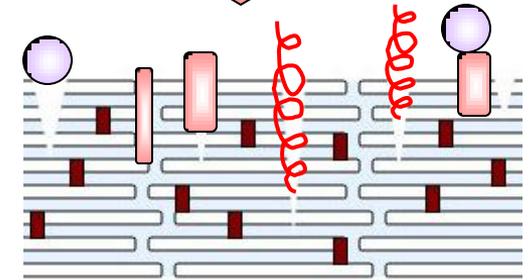
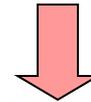
Water & cleansers disrupt lipid structure



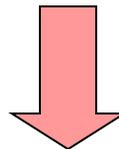
Skin barrier with defects



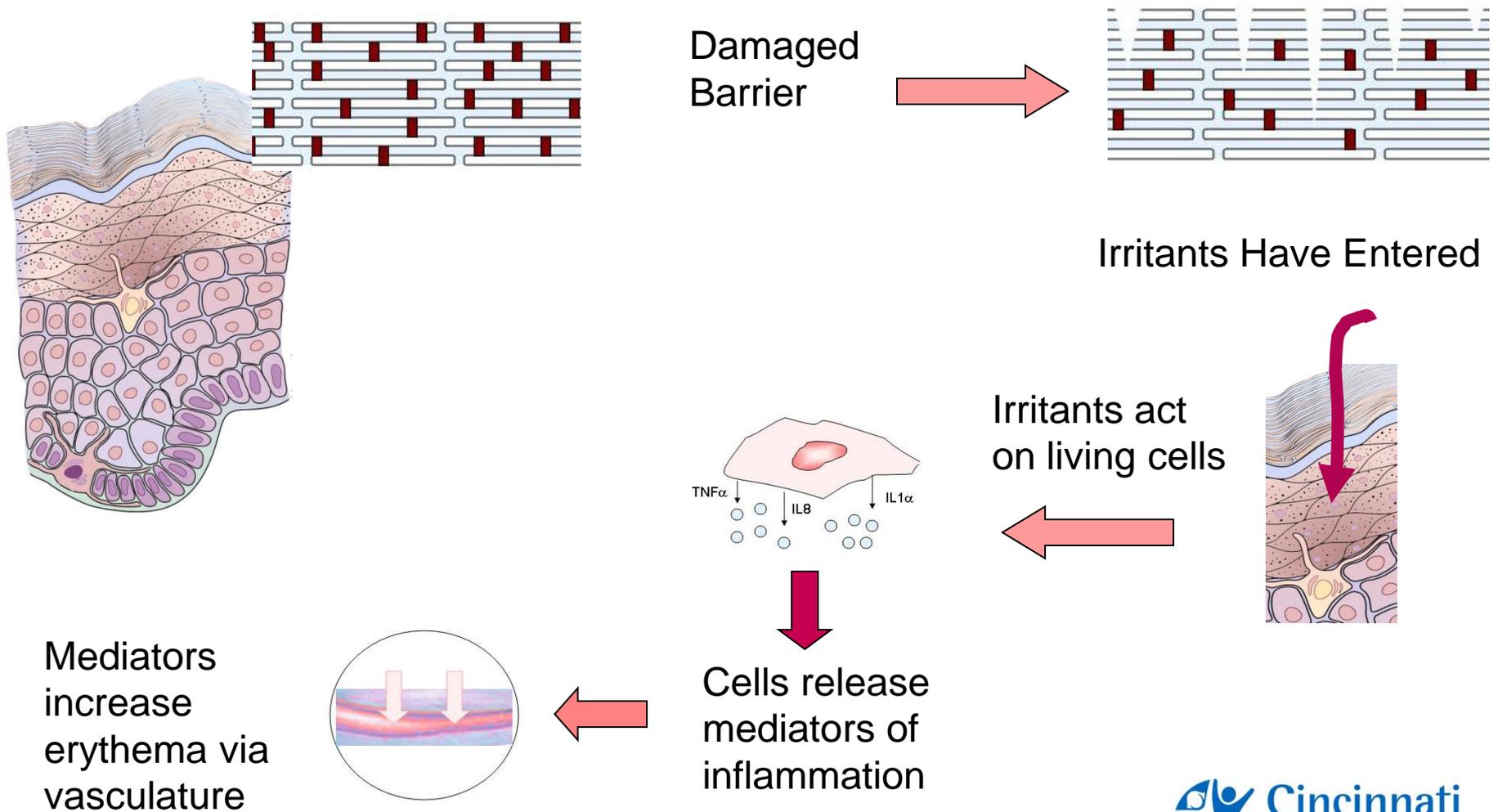
Irritants can penetrate



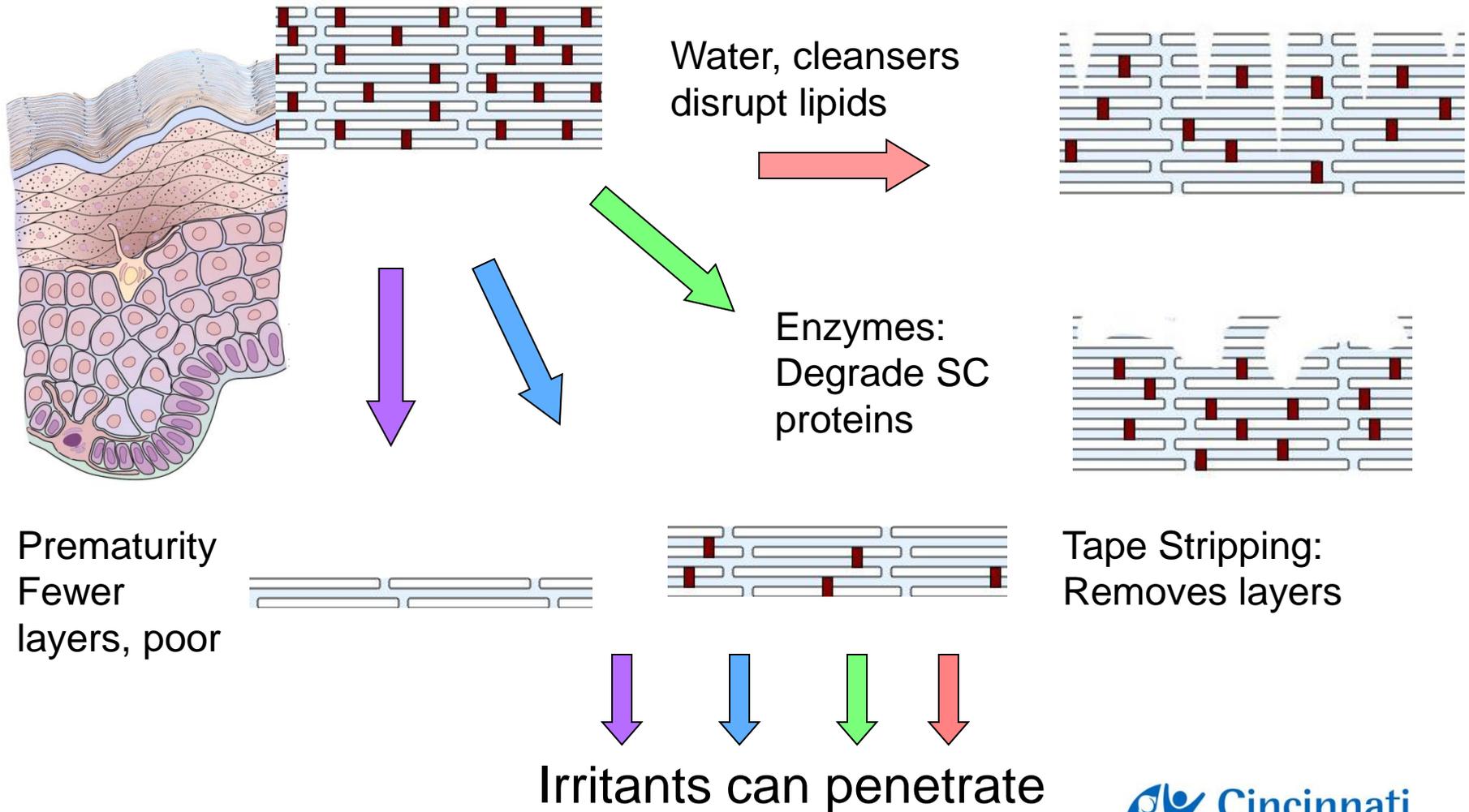
Microorganisms can enter to reach the Langerhans cells and epidermis



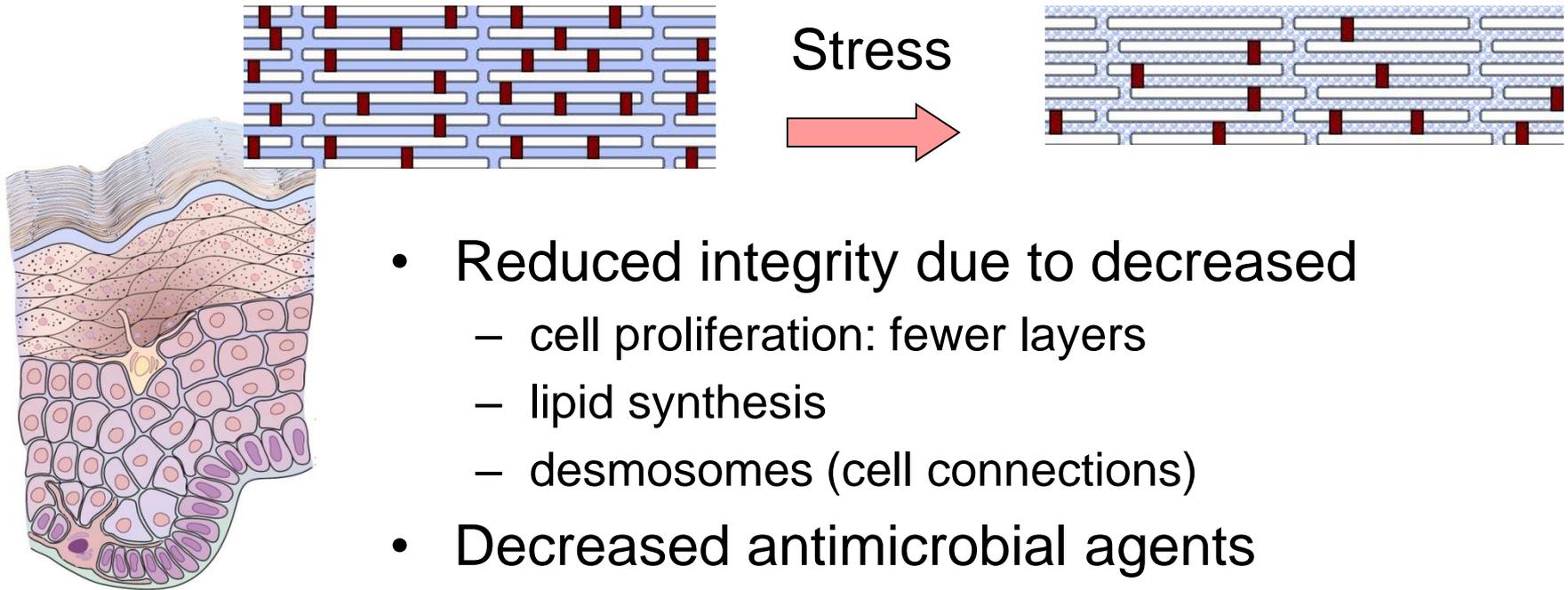
# Skin Compromise: 2



# Skin Compromise: 3



# Skin Compromise 4: Stress



- Reduced integrity due to decreased
  - cell proliferation: fewer layers
  - lipid synthesis
  - desmosomes (cell connections)
- Decreased antimicrobial agents
- Increased skin infection
- Delayed barrier recovery & wound healing

Choi, et al. *J Invest Dermatol* (2005);124:587-595.  
Aberg, et al. *J Clin Invest* (2007);117(11):3339-49.

# Skin Care Products & Regulations

- Topical skin products:
  - barrier creams
  - barriers
  - skin pastes
  - skin protectants
  - moisture barriers
- Many marketed under FDA Final Monograph: “Skin Protectant Drug Products for Over-the-Counter Human Use” (21 CFR Parts 310, 347, and 352)

# Skin Care Products & Regulations

- Under this monograph, skin protectants:  
“provide temporary relief from harmful or  
annoying stimuli”
- Some can claim: “temporarily protects minor  
cuts, scrapes, and burns”
- And/or: “helps prevent and temporarily protects  
and helps relieve chaffed, chapped, or cracked  
skin”

# Skin Protectant “Active Ingredients”

Ingredients	Allowed %
Cocoa Butter	50 - 100
Dimethicone	1 - 30
Glycerin	20 - 45
Mineral oil	50 - 100
Petrolatum	30 - 100

Ingredients	Allowed %
White petrolatum	20 - 45
Topical starch	1 - 30
Cod liver oil	5 - 13.56
Zinc oxide	12.5 - 50
Hard fat	50 - 100

# Examples

## *Original Ointment*



- **Petrolatum (53.4%), Lanolin (15.5%),** Cod Liver Oil (contains Vitamin A & Vitamin D), Fragrance, Light Mineral Oil, Microcrystalline Wax, Paraffin

## *Diaper Rash Cream*

- **Dimethicone (1%), Zinc Oxide (10%),** Aloe Barbadensis Extract, Benzyl Alcohol, Coconut Oil, Cod Liver Oil (Contains Vitamin A & Vitamin D), Fragrance, Glyceryl Oleate, Light Mineral Oil, Ozokerite, Paraffin, Propylene Glycol, Sorbitol, Synthetic Beeswax, Water

# Regulations

- Unlike prescription and certain OTC drugs, the FDA ***does not require*** randomized, controlled clinical trials ***that demonstrate effectiveness*** for approval.
- Do not assume that effectiveness has been shown in adequate, controlled clinical trials.

# Significance: Products

- Published information on the specific effects on skin barrier integrity and function within the NICU population is limited.

## *Assumptions*

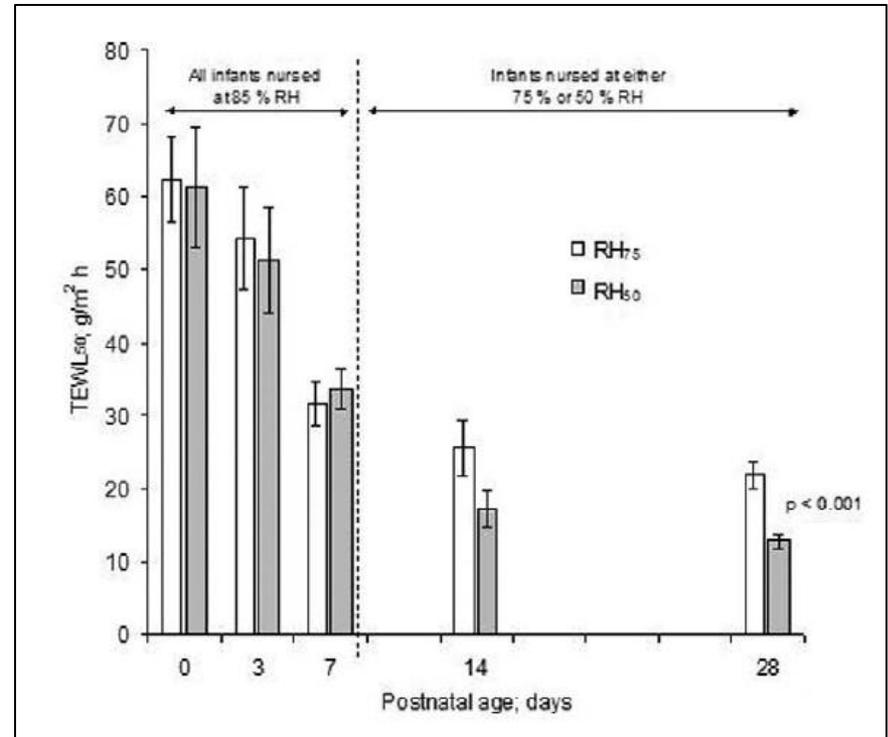
- Products sold for use on infant skin have extensive clinical trials on infants.
- Products tested on adults are automatically safe for infants.
- Infant skin and adult skin are the same.



# Premature Barrier Development

## *Effect of humidity*

- Premature infants 23-27 wks GA
- Incubator at ~80% RH for first week
- Randomized to 75% or 50% thereafter
- SC barrier maturation was more rapid at 50% vs 75% RH



*Agren et al, J Pediatrics, 2006, 148:613-7.*

# Vernix Caseosa

- Vernix caseosa coats the fetal skin surface during the last trimester.
- Vernix appears ~ 17 weeks in a head to toe, back to front pattern.
- Premature infants have little of no vernix.



# Vernix Research Findings

- ***Native vernix is a multifunctional skin cream with the following properties***
  - Skin moisturizer
  - Anti-infective
  - Anti-oxidant
  - Skin cleanser
  - Skin repair and wound healing, semipermeable
  - Barrier protectant, e.g. against enzymes

# Premature Skin: Topical Oils

- Daily massage with oils is a traditional cultural practice in many countries
- Benefits are prevention of infections and loss of heat
- However, mustard oil, a type commonly used in India, **delayed** skin barrier maturation.

*Darmstadt GL, et al. Acta Paediatr, 91(5), 546-554 (2002).*

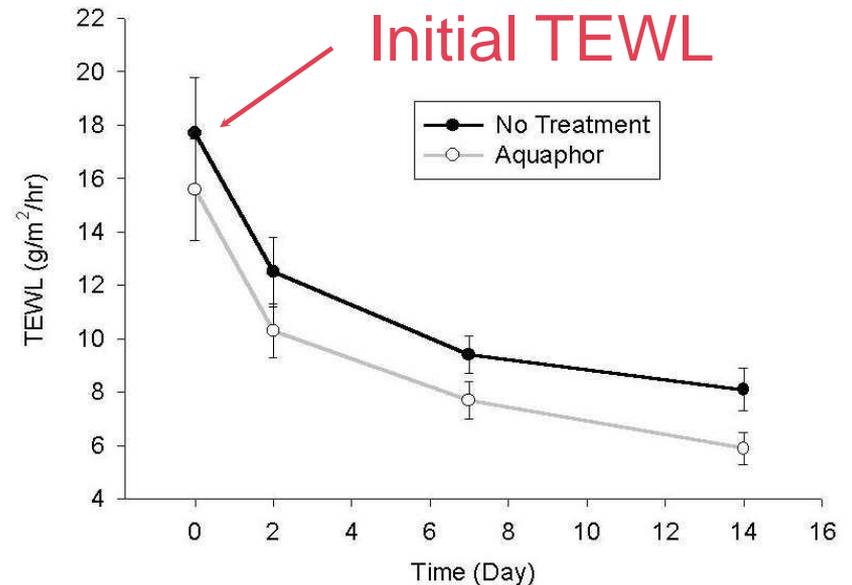
# Topical Oils: Sunflower Seed Oil

1. Sunflower seed oil enhanced skin barrier development.
2. Sunflower seed oil contains fatty acid (linoleic).
3. Application of sunflower seed and safflower oils significantly reduced nosocomial infection in preterm infants (< 33 wks GA) by 41% in Bangladesh.

*Darmstadt, et al. Lancet. 2005 365(9464):1039-45.*

# Premature Infants: Petrolatum

- 2x daily vs no treatment in 60 infants (29 wks)
- Petrolatum (Aquaphor<sup>®</sup>) group had significantly better skin condition, lower bacterial colonization, fewer positive cultures.
- TEWL decreased significantly for both.
- However, there was no difference when corrected for initial TEWL.



# Premature Infants: Petrolatum

## ***Multicenter Trial***

- Vermont Oxford Network, 54 NICUs
- Infants 500-1000g, mean GA = 26 weeks
- 610 infants: Petrolatum (Aquaphor<sup>®</sup>) 2x daily, 14 days
- 596 infants: Routine skin care
- A significantly **higher** incidence of nosocomial sepsis occurred in 501-750 g infants with Aquaphor<sup>®</sup>
- Organism responsible for sepsis was coagulase negative staph.

*Edwards, et al. Pediatrics. 2004 May;113(5):1195-203.*

# Premature Infants: Petrolatum

## ***Possible Explanation:***

- Aquaphor<sup>®</sup> behaved as an occlusive film in the trial, delaying barrier development and facilitating growth of microorganisms.

*Edwards, et al. Pediatrics. 2004 May;113(5):1195-203.*

# Premature Infants: Topical Oils

- Controlled trial among 457 infants  $\leq 33$  wks
- Nursery of Dhaka Shishu Hospital (Bangladesh)
- Daily treatment with **sunflower seed oil** (n = 159) or Aquaphor (n = 157) versus a no treatment (n = 181)
- Mortality rates were significantly reduced: 26% sunflower seed oil, 32% **Aquaphor**
- The results continue to support these treatments for use in developing countries.

*Darmstadt, et al. Pediatrics. 2008, 121(3):522-529.*

# Premature Infants: Topicals

- Application of certain topical treatments appears to be effective for improving skin condition in neonates.

## ***However.....***

- The mechanisms in human infants are not well understood.

# *Skin Care in the NICU Patient: Effects of Wipes versus Cloth & Water on Stratum Corneum Integrity*

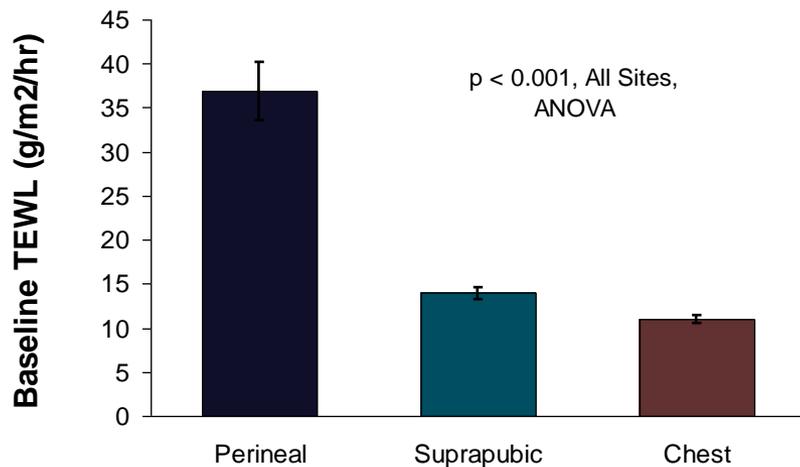
*Visscher, Odio et al. Neonatology (2009) 96:226-234*

# Subjects

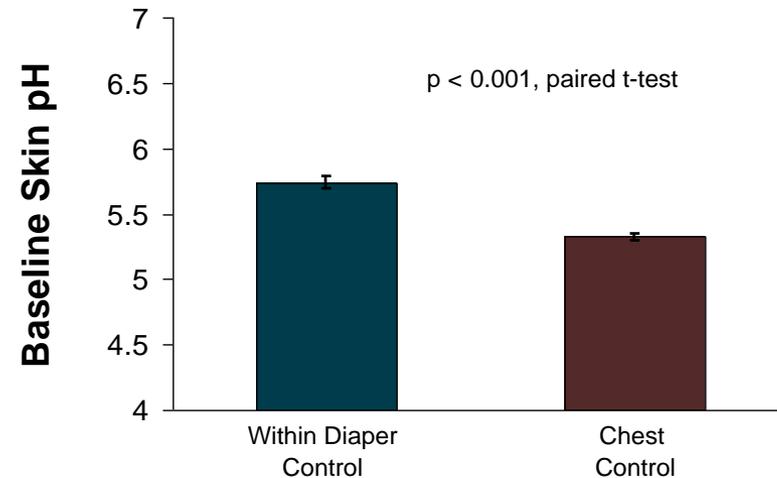
- 130 infants:
  - Wipe A = 45
  - Wipe B = 45
  - Cloth & Water = 40
- Mean gestational age: 34 wks (range 23 – 41)
  - Preterm = 97
  - Full term = 33
- Mean age at enrollment: 38 wks (range 30 – 51)
- Gender:
  - Males: 82
  - Females: 48

*Visscher, Odio et al. Neonatology (2009) 96:226-234*

# Regional Differences: Premature and Full-Term



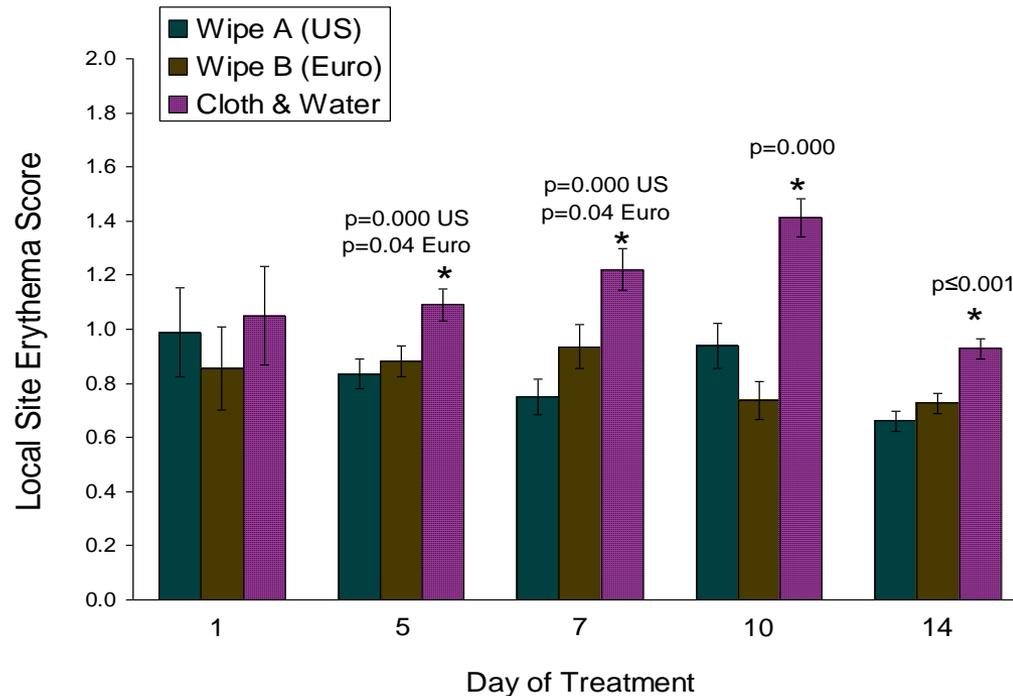
TEWL differed at for the perineal region, suprapubic area and chest.



Skin pH was significantly higher for diapered skin than the chest.

*Visscher, Odio et al. Neonatology (2009) 96:226-234*

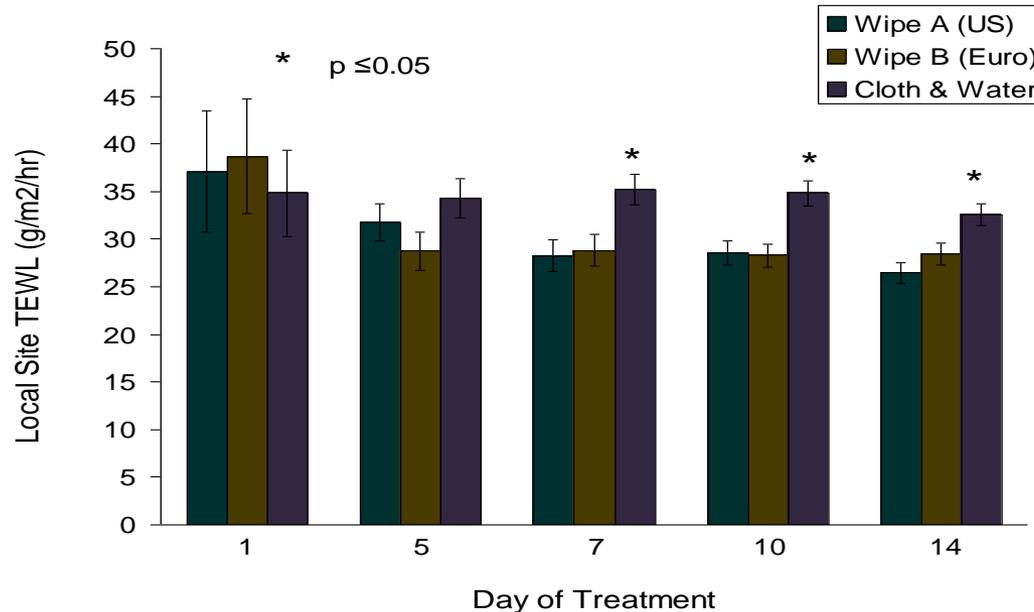
# Results: Local Perineal Erythema



- Local area (perineal) erythema scores were significantly **lower** for wipes than for cloth and water.

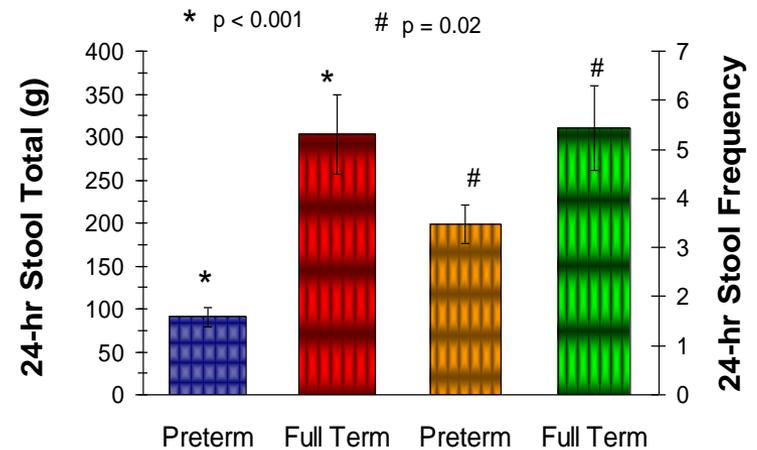
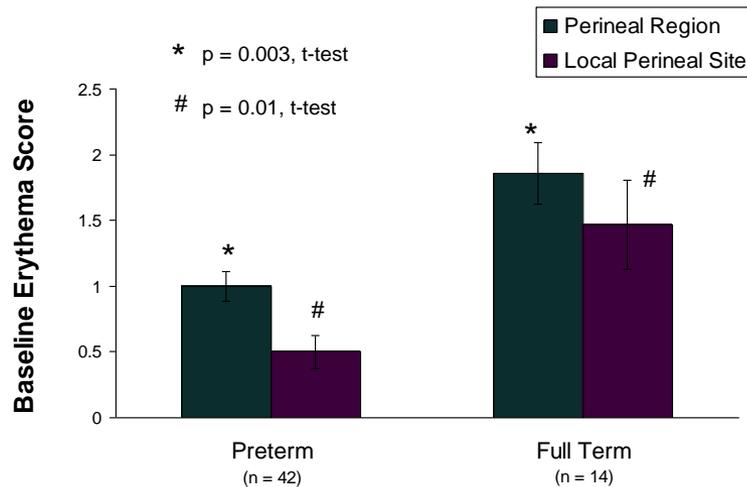
*Visscher, Odio et al. Neonatology (2009) 96:226-234*

# Results: TEWL Perineal Site



- TEWL at the perineal site was significantly **lower** for wipes treated skin than for cloth & water, reflecting a more normalized skin barrier.

# Effect of Gestational Age



- Perineal erythema scores were lower for preterm infants than for the full term group.
- The total stool exposure (g) influenced skin irritation.

Visscher, Odio et al. *Neonatology* (2009) 96:226-234

# Diaper Skin Breakdown: Prevention & Treatment

- ***Reduce hydration***
  - Use absorbent products to wick moisture from skin
  - Avoid diapers with plastic or non-breathable outer sheet
  - Minimize contact with urine, watery stools
  - Change diaper frequently
  - Insure that diaper fits properly
  - Dry the skin after cleansing

# Diaper Skin Breakdown: Prevention & Treatment

- ***Use gentle skin cleansing methods***
  - Soft implements
  - Avoid products with known irritants, fragrance, alcohol
  - Wipes without fragrance, irritants had lower erythema and rash than soft cloth and water
  - Minimize rubbing
  - If cream in place, remove only the soiled portion to minimize rubbing

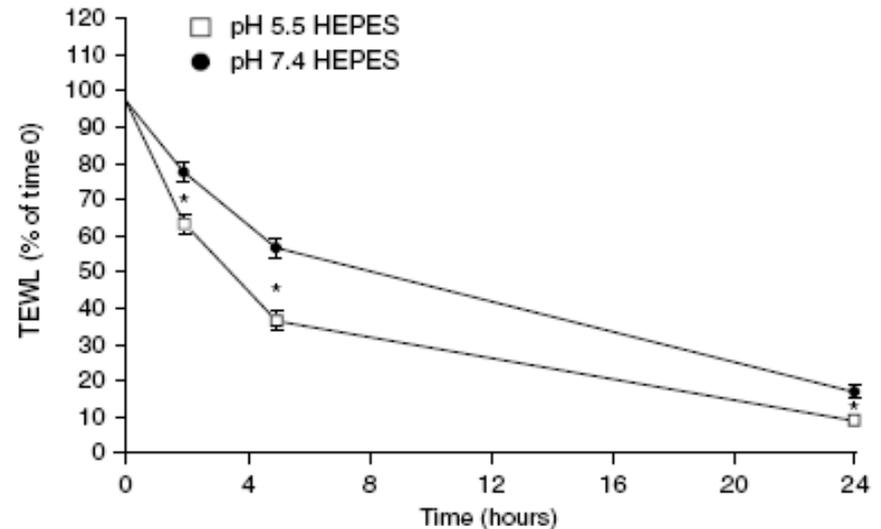
*Visscher M. Pediatric Health, Feb 2009, 3(1): 81-98*

# Diaper Skin Breakdown: Prevention & Treatment

- ***Apply topical treatments for barrier recovery and prevention of damage***
  - Provide a semipermeable layer
  - Provide a shield between skin and irritants
  - Use amount to balance “semipermeability” and physical shield
  - Use product that stays in place
  - Use products that can bind or deactivate irritants (bile salts, enzymes)

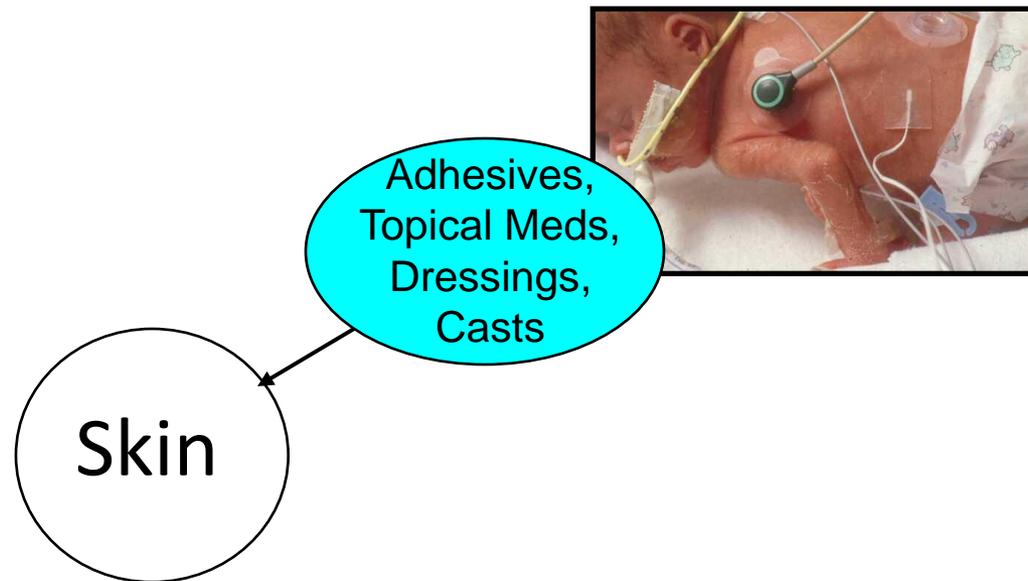
# Importance of an Acidic SC pH

- The rate of SC barrier recovery after tape stripping was increased with the application of an acidic (pH 5.5) buffer.
- Use of skin acidic (pH ~ 5) treatments may be a useful strategy for damaged infant skin.



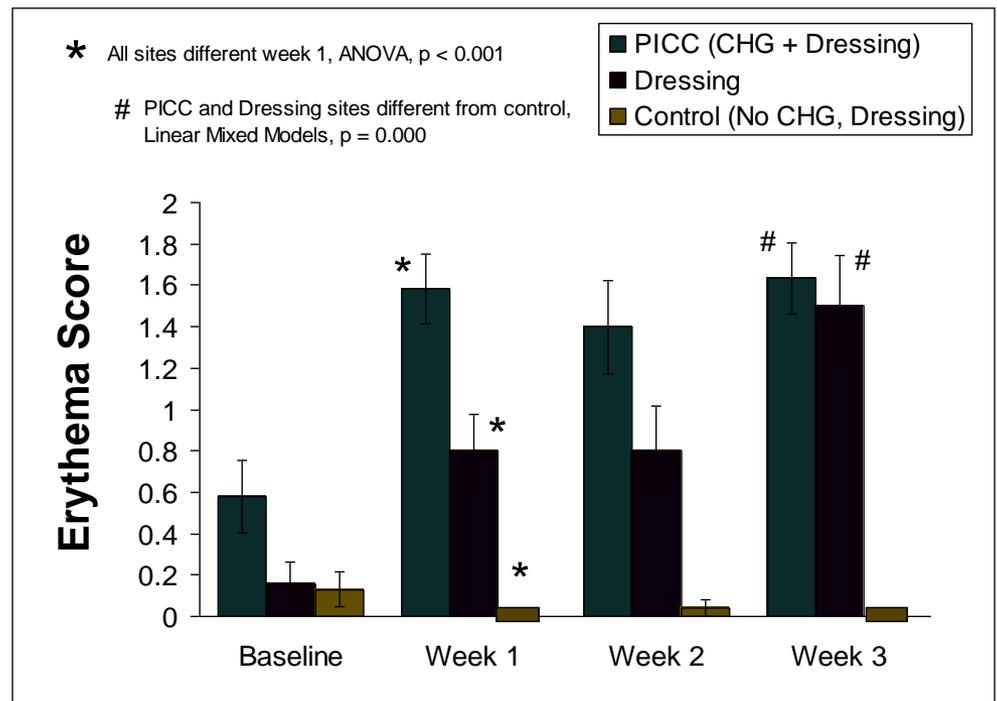
*Mauro, et al, Arch Dermatol Res. 1998, 290:215-222.*

# Effect of Chlorhexidine Gluconate (CHG) on the Skin Condition at PICC Line Sites



# Results: Skin Erythema

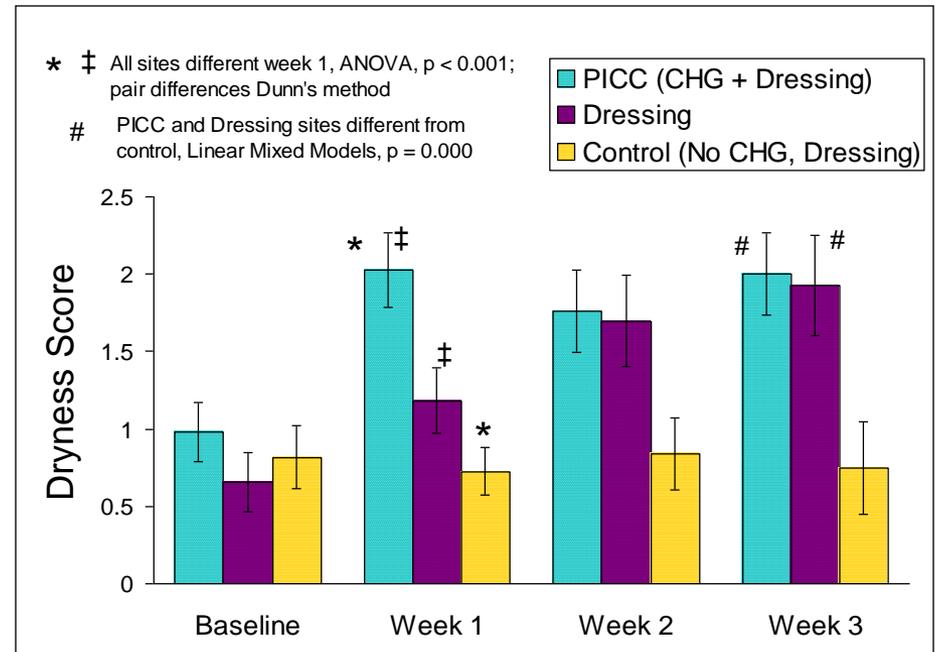
- At week 1, the sites were significantly different with the highest erythema at the PICC site
- By week 3, PICC and dressing sites were *comparable* and higher than the control.



Visscher, deCastro, Combs, Perkins, Winer, Schwegman, Burkhart, Bondurant. *J Perinatology* 2009;29(12):802-7.

# Results: Skin Dryness

- Dryness at baseline
- Week 1: dryness was significantly higher at the PICC site than the dressing and control.
- By week 3, PICC and dressing sites were comparable, with higher dryness than the control.



Visscher, deCastro, Combs, Perkins, Winer, Schwegman, Burkhardt, Bondurant. *J Perinatology* 2009;29(12):802-7 .

# Implications & Commentary

- The dressings, rather than CHG alone, contribute to skin breakdown.
- These results highlight the skin compromise issues associated with tapes and dressings.
- Dressings with inherently higher permeability may minimize skin breakdown.
- Investigation and/or development of alternatives is essential.

# Touch: Infant Skin Interactions

## *Specific Modalities:*

- Skin-to-Skin Contact (Kangaroo Care)
- Newborn Individualized Developmental Care and Assessment (NIDCAP)
- Infant Massage
- Tactile Stimulation

# Skin-to-Skin Contact

- Skin-to-skin contact
  - immediately following birth resulted in increased temperature and blood glucose, compared to swaddling next to the mother
  - for one hour shortly after birth impacted state organization and time spent sleeping

*Mazurek T, et. al. Med Wieku Rozwoj, 3(2), 215-224 (1999).  
Ferber SG, Makhoul IR. Pediatrics, 113(4), 858-865 (2004).*

# Skin-to-Skin Contact

- Infants 25-33 wks GA (n = 17)
- In mothers,
  - decreased salivary cortisol (32%)
  - decreased heart rate (7%),
  - decreased stress (89%)
  - increased mood (6%)
- In infants,
  - decreased heart rate
  - decreased pain scores
  - either increased or decreased cortisol



*Morelius E, et al. Pediatrics. Nov;116(5):1105-13, 2005*

# Developmentally Supportive Care

- Premature infants cared for with NIDCAP methods had significantly better
  - neurobehavioral function and more mature neuronal fiber structure
  - mother-child interaction (cluster communication), better hearing/speech and lower behavior symptom scores

*Als H, Duffy FH, McAnulty GB, et al. Pediatrics, 113(4), 846-857 (2004).  
Kleberg A, Westrup B, et. al. Early Hum Dev, 60(2), 123-135 (2000).*

# Tactile Stimulation

- Tactile stimulation via repeated stroking increased circulating lactate levels by 200% in the neonatal rat model

*Alasmi MM, Pickens WL, Hoath SB. Pediatr Res, 41(6), 857-861 (1997).*

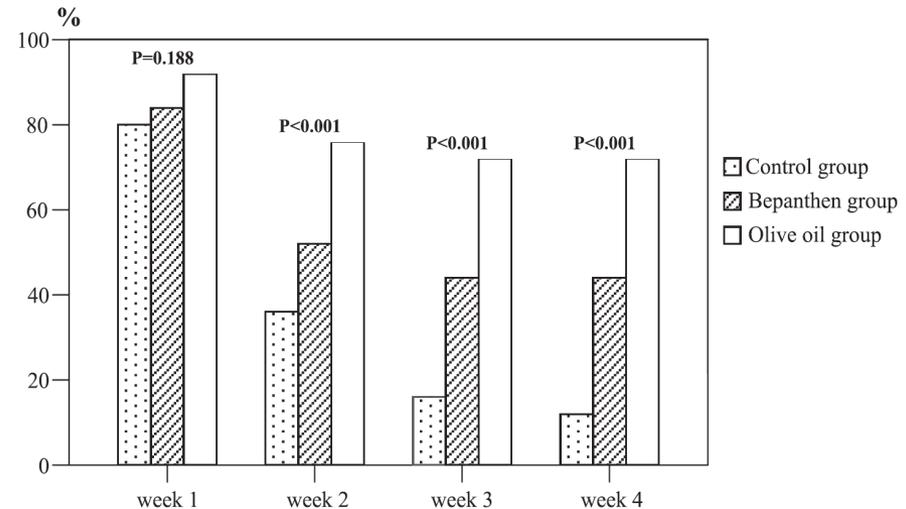
# Questions?????????



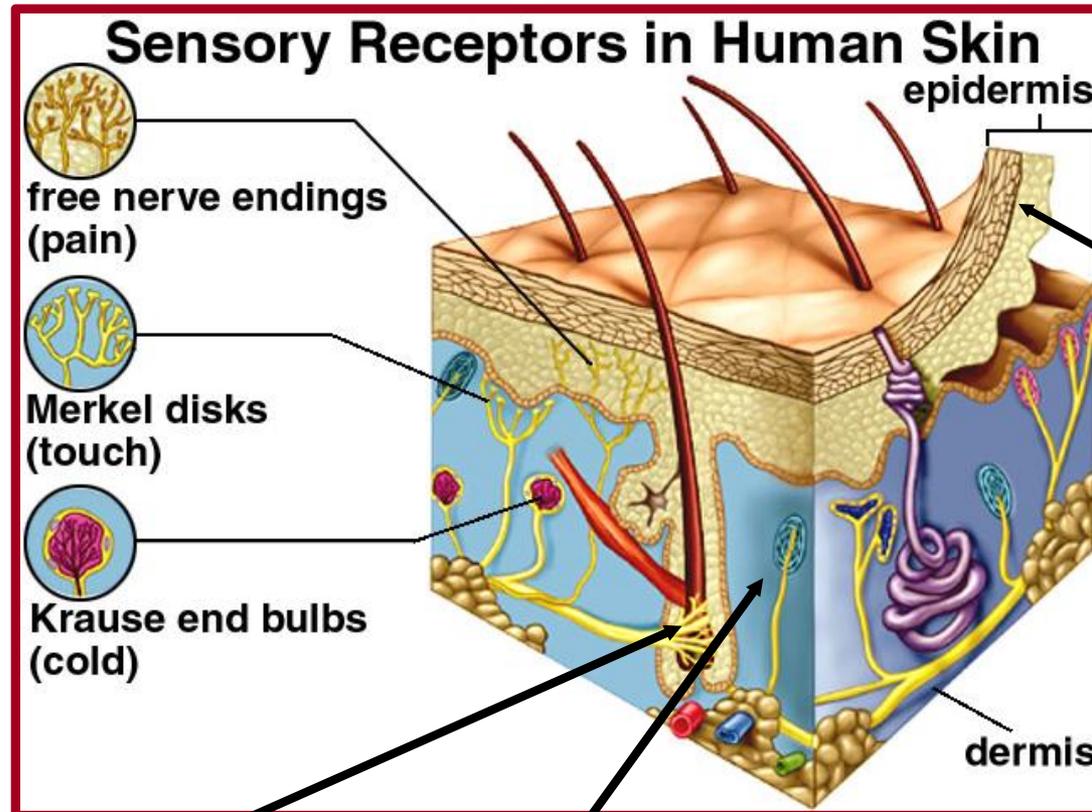
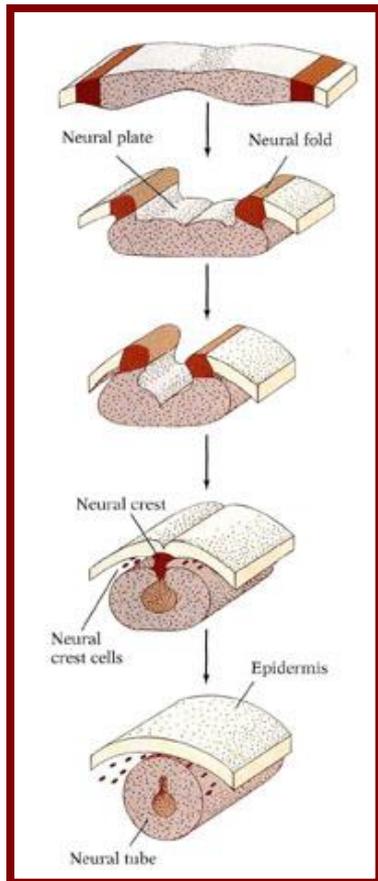
# Additional Information

# Premature Infants: Topicals

- 173 infants 25 – 36 wks GA
- 4 weeks with
  - Olive oil (fatty acid, linoleic) 30% and lanolin 70%
  - Bepanthen emollient (dexpanthenol, phenoxyethanol)
- Percent subjects with best skin condition was greater for olive oil vs. Bepanthen
- Both produced less dermatitis than control.



# Types of Cutaneous Nerve Endings



# Skin Statistics



***In an area the size of a quarter there are***

- Cells: > 3,000,000
- Sweat glands: 100 – 340
- Nerve endings: 50
- Blood vessels: 3 feet
- 640,000 sensory receptors
- 7 – 135 tactile points per cm<sup>2</sup>
- Sensory fibers from skin to spinal cord > 500,000

*Montagu A. Touching: The Human Significance of Skin, 1971, p. 7.*

# TEST

## Erythema

Area Increments	< 2%	2-10%	>10%	10-50%	>50%
-----------------	------	-------	------	--------	------

Severity Levels				
	Faint-Definite Pink	Definite Redness	Very Intense Redness	

## Rash

Area Increments	one	2-5	<10%	10-50%	>50%
-----------------	-----	-----	------	--------	------

Severity Levels	Papules	Pustules (automatic $\geq 2$ grade)
-----------------	---------	--

## Dryness

Area Increments	< 10%	10-50%	>50%
-----------------	-------	--------	------

Severity Levels	Slight powderiness	Early cracking	Moderate cracking & scales	High cracking & lifting scales	Bleeding cracks
-----------------	--------------------	----------------	----------------------------	--------------------------------	-----------------

# CONTROL

## Erythema

Area Increments	< 2%	2-10%	>10%	10-50%	>50%
-----------------	------	-------	------	--------	------

Severity Levels				
	Faint-Definite Pink	Definite Redness	Very Intense Redness	

## Rash

Area Increments	one	2-5	<10%	10-50%	>50%
-----------------	-----	-----	------	--------	------

Severity Levels	Papules	Pustules (automatic $\geq 2$ grade)
-----------------	---------	--

## Dryness

Area Increments	< 10%	10-50%	>50%
-----------------	-------	--------	------

Severity Levels	Slight powderiness	Early cracking	Moderate cracking & scales	High cracking & lifting scales	Bleeding cracks
-----------------	--------------------	----------------	----------------------------	--------------------------------	-----------------

# TEST

## Erythema

Area Increments	< 2%	2-10%	>10%	<del>10-50%</del>	>50%
-----------------	------	-------	------	-------------------	------

Severity Levels			<del></del>	
	Faint-Definite Pink	Definite Redness		Very Intense Redness

## Rash

Area Increments	one	<del>2-5</del>	<10%	10-50%	>50%
-----------------	-----	----------------	------	--------	------

Severity Levels	<del>Papules</del>	Pustules (automatic $\geq$ 2 grade)
-----------------	--------------------	--

## Dryness

Area Increments	< 10%	<del>10-50%</del>	>50%
-----------------	-------	-------------------	------

Severity Levels	Slight powderiness	Early cracking	<del>Moderate cracking &amp; scales</del>	High cracking & lifting scales	Bleeding cracks
-----------------	--------------------	----------------	---	--------------------------------	-----------------

**Erythema = 2.0**  
**Rash = 1.0**  
**Dryness = 2.5**

# CONTROL

## Erythema

Area Increments	<del>&lt; 2%</del>	2-10%	>10%	10-50%	>50%
-----------------	--------------------	-------	------	--------	------

Severity Levels	<del></del>			
	Faint-Definite Pink	Definite Redness	Very Intense Redness	Very Intense Redness

## Rash

Area Increments	one	2-5	<10%	10-50%	>50%
-----------------	-----	-----	------	--------	------

Severity Levels	Papules	Pustules (automatic $\geq$ 2 grade)
-----------------	---------	--

## Dryness

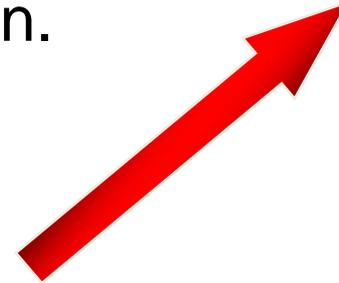
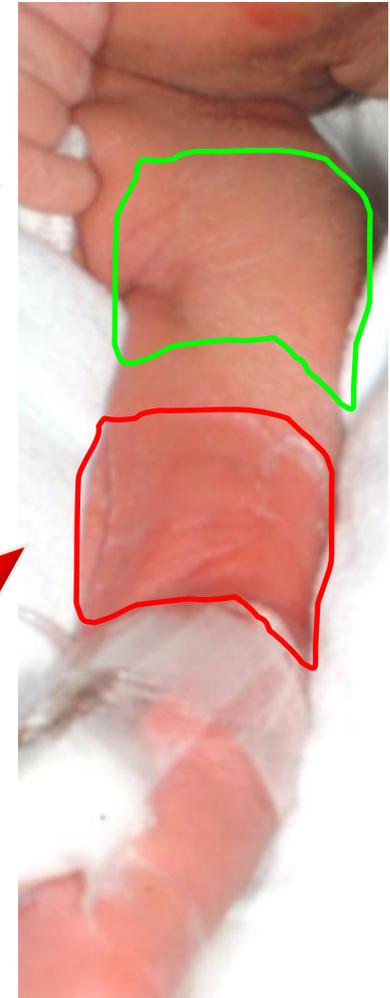
Area Increments	< 10%	10-50%	>50%
-----------------	-------	--------	------

Severity Levels	Slight powderiness	Early cracking	Moderate cracking & scales	High cracking & lifting scales	Bleeding cracks
-----------------	--------------------	----------------	----------------------------	--------------------------------	-----------------

**Erythema = 0.5**  
**Rash = 0**  
**Dryness = 0**

# Tape Irritation

- Removal of dressings and tapes can cause stripping of some of the outer layers of skin, creating a superficial wound.
- As a result, the skin is more permeable to irritants and susceptible to infection.



## Erythema

Area Increments	< 2%	2-10%	>10%	10-50%	<del>50%</del>
Severity Levels					
	Faint-Definite Pink		Definite Redness	Very Intense Redness	

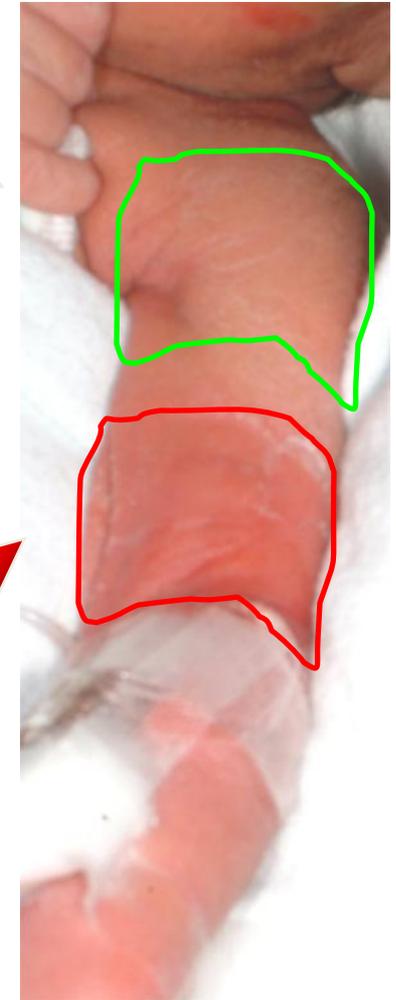
Erythema = 2.5

# Tape Irritation

Score	Description	Area
0	None	---
0.5	Slight powderiness	< 10%
1.0	Slight powderiness or early cracking	10-50% < 10%
1.5	Slight powderiness or early cracking	>50% 10-50%
2.0	Early cracking or moderate cracking & scales	>50% <10%
2.5	Moderate cracking & scales	10-50%
3.0	Moderate cracking & scales	>50%
3.5	High cracking & lifting scales	10-50%
4.0	High cracking & lifting scales	>50%
4.5	Bleeding cracks	10-50%
5.0	Bleeding cracks	>50%

Control

Dryness = 2.0



## Erythema

Area Increments	< 2%	2-10%	>10%	10-50%	>50% <del>X</del>
Severity Levels					
	Faint-Definite Pink		Definite Redness	Very Intense Redness	

Erythema = 2.5