

**Neonatal Skin Health:  
Evidence-Informed  
Care in Early Life**



## **Marty O. Visscher, PhD**

James L. Winkle College of Pharmacy,  
University of Cincinnati

- World-renowned expert in neonatal and infant skin health
- Over 30 years of active skin research
- Specialized expertise in:
  - Skin barrier development & adaptation
  - Vernix biology and early-life skin care
  - Prevention of skin injury in NICU settings
- Author of numerous seminal publications on neonatal skin
- Frequent CE speaker at national professional associations

# Objectives

- 1 Premature and full-term infant skin structure, function and changes over the first few months.
- 2 Skin care practices that facilitate healthy skin starting at birth.
- 3 Diaper dermatitis, its causes and evidence-based preventive skin care practices.
- 4 Scientific and clinical research support for skin care practices

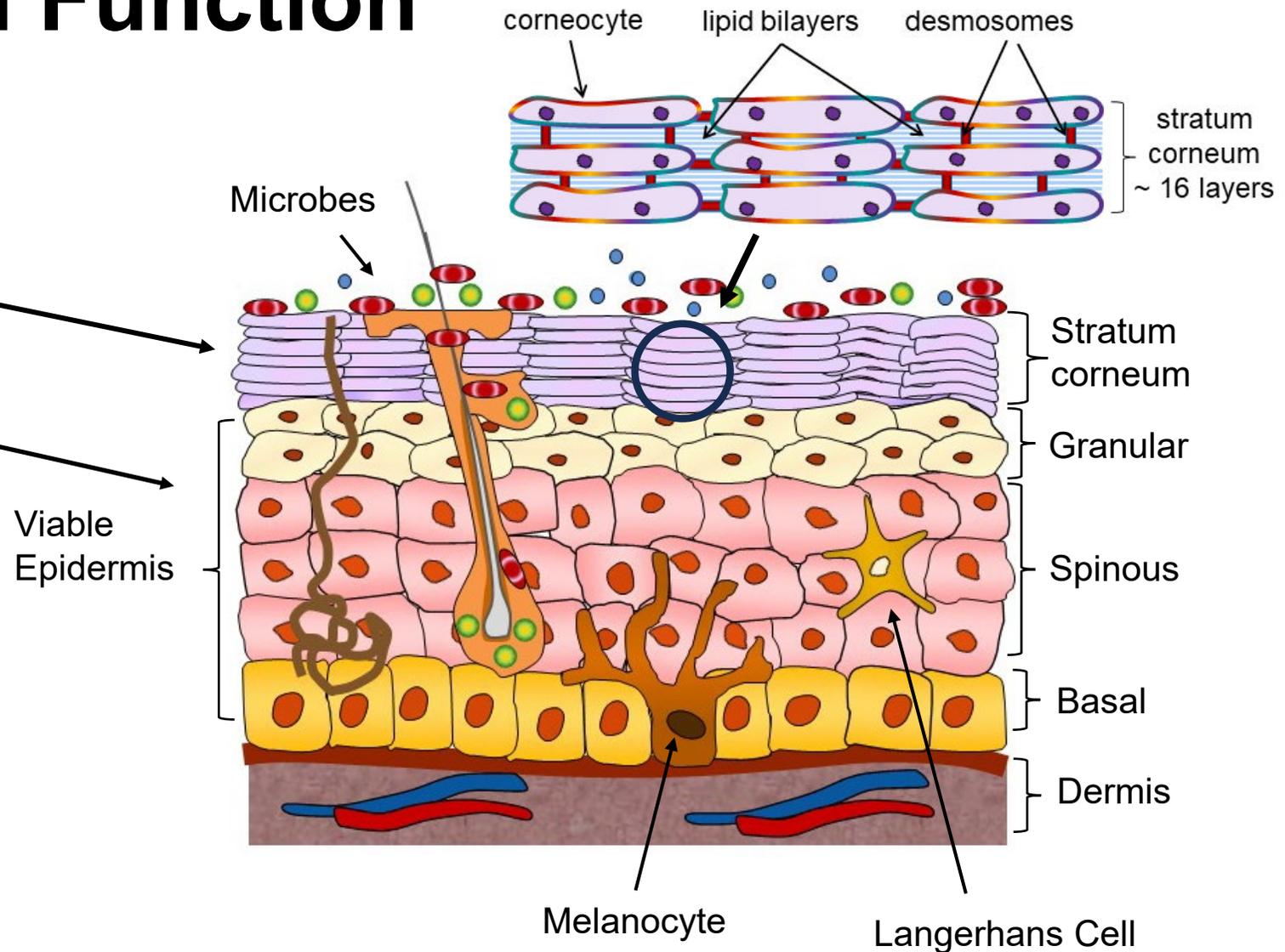


# Life-Saving Functions of Neonatal Skin

- Skin - the only self-renewing organ, turns over every 28 days
- The skin forms from ectoderm, the same tissue as the brain
- Constantly senses the environment
  - Superb “threat detector” with rapid response
  - Continually repairs itself from “assault” and damage
- Newborn baby skin = **Perfection**
- Irresistibly touchable

# Skin Structure and Function

- **Stratum Corneum (SC)**
  - Physical barrier
  - Acid mantle
  - Tactile discrimination
- **Viable Epidermis**
  - Generates SC
  - Langerhans cells (immunity)
  - Melanocytes: color, protection from UV
- **Dermis**
  - Structural proteins (e.g., collagen)
  - Thermoregulation
  - Blood supply
  - Resiliency, protects from mechanical stress



# Birth: **COLOSSAL** Upheaval

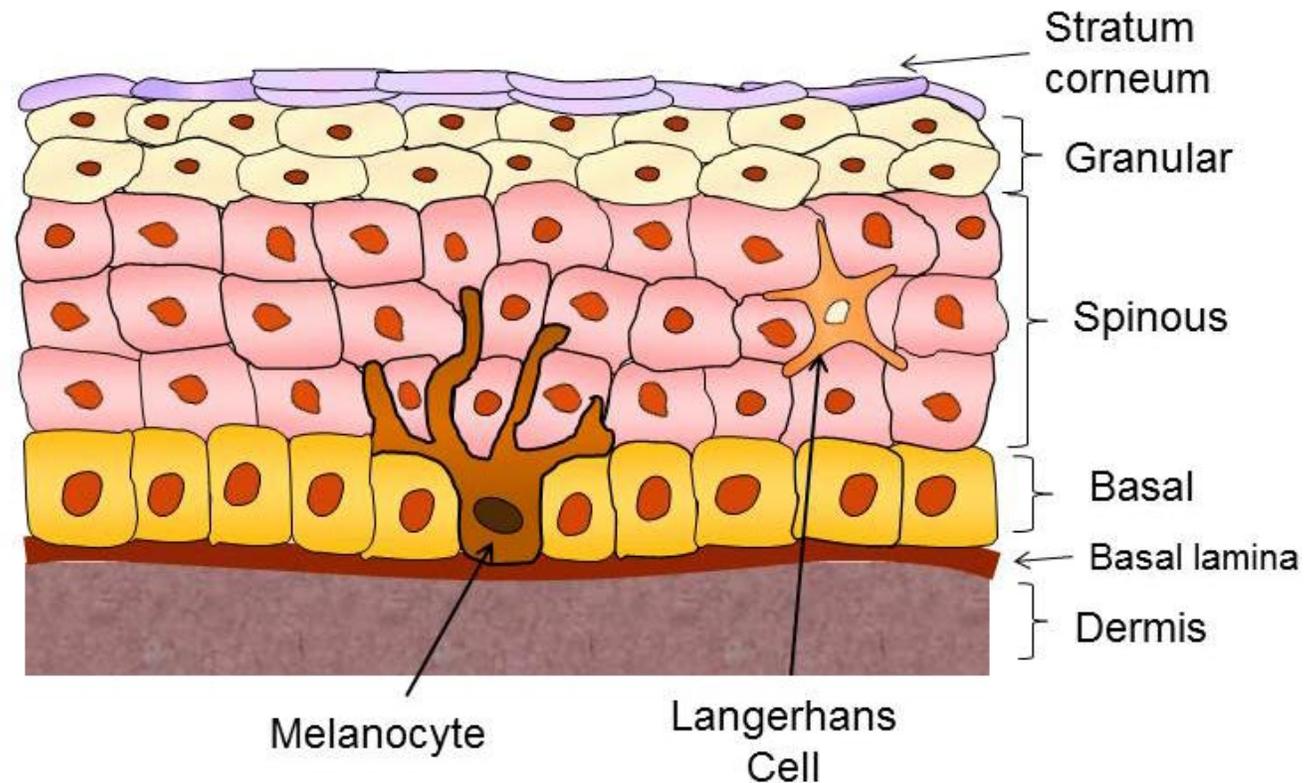


**WAIT!!!!**

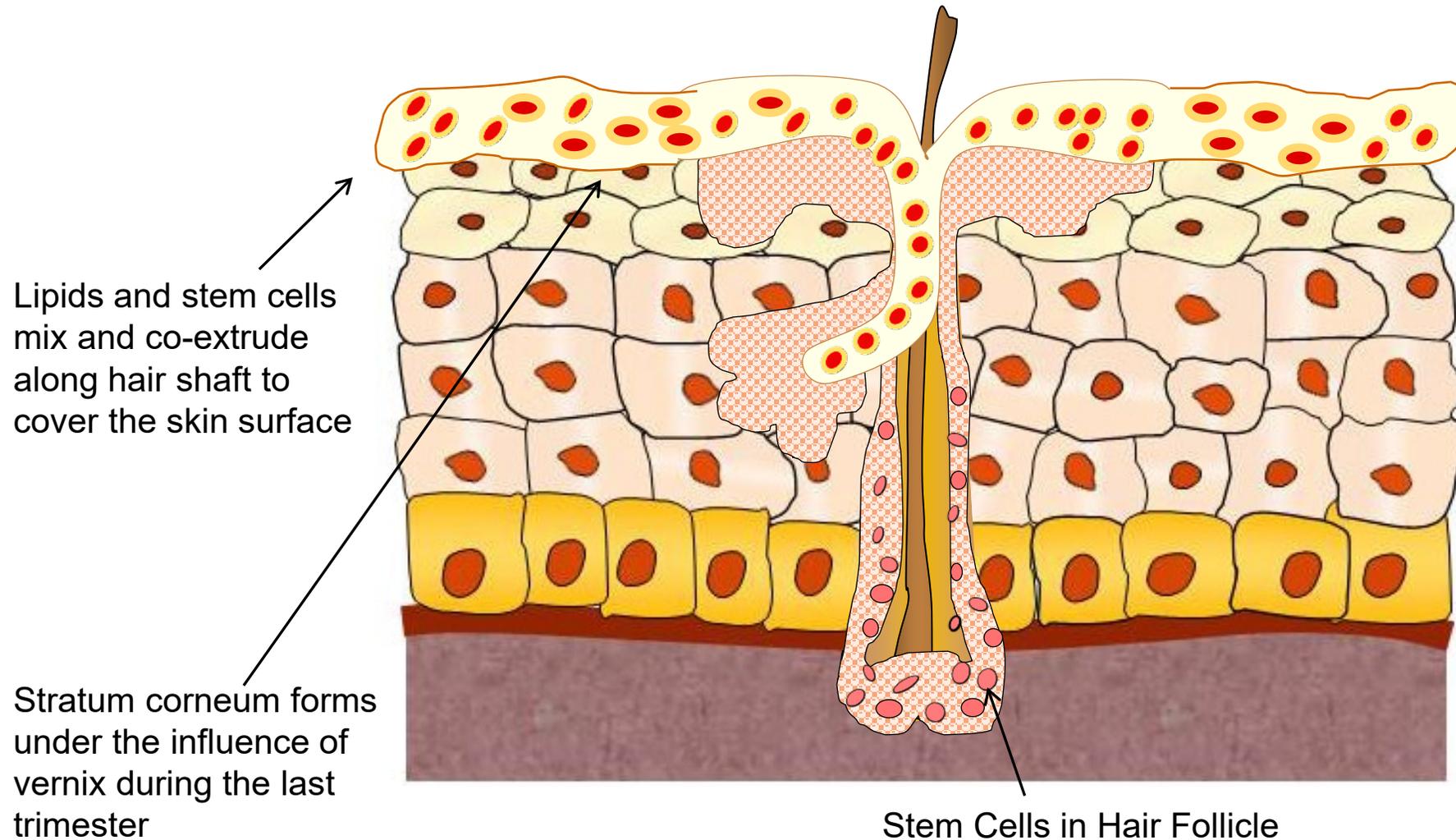
How does the infant develop excellent skin while soaking in water and urine before birth?

# Fetal Skin Development

At birth, the skin is thin, pink, and wrinkled. The epidermis is composed of a single layer of cells, and the dermis is composed of a few layers of cells. The skin is covered in a protective layer of mucus, and a protective layer of keratin appears.

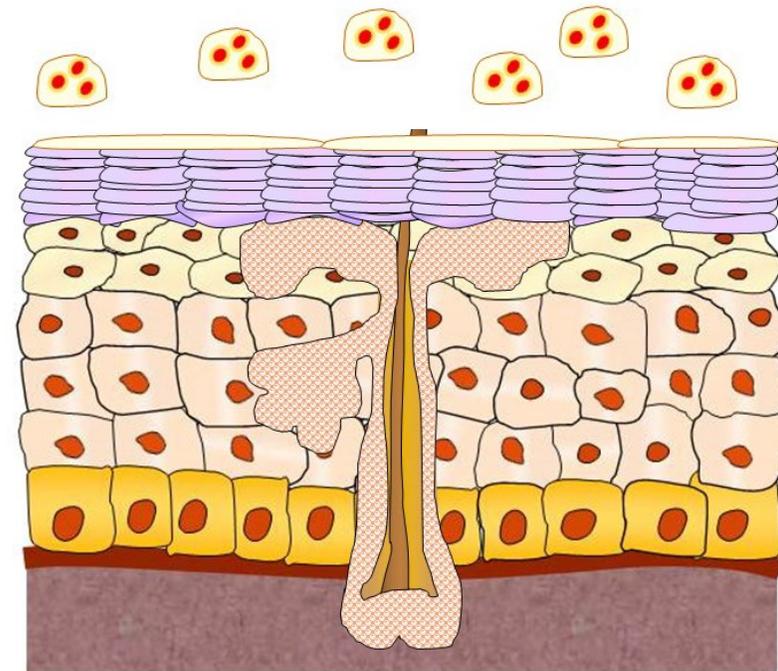


# Skin Development During Gestation



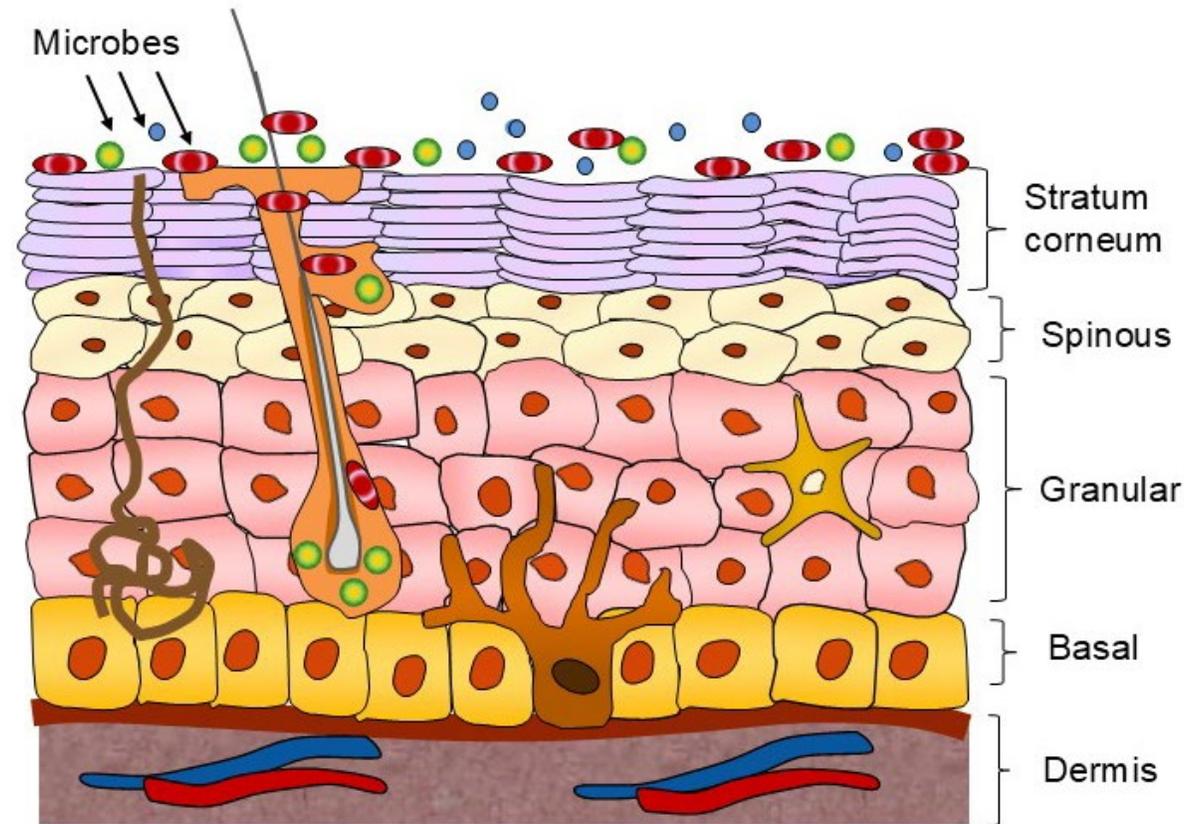
# Lung Maturity

- Mature lungs secrete phospholipid surfactants that detach vernix from the skin surface
- Causes cloudy amniotic fluid
- Infant swallows the amniotic fluid
- Vernix provides nutrients and primes the intestine for extra-utero feeding.

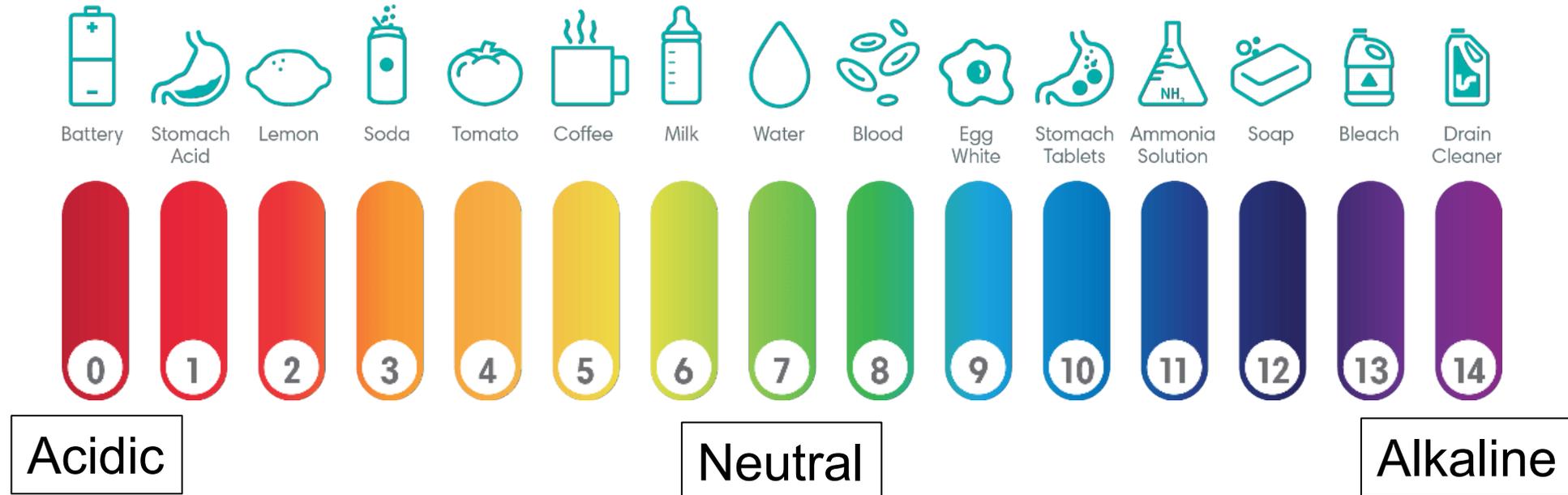


# Skin Microbiome

- Huge surface for microbe interaction
- Microbes: bacteria, virus, fungi, colonize the surface, hair follicles & eccrine glands
- Microbes cause the skin to make **beneficial** agents, e.g., antimicrobial proteins & fatty acids.
- Microbes inhibit pathogenic bacteria
- Microbes trigger keratinocytes to make immune mediators.



# The pH Scale



# Importance of an Acidic Skin Surface

## Stratum Corneum

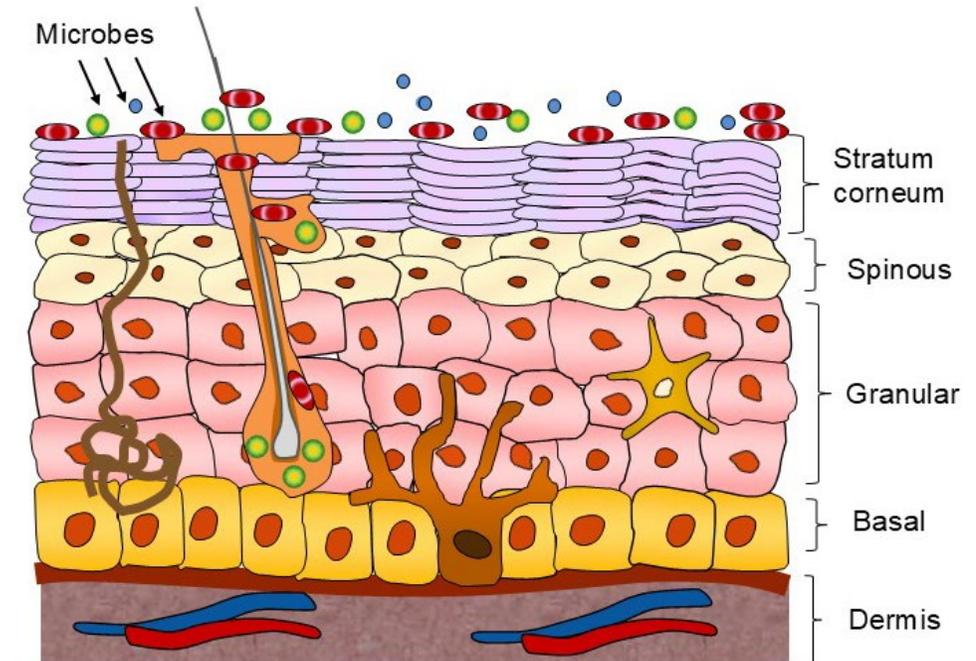
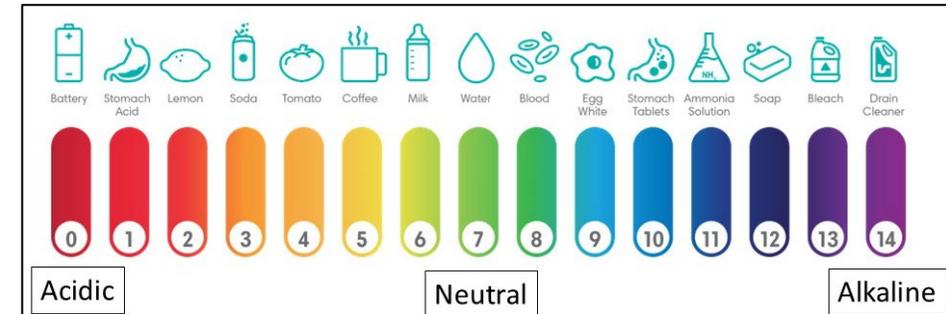
- Formation, Integrity
- Lipid metabolism & structure
- Cohesion
- Desquamation

## Bacterial homeostasis

- Colonize with appropriate bacteria, i.e., *S. epidermidis* attachment to skin
- Inhibit pathogenic bacteria, e.g., *S. aureus*

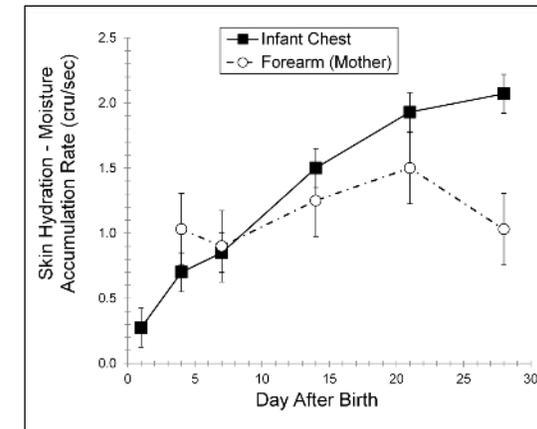
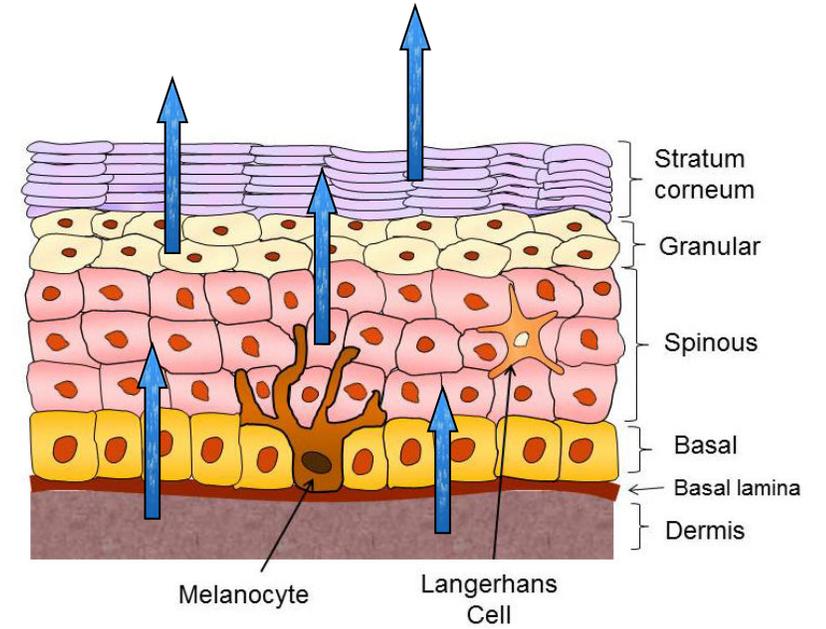
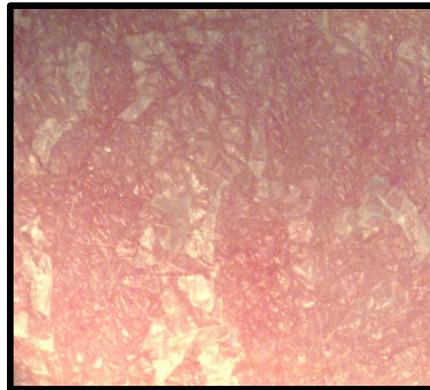
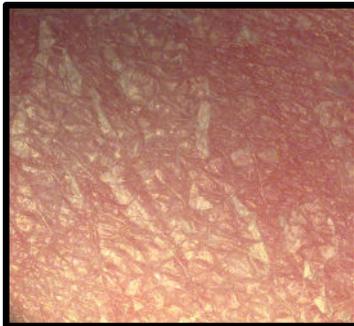
## Mechanisms

- Filaggrin proteolysis to NMF
- Lamellar phospholipids to FFA
- NHE1 acidifies extracellular domains



# Full-Term Infant Skin: Adaptation

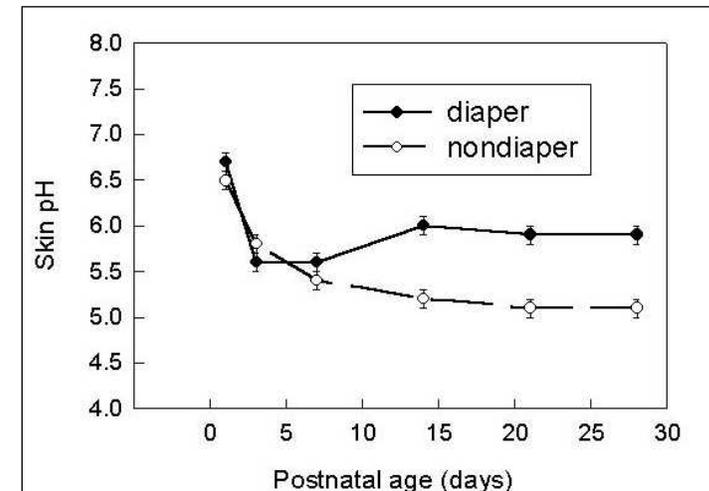
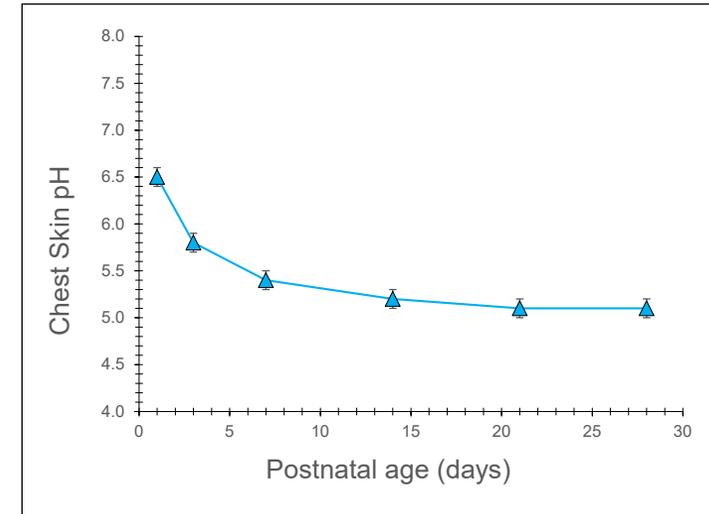
- Competent barrier - low transepidermal water loss (TEWL) at birth ( $\sim 5\text{-}6\text{ g/m}^2\text{/hr}$ )
- Skin hydration decreases rapidly (day 1) then increases over first month
- Visible dryness/scaling due to low levels of NMF, water binding amino acids
- Parents will likely see the dryness after discharge



Visscher, Hoath, et al., *Pediatr Dermatol*, 2000; 17(1):45-51.  
 Nikolovski J, et. al. *J Invest Dermatol* 2008 128(7):1728-36.  
 Visscher, Hoath, et al., *Skin Res Tech*, 1999; 5: 213-220.

# Full-Term Infant Skin: Adaptation

- Skin pH decreases rapidly over days 1-4 and continues to decrease as the acid mantle develops
- Decreases more gradually for several months
- After the initial decrease, the skin pH is higher in the diaper area than the nondiapered site (chest)



# But, What About Vernix?

## Composition

Water (80%)

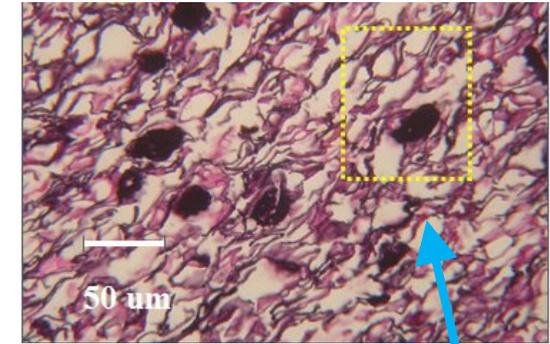
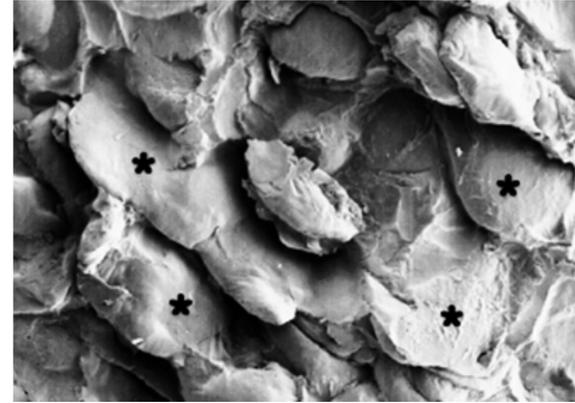
more than Eucerin, Aquaphor

Lipids (9.7%)

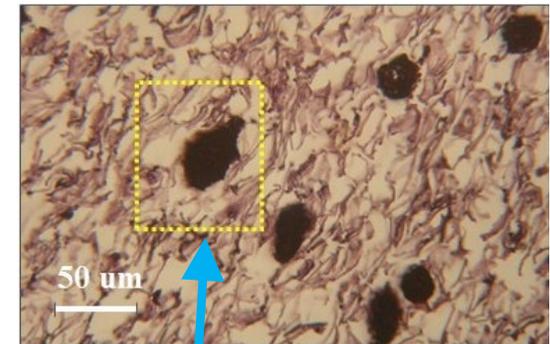
Protein (10.3%)

flattened cells “coated” with lipids

Water is associated with cells



**Lysozyme**



**Lactoferrin**

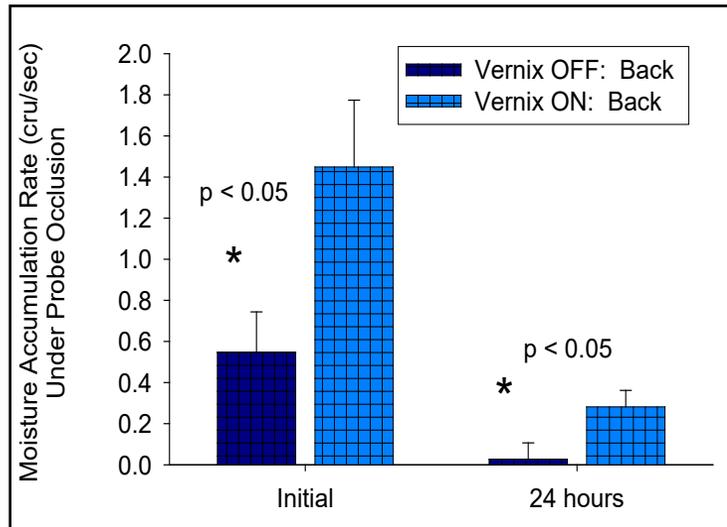
**Antimicrobials** in “granules” for “quick release” to confront infection;

- ✓ effective against specific perinatal pathogens, i.e., group B *Streptococcus*, *K pneumoniae*, *L monocytogenes*

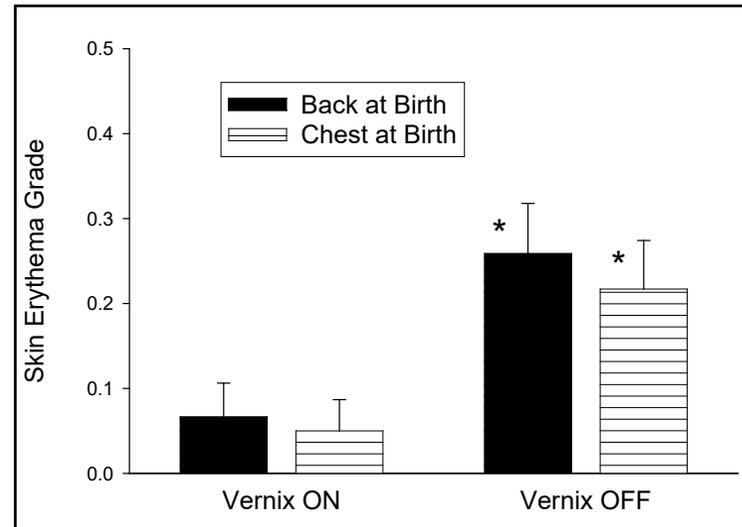
**Proteins** = 41

- ✓ 16 with *innate immunity*
- ✓ 12 with *antimicrobial function*

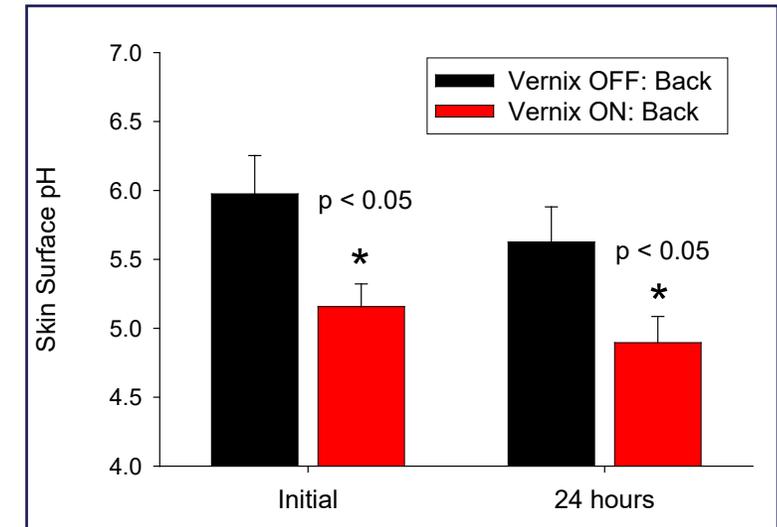
# Vernix *Retained* Infant Skin after birth



1.....more hydrated



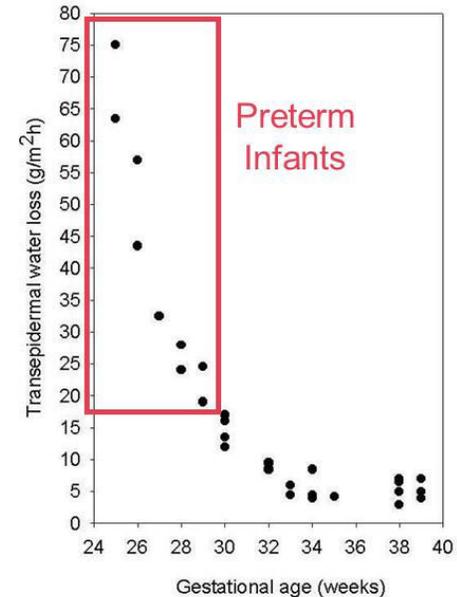
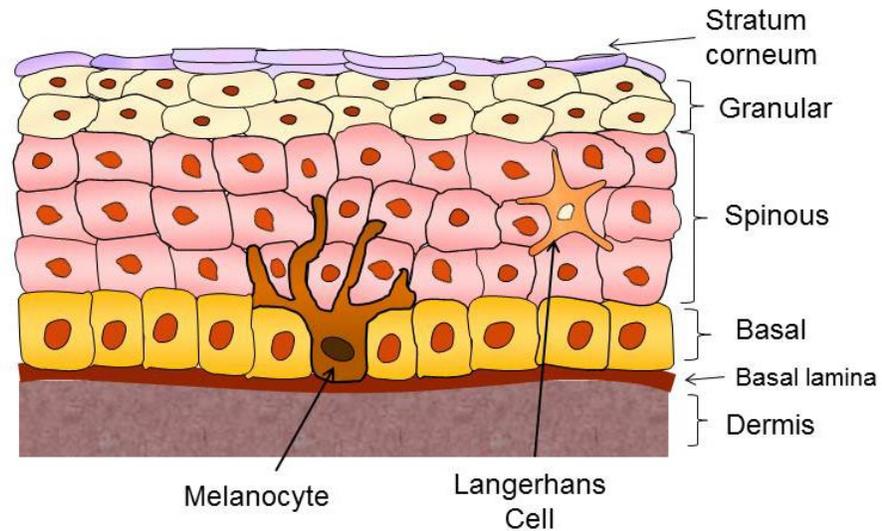
2....less erythematous



3.....lower skin surface pH

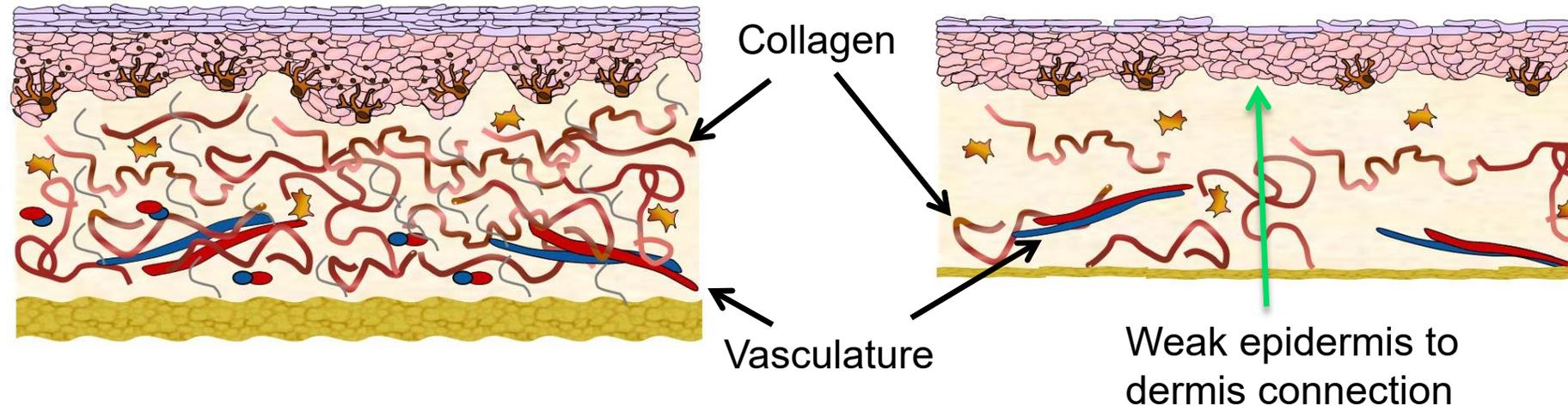
- Vernix facilitated hydration and lower skin pH acid
- Vernix retained contains natural moisturizing factor, retained on infant skin
- Bathing: World Health Organization says wait at least 6 hours before the first bath.

# Premature Infant Skin



1. Stratum corneum (SC) is absent or only a few layers
2. Thin epidermis
3. Skin barrier integrity varies with GA
  - TEWL at < 25 weeks very high due to few SC layers
4. One month after birth, **ELBW TEWL** was *significantly higher* than **full-term TEWL**

# Full-Term & Premature: Difference in Dermis

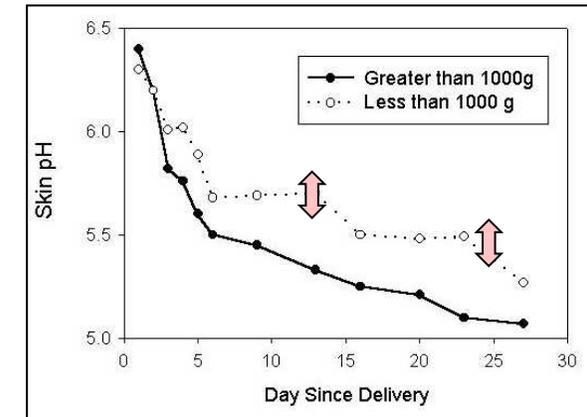
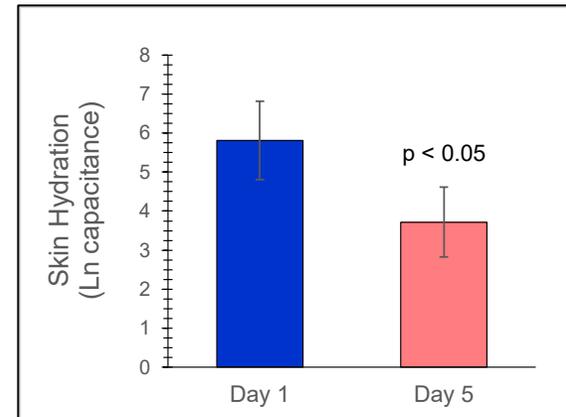
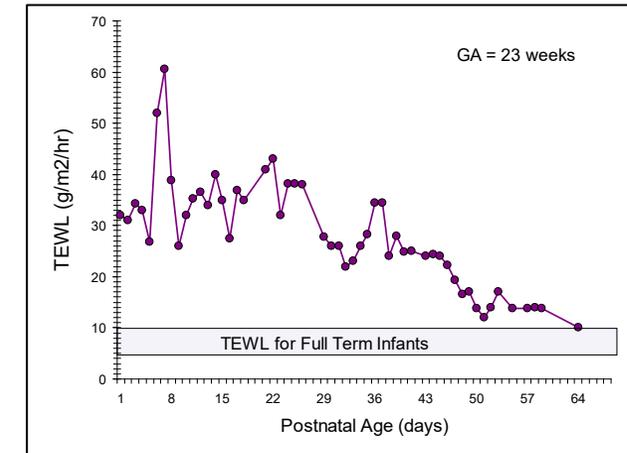
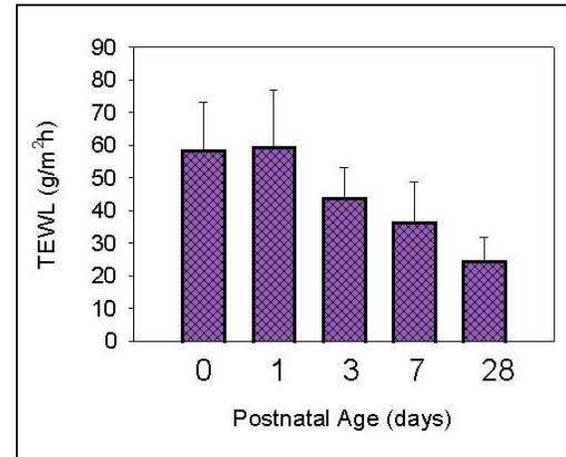


## ***Premature Dermis***

- Structural proteins deficient, less organized, low collagen bundle density
- Low elastin and under developed fiber networks
- NOT resilient to mechanical trauma, e.g., ***easily torn with adhesive removal and significantly compressed with pressure from devices, e.g., CPAP***

# Premature Skin Maturation after Birth

- One month post birth, **TEWL** was *higher* for the early preterms versus in full-terms (~5-6 g/m<sup>2</sup>/hr).
- TEWL for 23 weeks GA preterms reached full-term values at 9 weeks.
- Skin hydration was higher on day 1 versus day 5 in infants < 26 wks GA.
- Skin pH varied with GA; smaller preterms had a higher pH for longer.

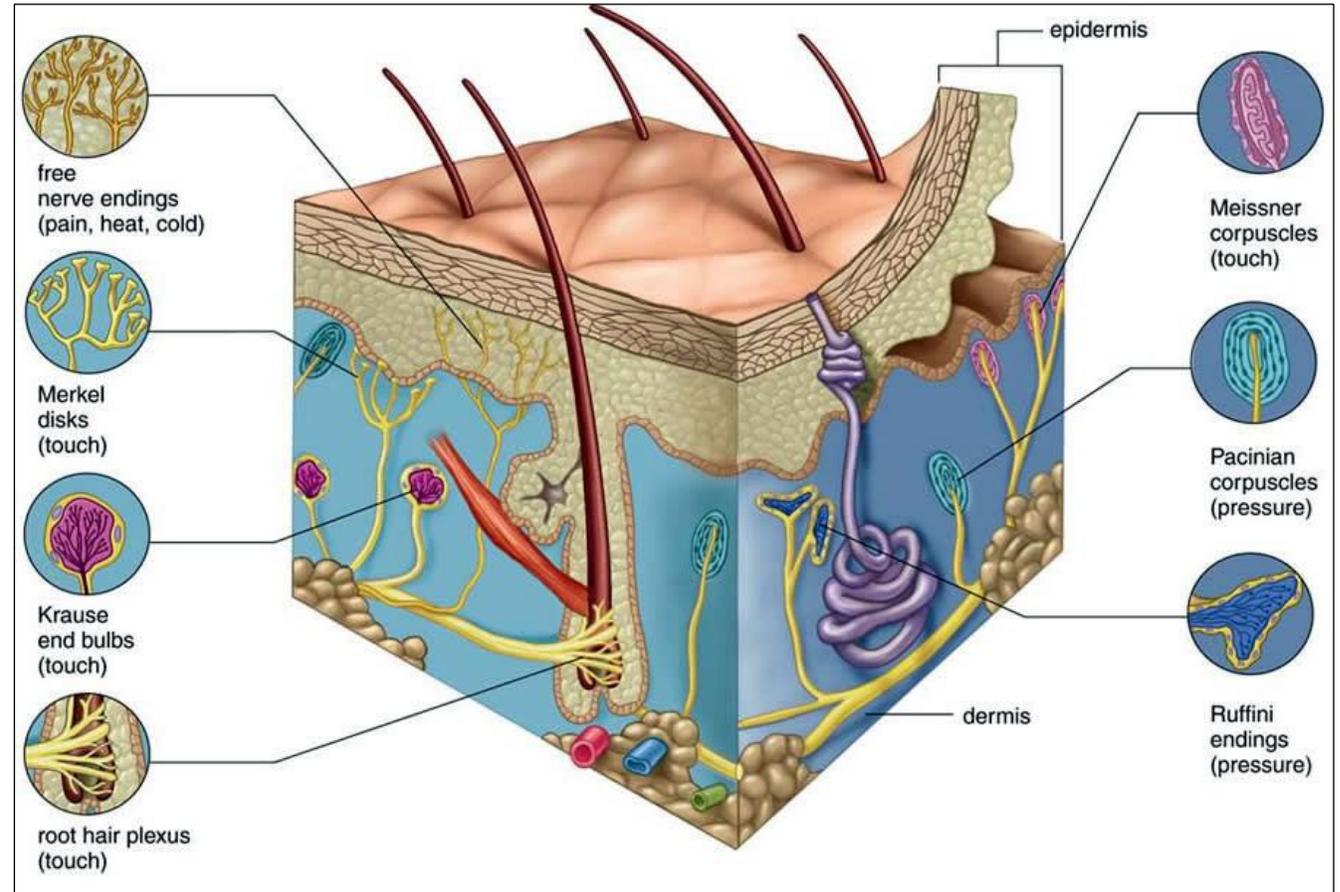


Agren et al, *Acta Paediatr Scand*, 1998, 72(5): 721-728; Kalia et al., *J Invest Dermatol*, 1998, 111:320-326

Okah, Wickett, Pickens, Hoath, *Pediatrics*, 1995, 96(4): 668-692; Fox, et al, *J Perinatology*, 1998, 18(4): 272-275

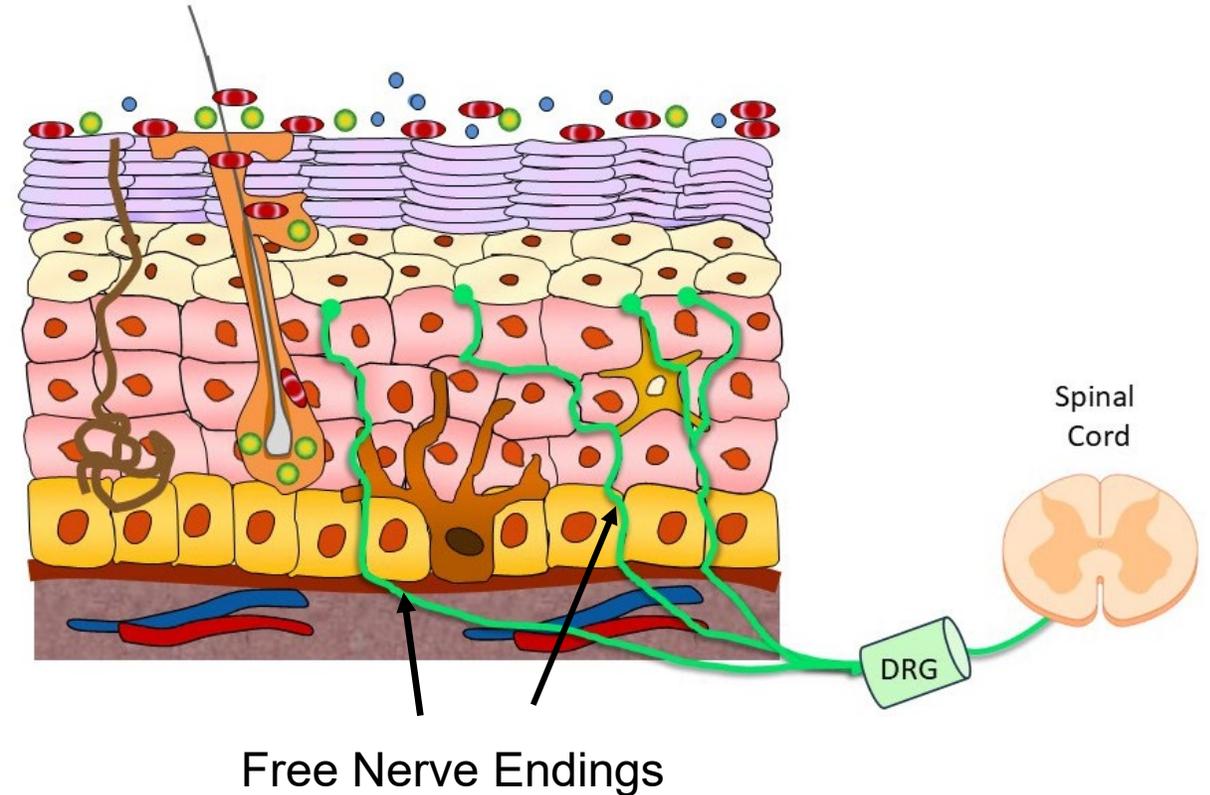
# Skin Sensory System

- Free nerve endings – pain, heat, cold
- Meissner corpuscles - vibration
- Pacinian corpuscles - vibration
- Ruffini endings - stretch
- Krause end bulbs - cold
- Merkel cells - sustained touch

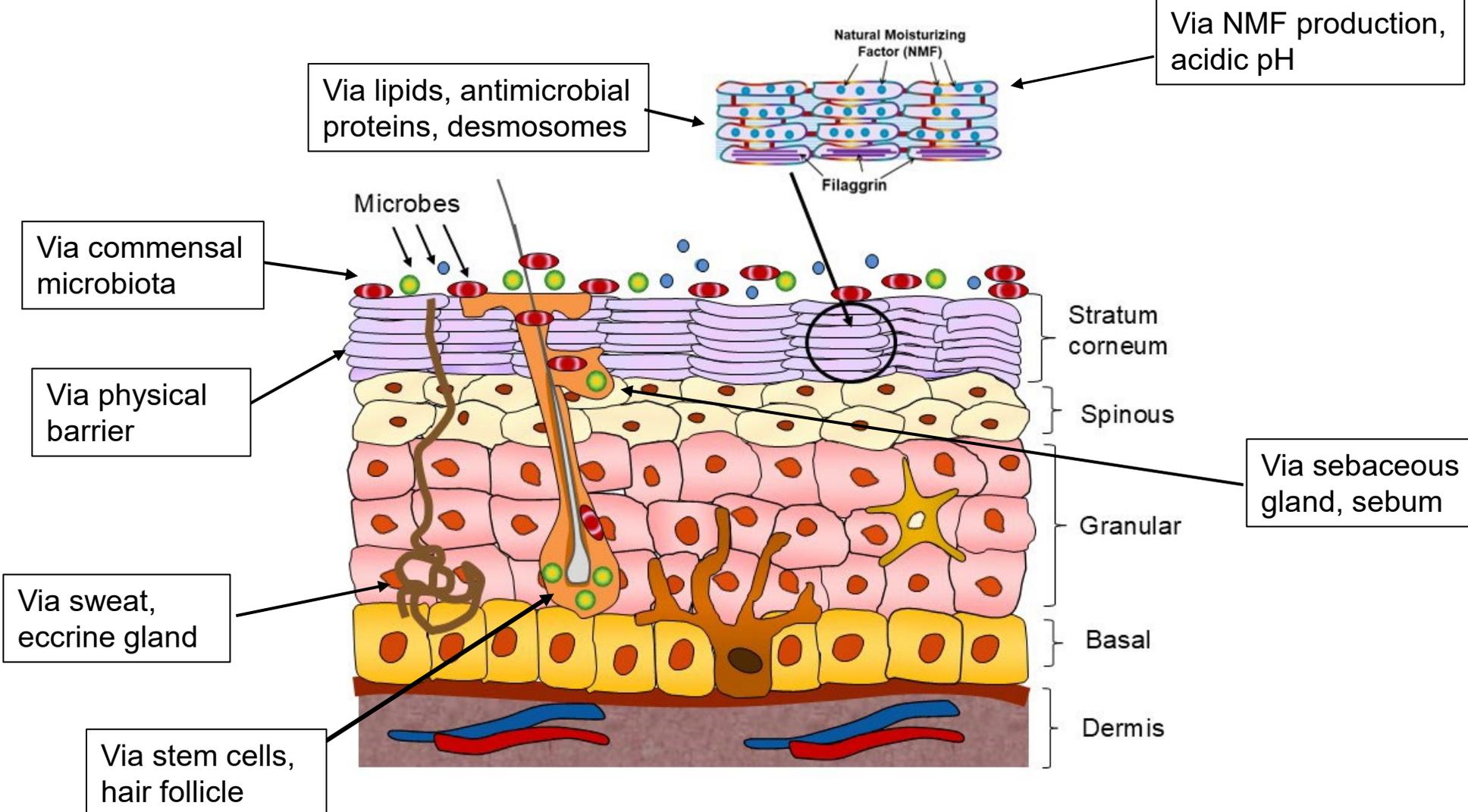


# Sensory Nerves and the Skin Barrier

- Keratinocyte receptors sense mechanical, thermal, and chemical stimuli and activate responses.
- Free nerve endings between keratinocytes detect and transmit stimuli.
- Keratinocytes express multiple transient receptor potential channels that:
  1. Induce heat sensation itching; suppresses sebaceous lipid and synthesis
  2. Shift keratinocytes activity towards differentiation
  3. Regulate epidermal barrier formation
  4. Increase pro-inflammatory cytokine release



# Overview: Skin Immune Functions



# **Caring for Neonatal Skin**

**Educational insights to support  
healthy skin from day one**



## **Andrew N. Carr, PhD**

### **Procter & Gamble – Baby Care Clinical Research**

- Clinical scientist leading design and oversight of baby care clinical studies
- Over 18 years of experience in clinical research at Procter & Gamble
- Expertise in:
  - Skin health and development
  - Sleep science
  - Infant microbiome
- Extensive collaboration with regulatory and professional organizations (FDA, EMEA, CHPA)
- Author of 70+ peer-reviewed publications, abstracts, and book chapters

# Objectives

- 1 Discuss diaper dermatitis, including causative factors, incidence rates, and how the factors interact.
- 2 Describe the new clinical research that supports the recommended skin care practices.
- 3 Describe impact of skin type and diapering products on skin health outcomes

# Diapered Area: A Unique Environment

Attribute	Undiapered Skin	vs.	Diapered Skin
Coverage/Wear time	Clothes/intermittent		Diaper/nearly exclusive
Topography	Largely flat		Convex, concave, crevices
External exposures	UV		Urine, feces
Humidity	~35%-45%		Dry: ~55%; Wet: >90%
Temperature	~22-25°C		~29-34°C
Cleaning	Daily/weekly		Frequent, daily

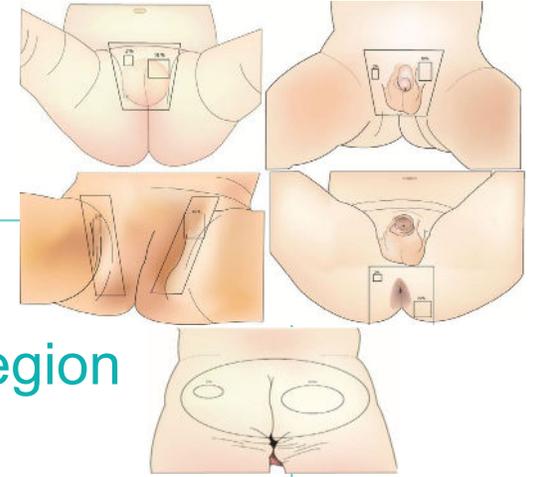
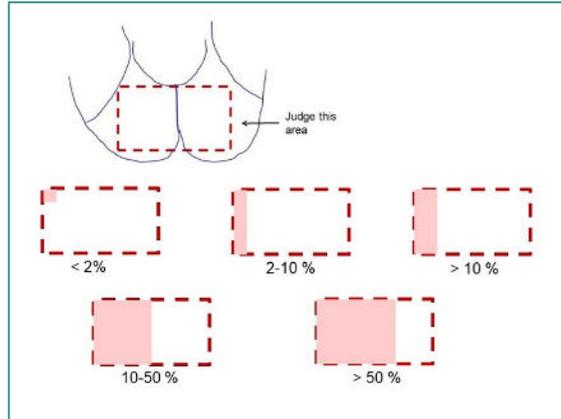
# Dermatitis in the Diapered Area (DDA)

An acute, episodic **inflammatory reaction** of skin in the area covered by the diaper: 4 signs of inflammation include pain, heat, redness and swelling.



- The most common skin ailment for infants.
- Results from skin damage by physical, chemical, enzymatic and microbial factors.
- Characterized by erythema (redness), and/or papules and/or pustules.
- In older infants, the incidence is highly variable (16-65%) and typically peaks between 6-12 months of age.
- Incidence in the first week of life **~70%**.
- Incidence in the NICU **~25-70%**; Neonatal Opioid Withdrawal Syndrome **~86%**.

# Assessment of Diaper Dermatitis: Clinical Tool



- Scoring includes:
  - Specific anatomical region
    - Perianal
    - Buttocks
    - Genitals
    - Intertriginous
  - Key Attributes
    - *Percent coverage of erythema*
    - *Intensity of erythema*
    - *Papules*
    - *Pustules*
  - Scoring is 0-3 (or 0-4) with 0.5 severity increments

Erythema					
Area Increments	None	< 2%	2-10%	10-50%	>50%
Severity Levels					
	Faint-Definite Pink	Definite Redness	Very Intense Redness	Very Intense Redness & <b>Bleeding</b>	

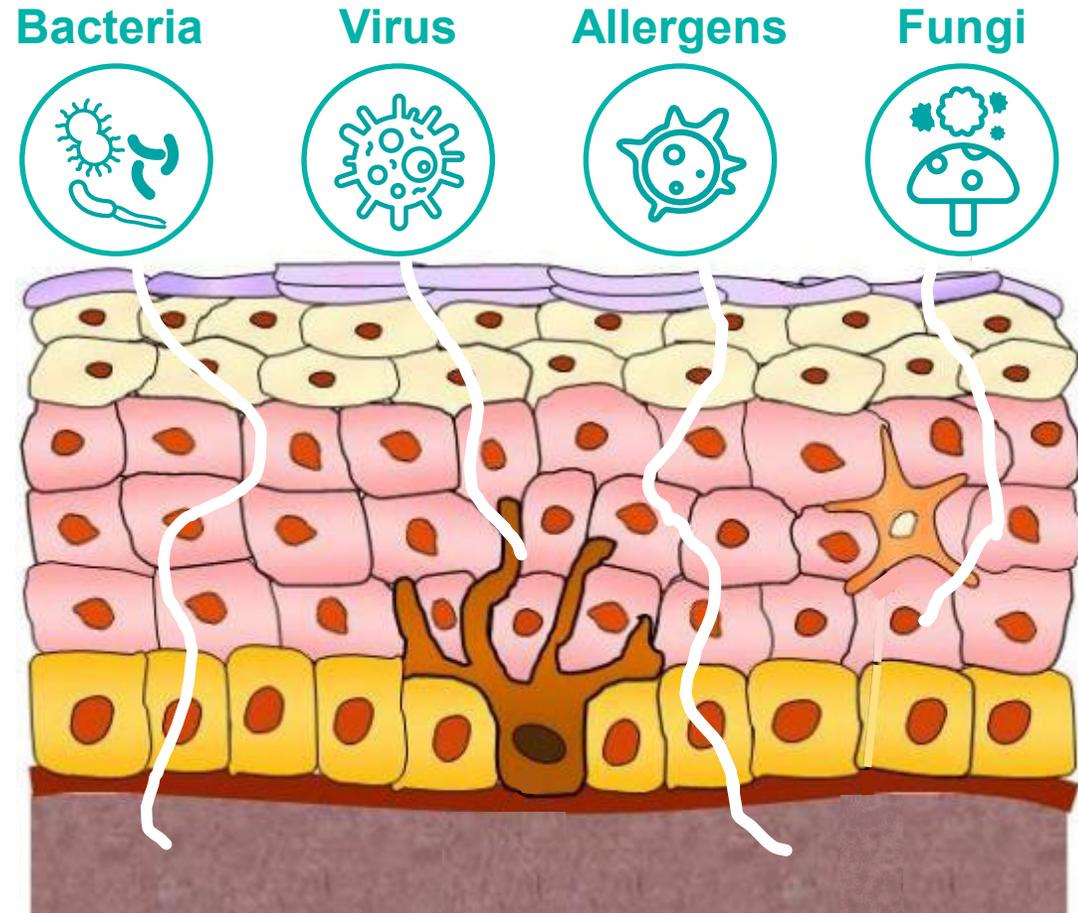
Jordan et al. *Pediatr Dermatol.* 1986;3(3):198-207.

Odio et al. *Dermatology.* 2000;200:238-243.

Lukacovic, Visscher, et al. *J Soc Cosmet Chem.* 1988;39:355-366

Visscher. *Newborn & Infant Nursing Reviews* 2014;14:147-152.

- Subsequent to skin damage, the skin is breached and allows the entry of bacteria, viruses, allergens and fungi
- This leads to activation of the immune system and signs of inflammation (dermatitis)



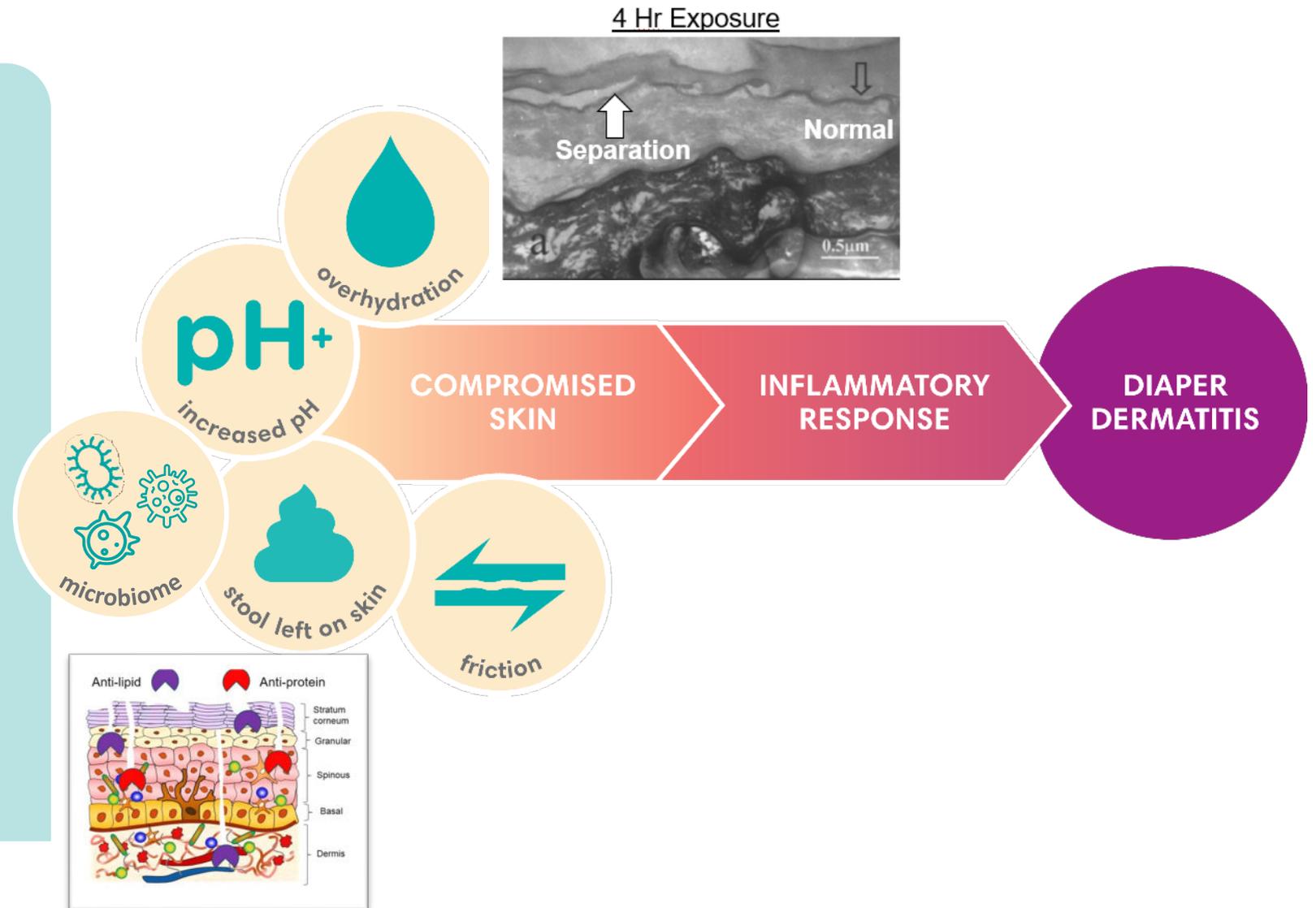
**Inflammation!!!**

# Model of Dermatitis in the Diapered Area

## Contributing Factors

What is happening to baby (complications/interventions):

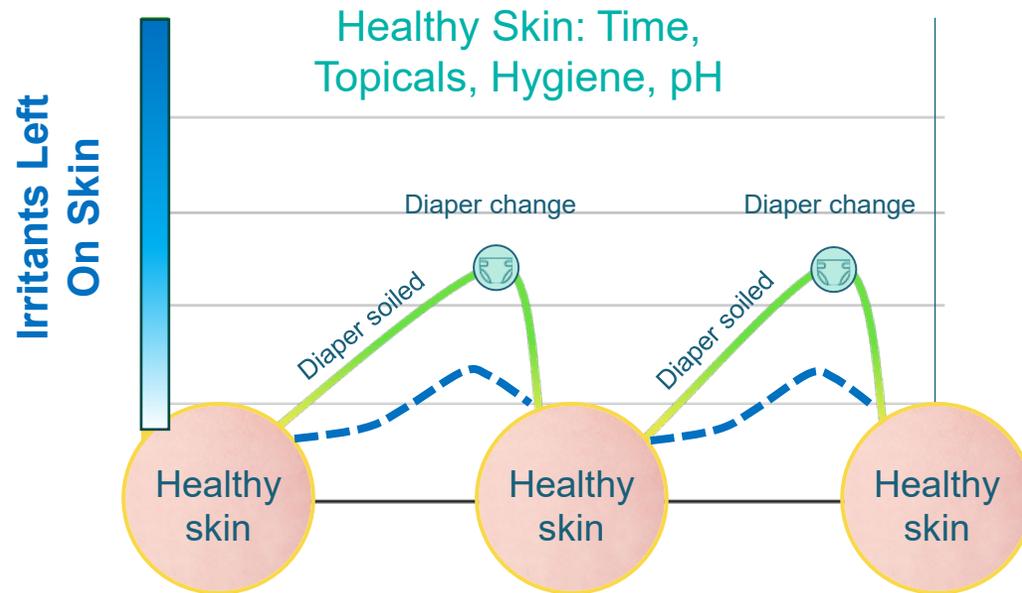
- Antibiotic/Prescription use
- Allergies
- Change in diet or fortification
- Opioids
- Underdeveloped skin
- Diarrhea/Frequency of loose stools





# Did You Know...

## Diapered skin is always under attack



- Frequent diaper changes
- Skin protectants
- Irritants removed (Hygiene)
- Reset skin = maintain Healthy Skin

- Infrequent diaper changes (elevated %RH)
- Irritants (urine/stool) left on skin
- Skin exposed to repetitive damage
- Cumulative insults from wetness & humidity

# The Gut-Brain-SKIN Axis & Disease

## Skin Inflammation & Brain and Gut Signalling

For Babies: ...involves education, *skincare*, ...targeting **skin inflammation** and barrier repair, ...**[p]roactive therapy**, addressing **subclinical inflammation** ...for preventing eczema flares.

For Mothers: “...*stress management*, nutritional guidance, *holistic* consideration of overall **infant [health]**.”

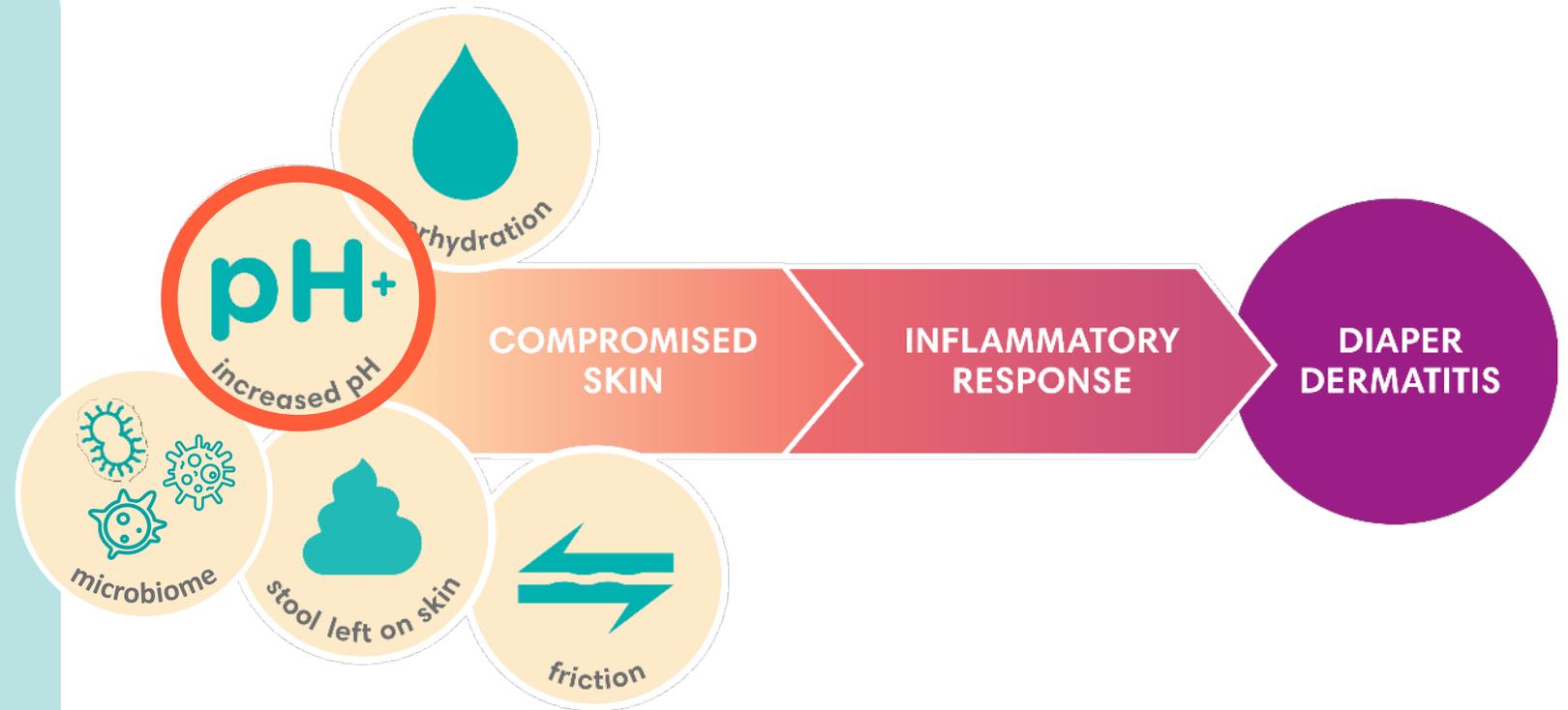


# Model of Dermatitis in the Diapered Area

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What is happening to baby (complications/interventions):

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# Basic *pH*acts – What Is pH?

- 01** “p” is the “power” and “H” is “hydrogen”, so pH is the “power of hydrogen”

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- 02** pH is the concentration of hydrogen ions ( $[H^+]$ ) in an aqueous solution

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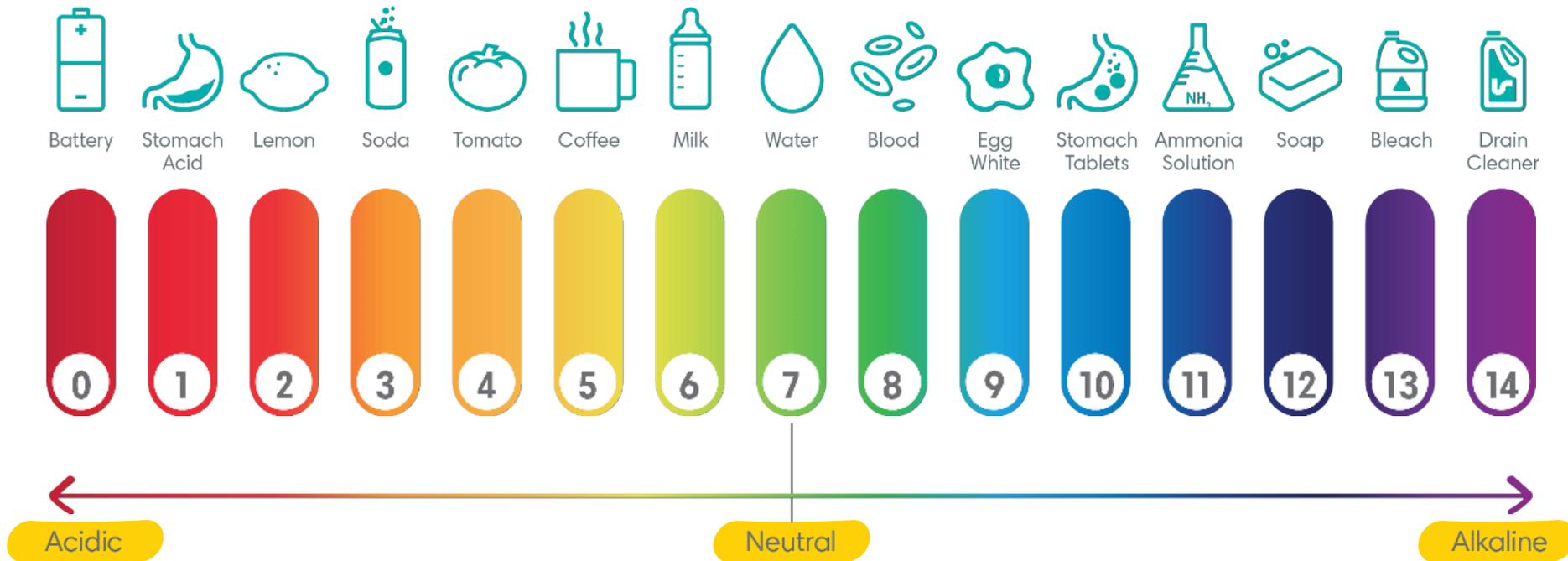
- 03** Expressed as the “negative log (-log)” of  $[H^+]$ , which means a “one unit” change in pH = 10x difference in  $[H^+]$



Many biological processes are impacted by pH ...including those involved in skin development!

# pHacts About pH & Buffering Capacity

## THE pH Scale



### BUFFERS

Substances that resist changes in the pH.

(i.e., "hold the pH")

# Magic of

# 5

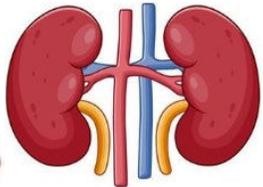
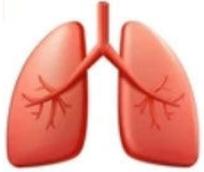


**Fingers**

**Toes**



**Vital Organs**



**Senses**



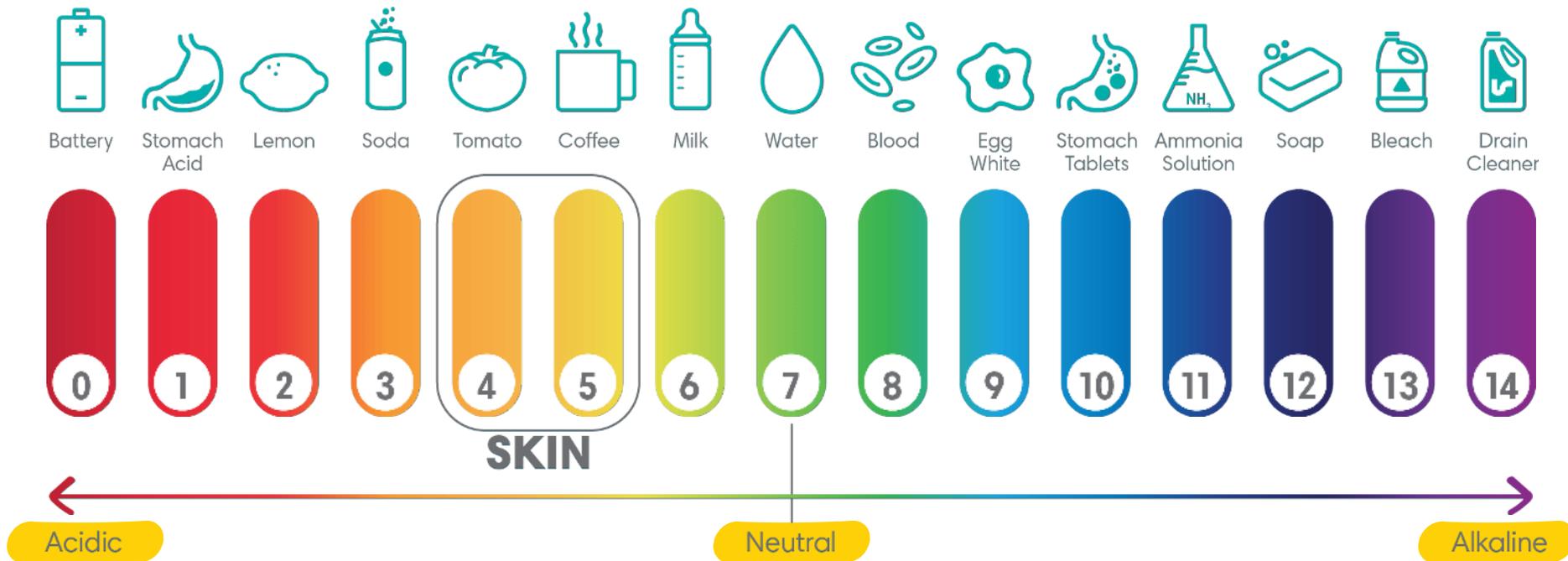
**Liters of blood**

# What pH should the SKIN BE????



# pHacts About pH & Buffering Capacity

## THE pH Scale



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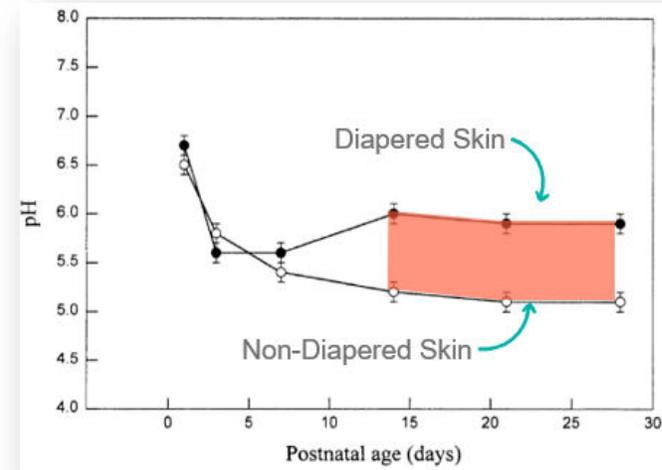
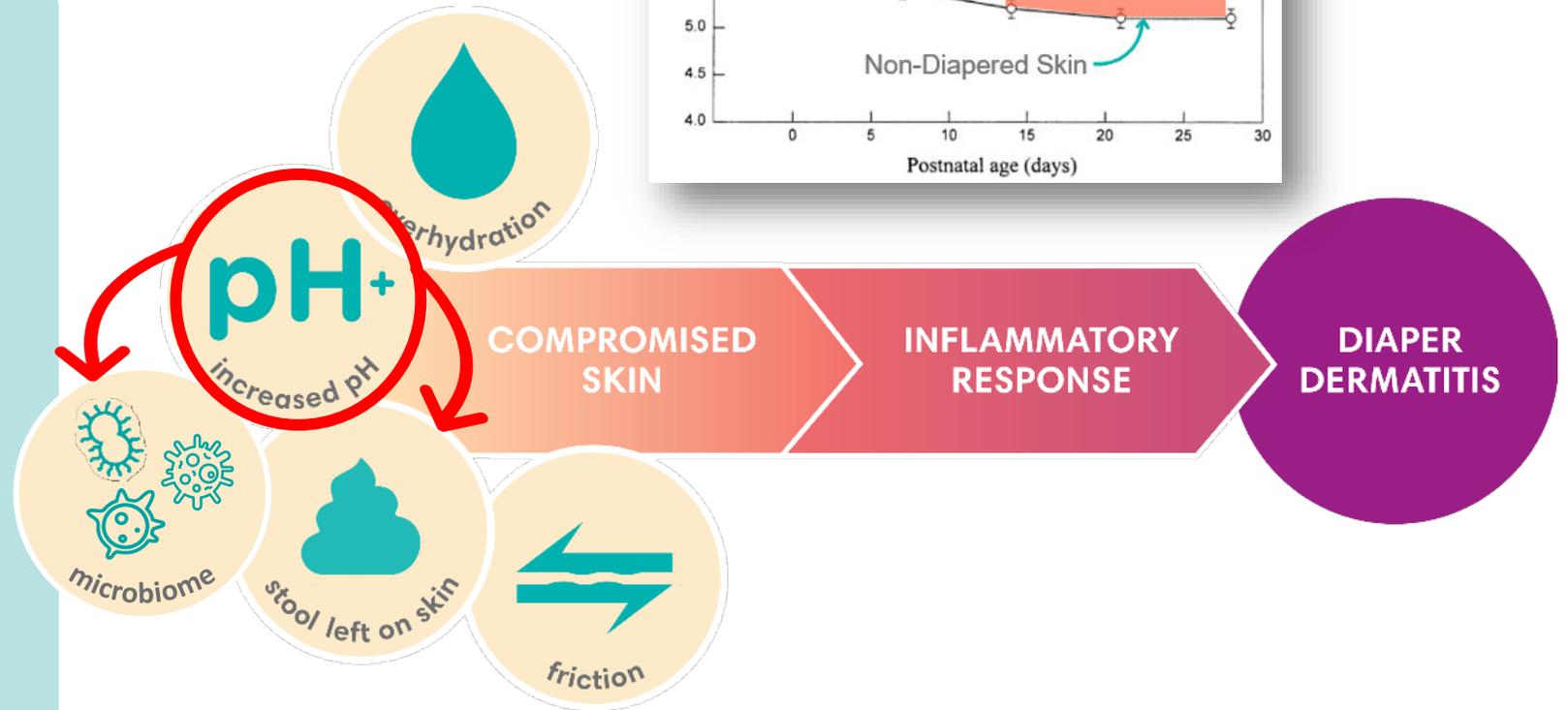
# Breaking Down the Causes of Skin Breakdown

# Root Causes of DDA

## Elevated Skin pH

Skin pH found in the diapered area can be elevated by occlusion, exposure to urine/stool, dysbiosis

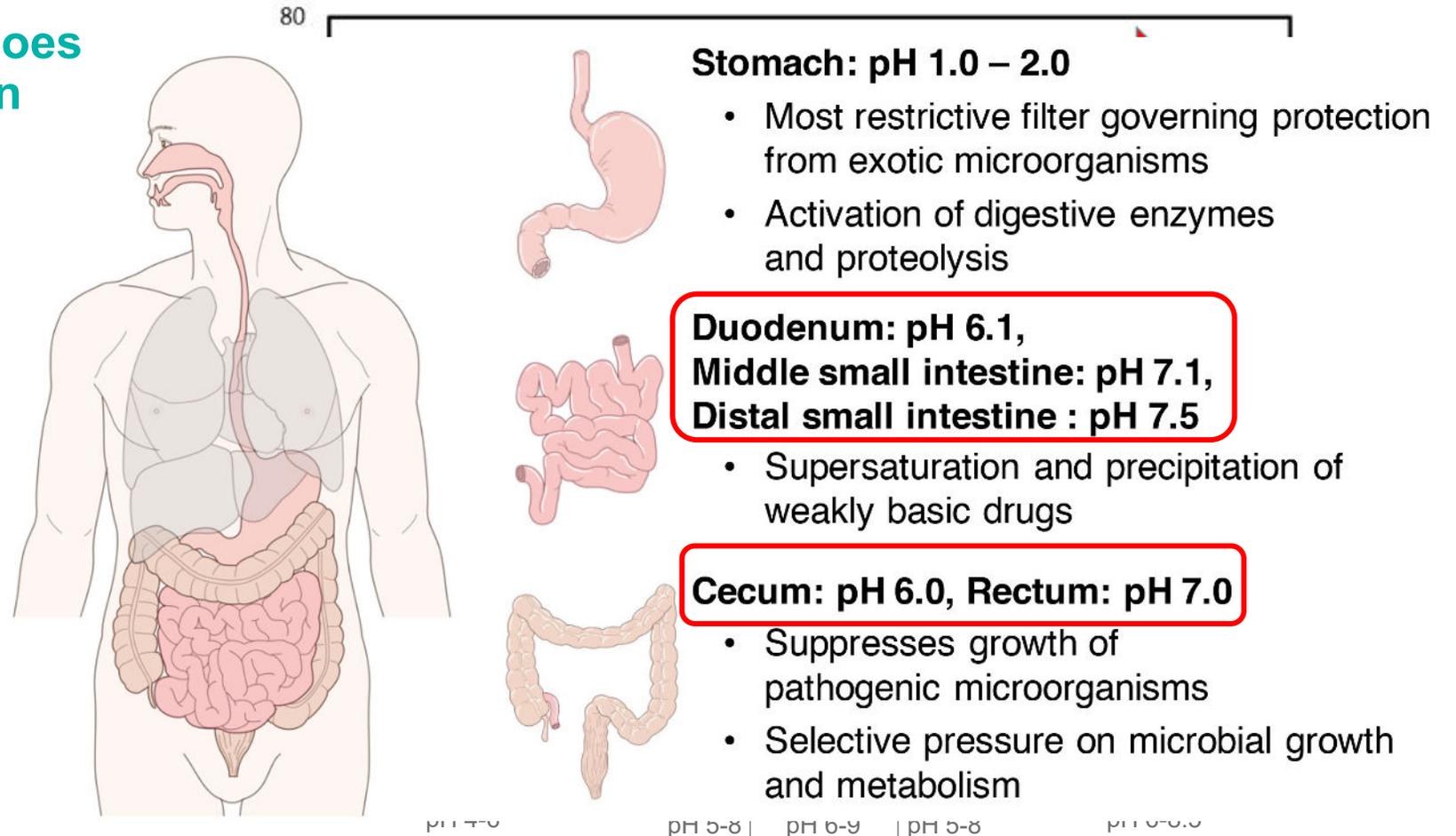
- Activates fecal enzymes (more active at intestinal pH)
- Disrupts normal skin function: e.g., desquamation
- Slows skin healing
- Shift in microbiome towards *S. aureus*, *C. albicans* growth



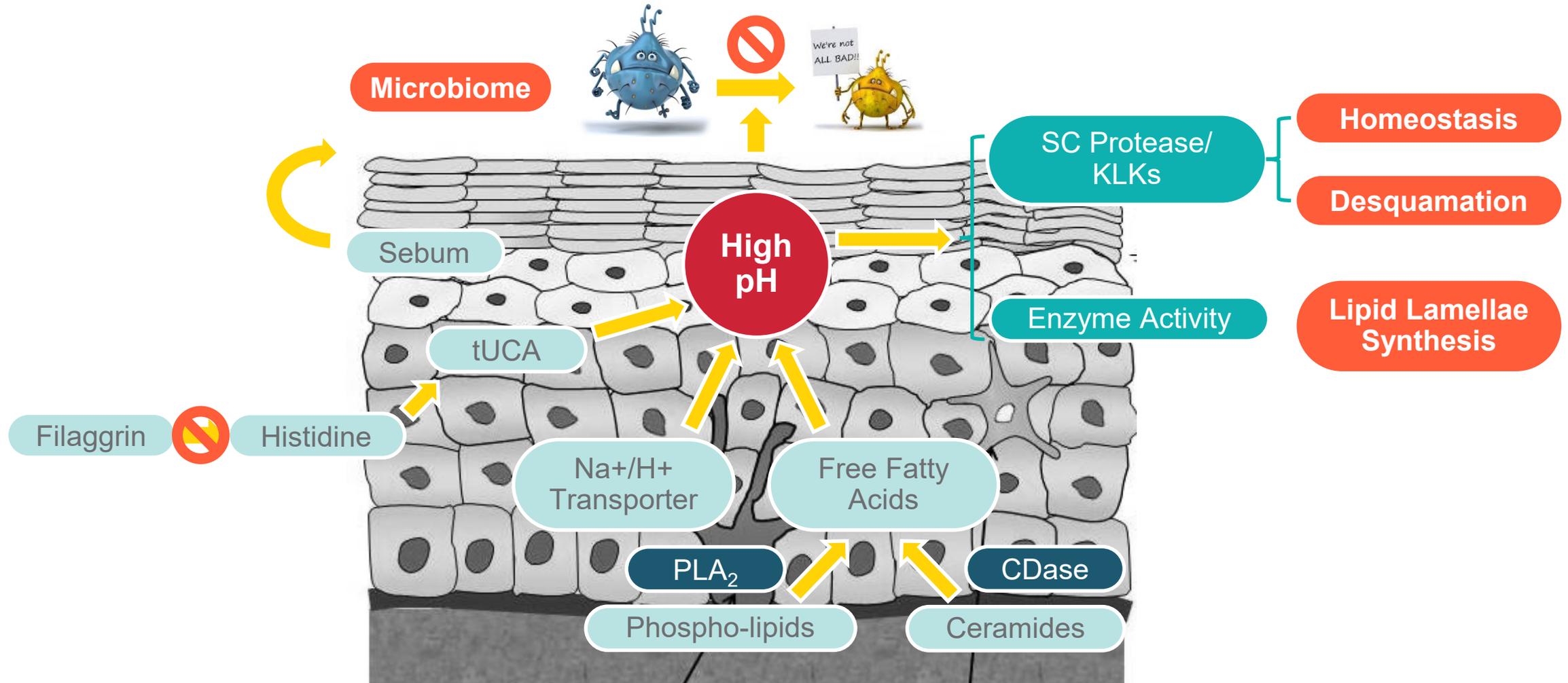
# pHact: Fecal Enzyme Attack Is pH-Sensitive

## As stool pH increases, so does fecal enzyme toxicity to skin

- Stool pH collected in n=224 babies across 3 geographies (USA, Mexico, Japan)
- Over 60% of stools pH > 6.0
- Trypsin protease activity is > 40% at pH 6.0
- Thus, most stool exhibits toxicity to skin (high degradation potential)



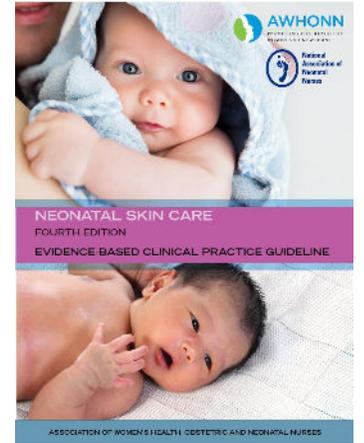
# pHact: Elevated pH Is a Warning Sign



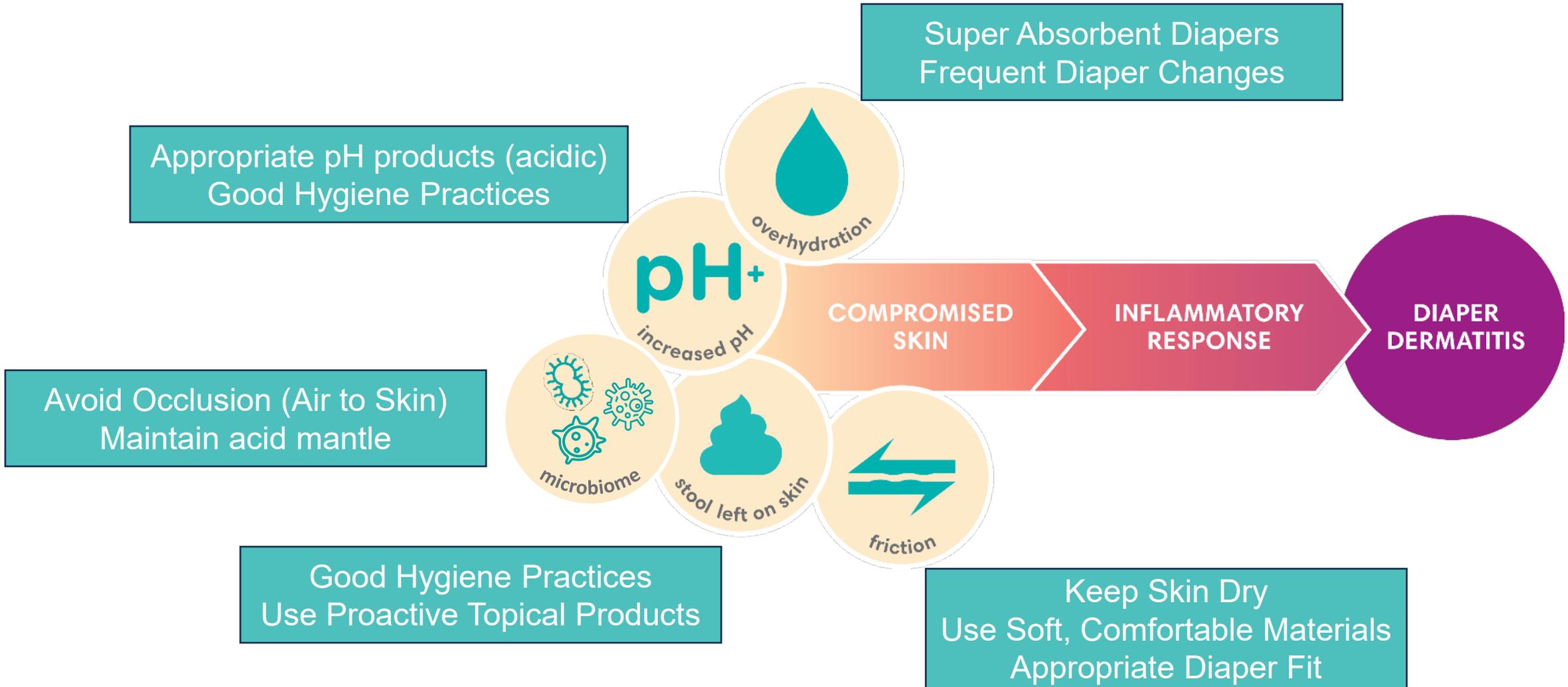
# Preventing DDA

AWHONN/NANN Skin Care Guideline, Fourth Edition

- “Prevention strategies accompanied by a focused skin assessment remain the best intervention for diaper dermatitis.”



# Prevention of DDA

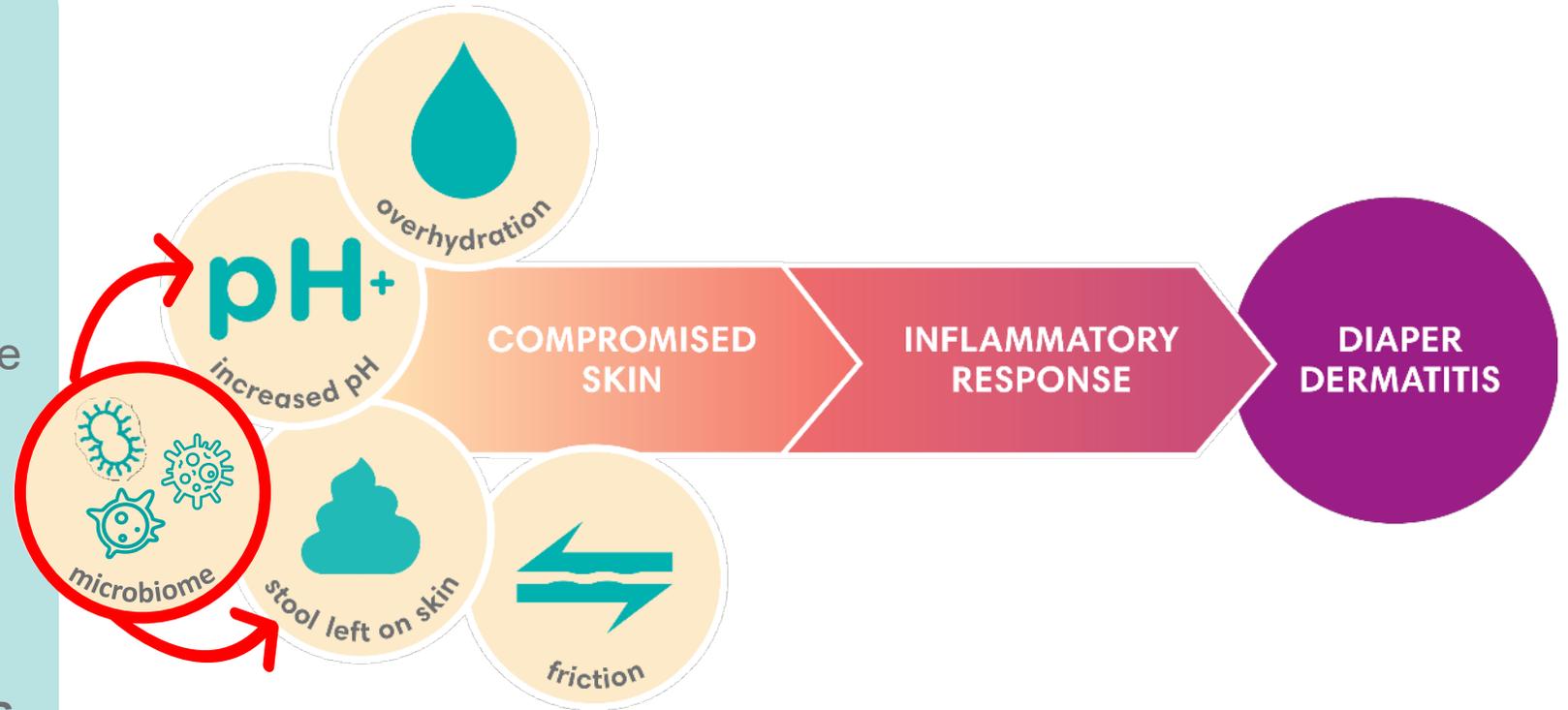


# Root Causes of DDA

## Elevated Skin pH

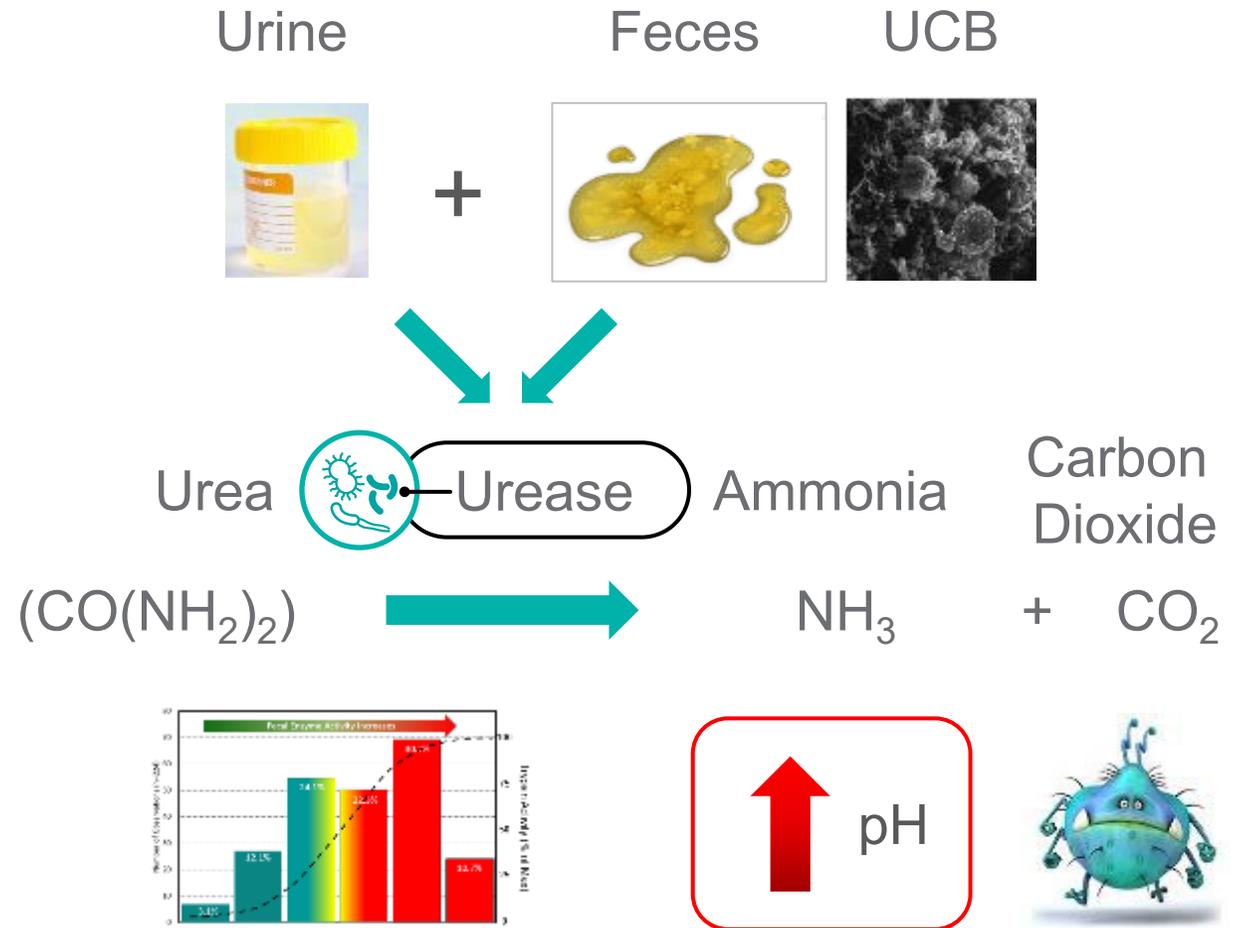
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- Slows skin healing
- **Shift in microbiome towards *S. aureus*, *C. albicans* growth**



# Skin Microbiome and pH in DDA

- *Candida* (fungi/yeast) present in ~30% of DDA cases
- Urease containing bacteria (UCB) in the stool can convert urea to ammonia driving up pH
- Increased pH:
  - Increased fecal enzyme activity
  - Dysbiosis favoring pathological organism growth (*S. aureus*, *C. albicans*)



# Evidence-Based Clinical Practice

Evidence-based practice is the process by which healthcare professionals review and assess the most current, *high-quality research* to improve clinical practice and patient outcomes.

A key source of scientific data comes from *clinical trials* and how those studies are *designed, conducted and analyzed* all of which are critical to interpreting the data to guide patient care.

# Global Rash Study

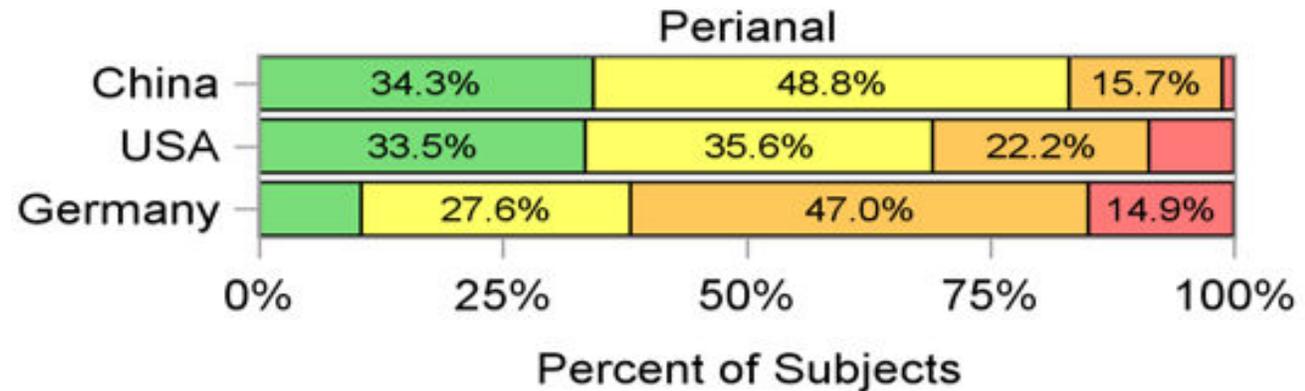
**1,800 Babies**  
*(n=600 per country)*

 **China:**  
**Ages 2-8 Months**

 **Germany & U.S.:**  
**Ages 2-18 Months**



## Diaper Rash Severity 2-8 Months of Age

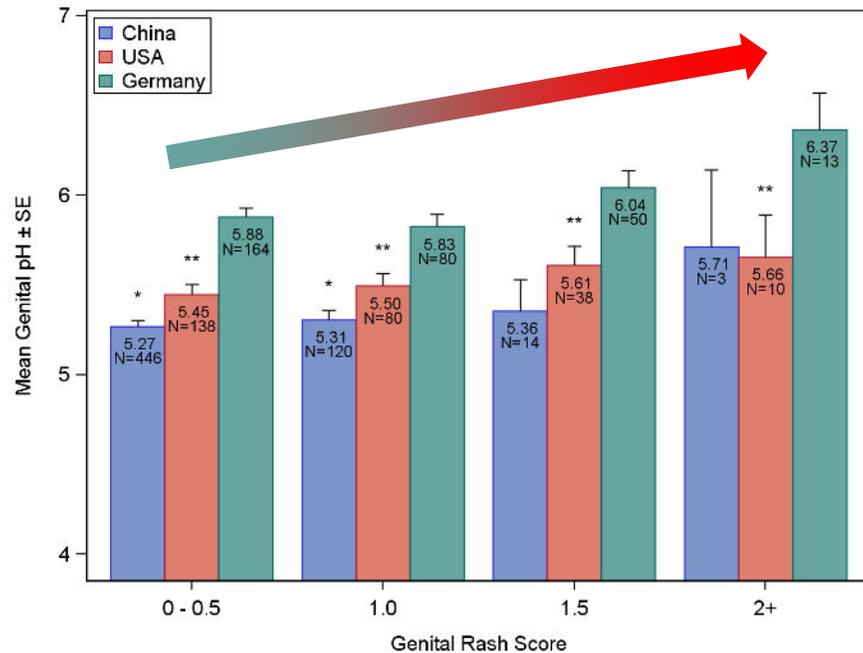


Rash Grade ■ 0-0.5 ■ 1.0 ■ 1.5 ■ 2-3

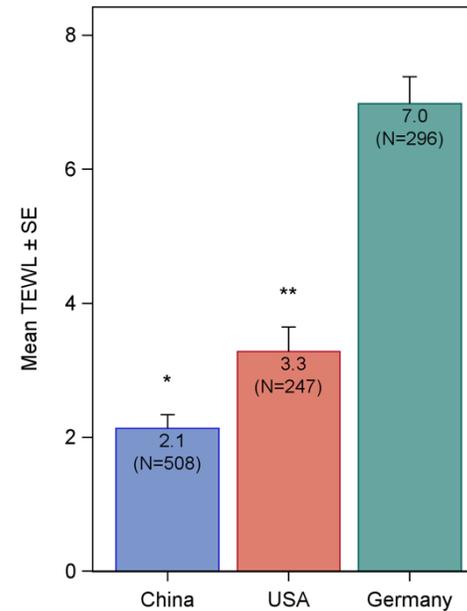
**Rash Free** **Mild-Mod** **Mod** **Severe**

# Global Rash Study: Skin Characteristics

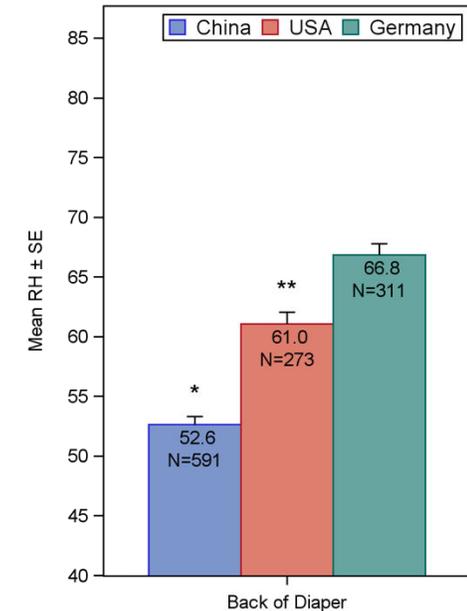
## Genital Skin pH



## Skin Barrier Function



## Within Diaper Humidity

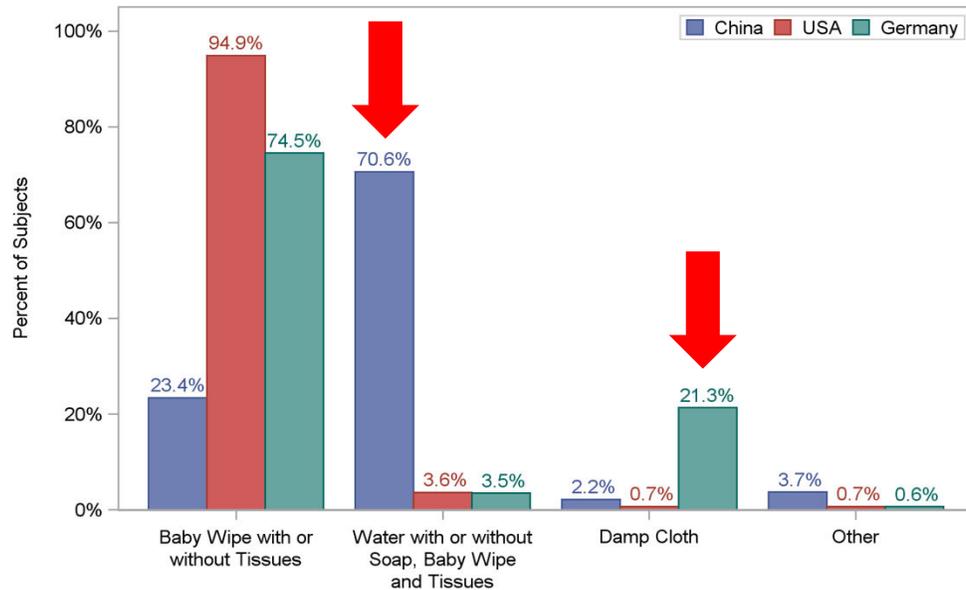


**Reduced Diaper Dermatitis Incidence and Severity Mirrored**

- Lower Skin pH and Diaper Humidity
- Better Skin Barrier Function (Lower TEWL)

# Global Rash Study: Caregiver H&P

## Cleaning Stool Off Skin

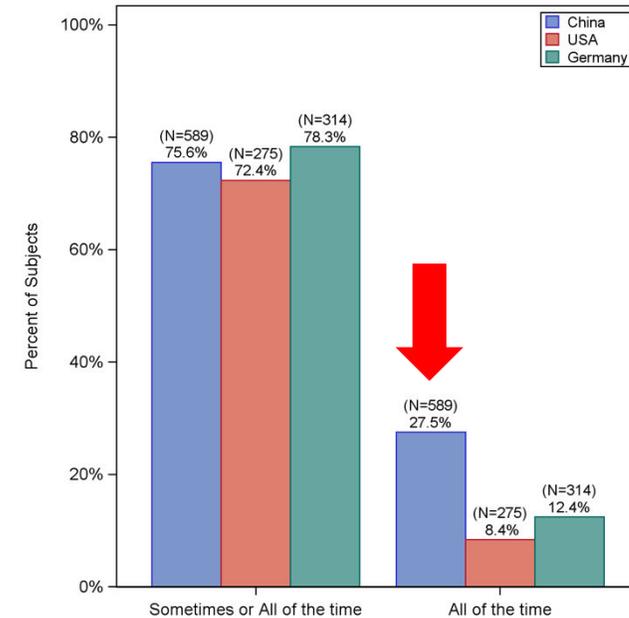


### China: Cleaning Implement

- Extensive diaper area cleaning post-stool

### Germany: Highest Cloth/Water Usage

## Topical Product Usage



### China: Topical Product Use

- Highest prophylactic use

# Bathing Frequency: Including Post-Stool Cleaning

Bathing Frequency			
	<b>China</b> (n=589)	<b>USA</b> (n=274)	<b>Germany</b> (n=314)
“Bathing” diapered skin after stooling*	<b>416 (70.6%)</b>	10 (3.6%)	11 (3.5%)
≥ 1 per day	42 (7.1%)	58 (21.2%)	13 (4.1%)
Every Other Day	60 (10.2%)	<b>156 (56.9%)</b>	53 (16.9%)
3x Per Week	2 (0.3%)	2 (0.7%)	1 (0.3%)
2x Per Week	83 (14.1%)	48 (17.5%)	<b>124 (39.5%)</b>
Once Per Week	249 (42.3%)	7 (2.6%)	<b>120 (38.2%)</b>
Other	153 (26.0%)	3 (1.1%)	3 (1.0%)

 Diapered area skin cleansing frequency is inversely related to DDA

# Diaper Change Frequency & Diet

			
	<b>China</b> (n=589)	<b>USA</b> (n=274)	<b>Germany</b> (n=314)
<b>Hours in Diaper</b>			
Overnight	6.0 ± 2.27	7.9 ± 2.56	8.5 ± 2.92
<b>Diet</b>			
Exclusive Milk	100%	29.5%	26.3%
Human Milk*	75.7%	50.6%	65.1%

 Diaper rash severity mirrored nighttime diaper wear time

Chinese babies were exclusively milk fed, mostly human milk

# Risk Factors & Reduction of DDA

TABLE 1

## Prevention of Diaper Dermatitis by Elimination of Causative Factors

Causative Factor	Effect	Intervention
Prolonged and excessive humidity	Friction	<ul style="list-style-type: none"> <li>Frequent diaper change</li> <li>Superabsorbent diaper</li> </ul>
Alkaline urine feces	<ul style="list-style-type: none"> <li>Disruption of pH balance</li> <li>Microbial overgrowth</li> <li>Activation of fecal lipases, endogenous and exogenous proteases</li> <li>Skin maceration</li> <li>Increased permeability</li> </ul>	<ul style="list-style-type: none"> <li>Superabsorbent diaper</li> <li>Cleansing with wipes or cotton wool and water</li> <li>Topical emollient</li> <li>Education</li> </ul>
Cleansing using soap and detergents	Further skin barrier breakdown	<ul style="list-style-type: none"> <li>No use of soaps and detergents</li> <li>Cleansing with wipes or cotton wool and water</li> <li>Topical emollient</li> </ul>

## Causes of DDA

- High humidity/Skin wetness
- Alkaline urine
- Fecal material

## Reduction of DDA includes

- Frequent diaper changes
- Super absorbent diapers
- Topical emollient
- Skin hygiene via wipe, cotton, water

# Fitzpatrick Skin Types I-VI



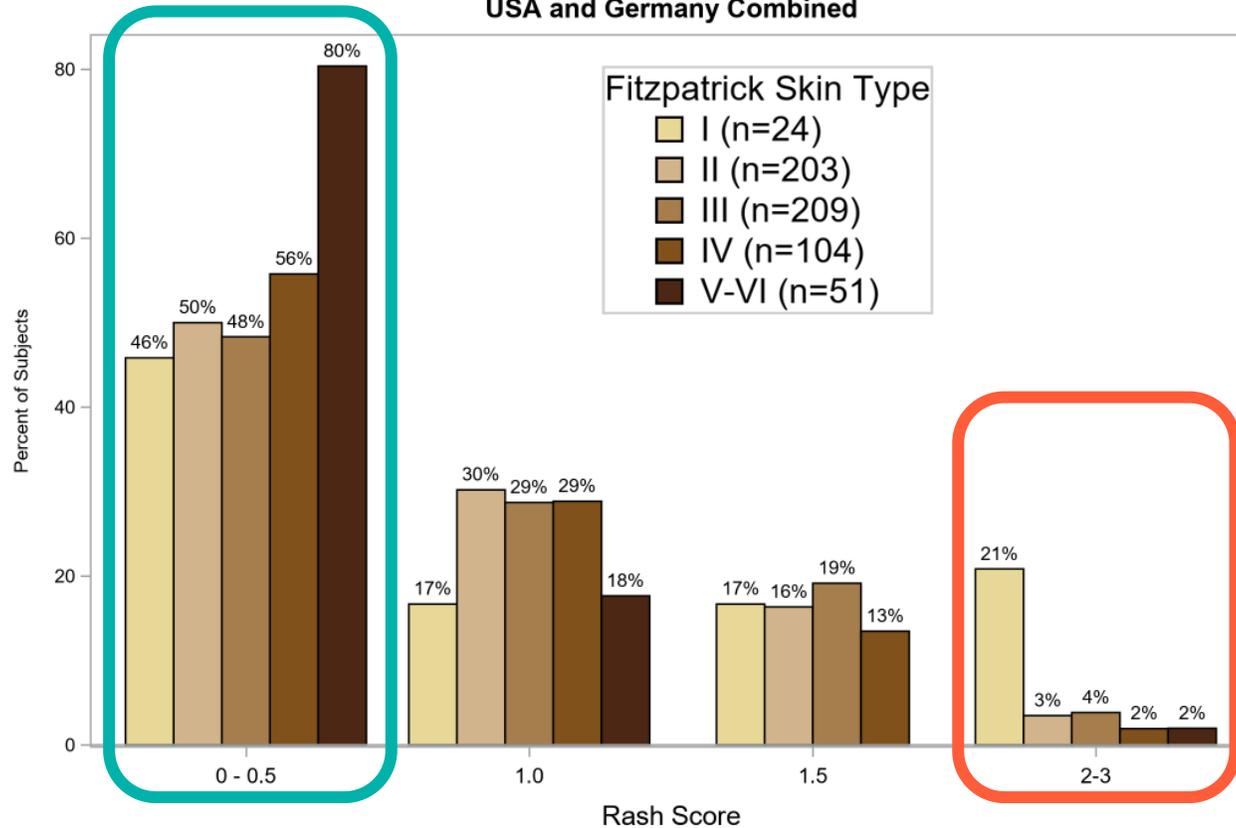
Personal Characteristics	Light skin, Red hair	Fair Skin, Light hair	Medium, white- to-olive skin	Olive, moderate brown	Brown, dark brown skin & hair	Black, very dark brown
Sun Sensitivity	Always burns, never tans	Usually burns, Difficult tanning	Sometimes burns, gradually tans	Rarely burns, easily tans	Very rarely burns, tans very easily	Never burns, deeply pigmented

# DDA: Fitzpatrick Skin Type

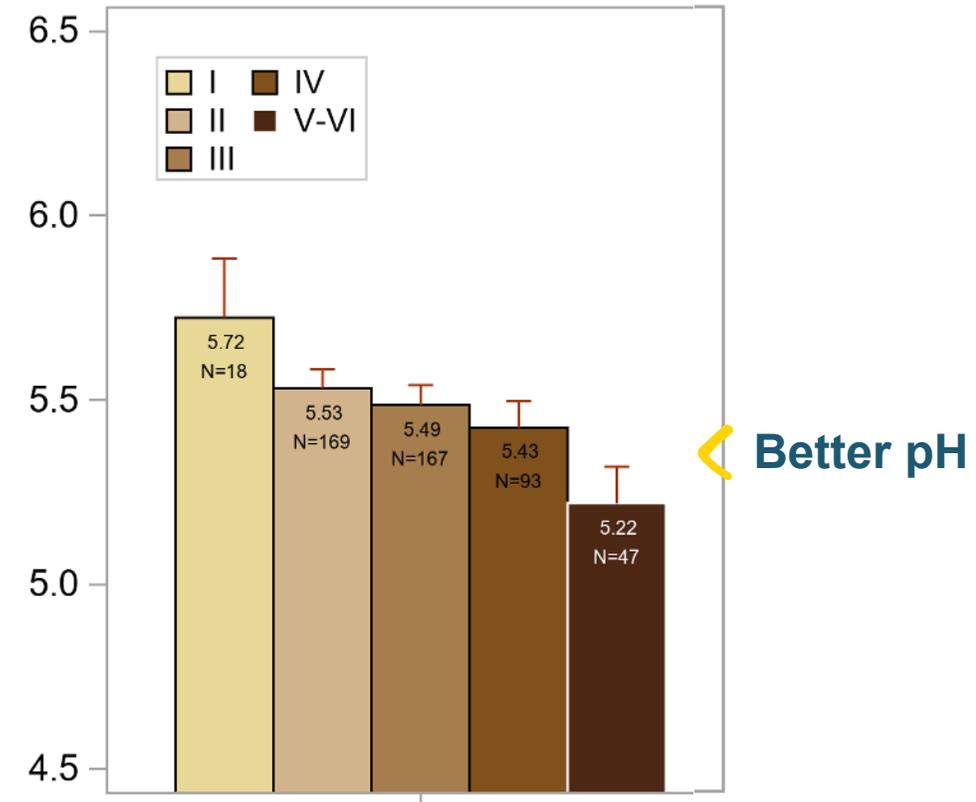


## Perianal Dermatitis

Genitals Rash Score by Fitzpatrick Skin Type - Ages 2-8 Months  
USA and Germany Combined



## Skin pH (Buttocks)



**Wash Cloth & Water**  
**vs.**  
**Acidic, pH-Buffered Baby Wipe**  
**NICU Clinical Study**

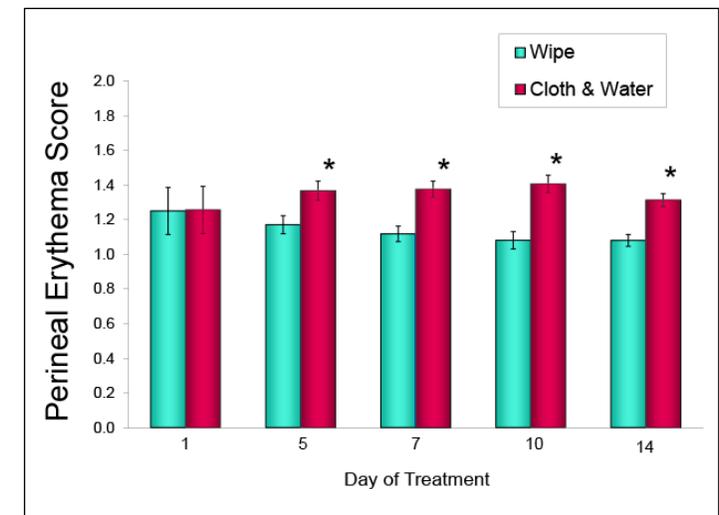
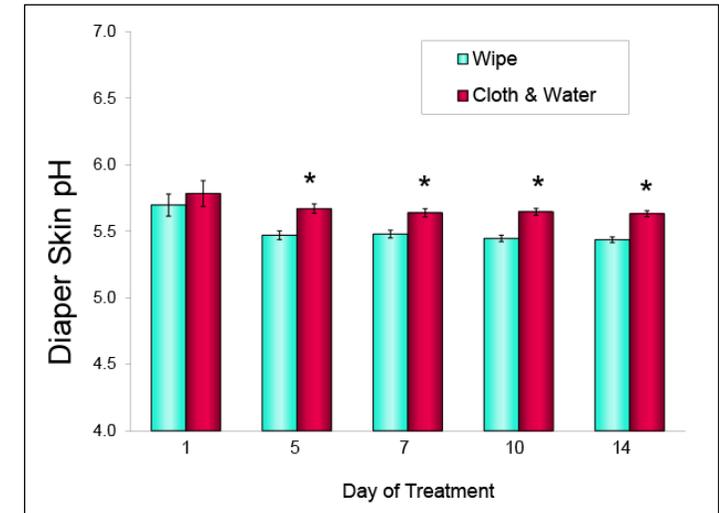


# Skin Benefits of a Mildly Acidic, pH-Buffered Wipe

## OBJECTIVE

To compare skin mildness of a low-pH disposable wipe vs. Cloth & Water (CW) in the NICU setting.

- Randomized 130 NICU patients (31-50 wks)
- Use for up to 14 days.
- Acidic, pH-buffered Baby Wipe:
  - Better Skin Barrier
  - Lower Skin pH
  - Reduced Erythema (Redness)

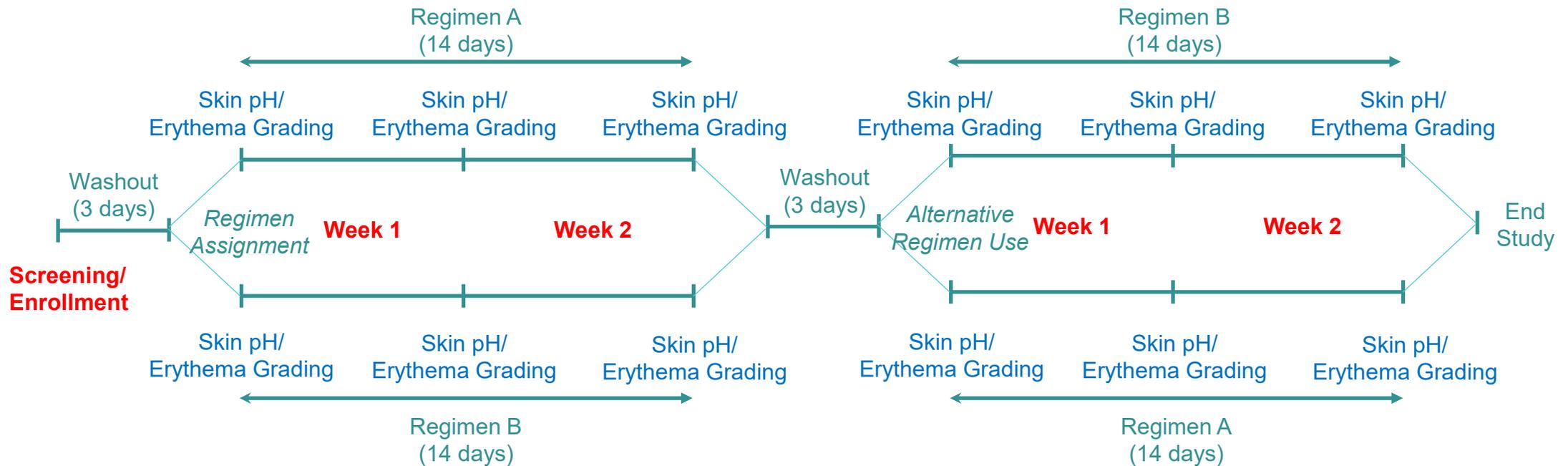


# Do Diapers & Wipes Play a Role in Baby Skin Health?

Comparison of Diaper and Wipe Regimen

# Diapers & Wipes Regimen Clinical Study Design: 2 Clinical Studies

- Two, IRB approved, randomized, blinded, crossover clinical studies
- Healthy, newborn population (>7 days, < 8 weeks of age);
- Exclusive Regimen usage for 3 (n=38) or 14 (n=80) days;
- No topical product usage



# Diaper + Wipe Regimen Product Features

## Regimen A

## Regimen B

Diaper Features



Diaper with Barrier Ointment

+

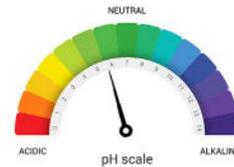
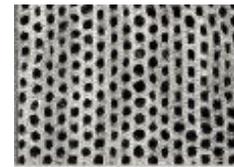


Absorb-Away Liner™

+



pH Buffering Wipes



No Emollient

+

Non-Apertured  
Topsheet

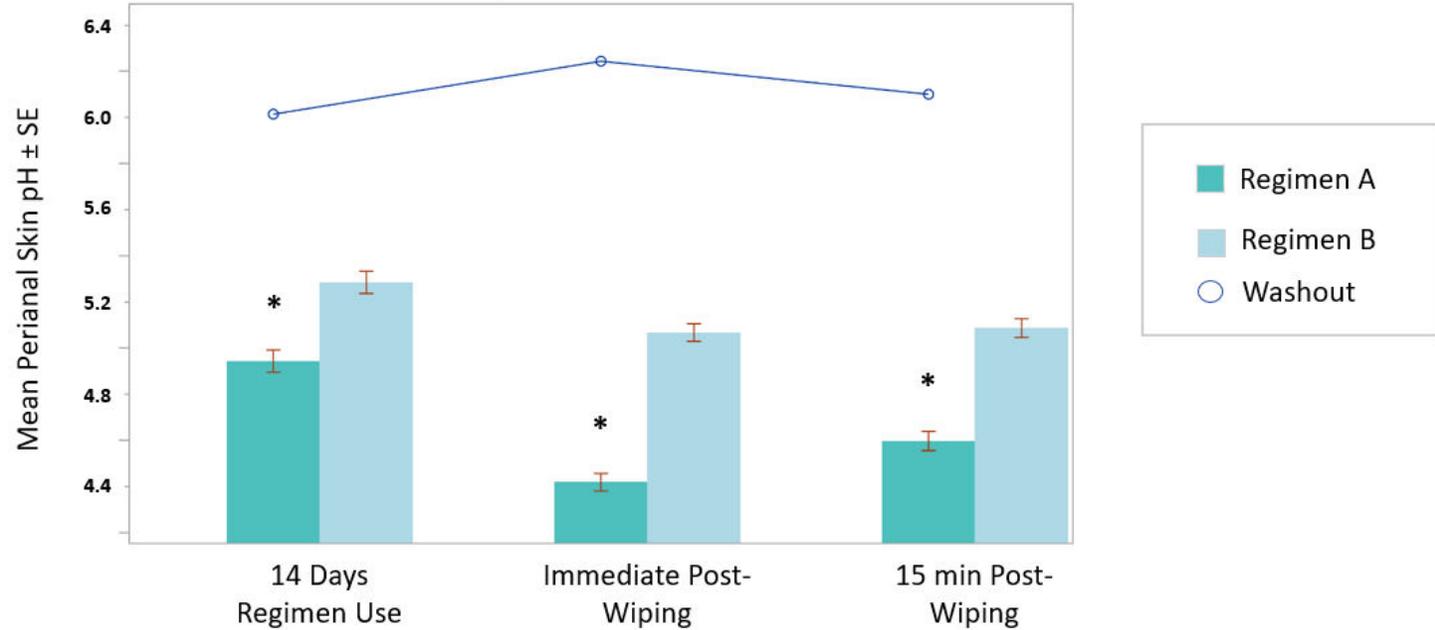
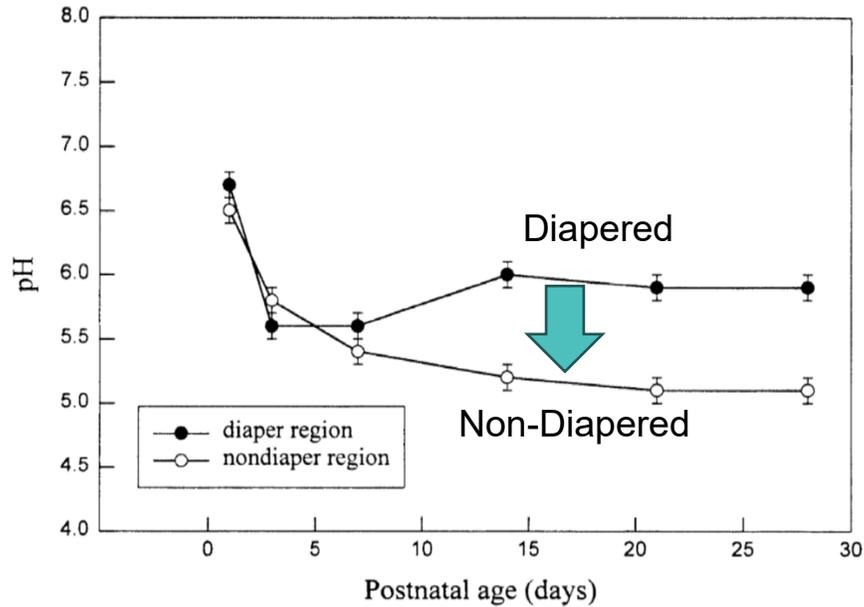
+

Mildly acidic,  
limited pH  
buffering

Wipe Features

# Diapers & Wipes Regimen: Impact on Skin pH

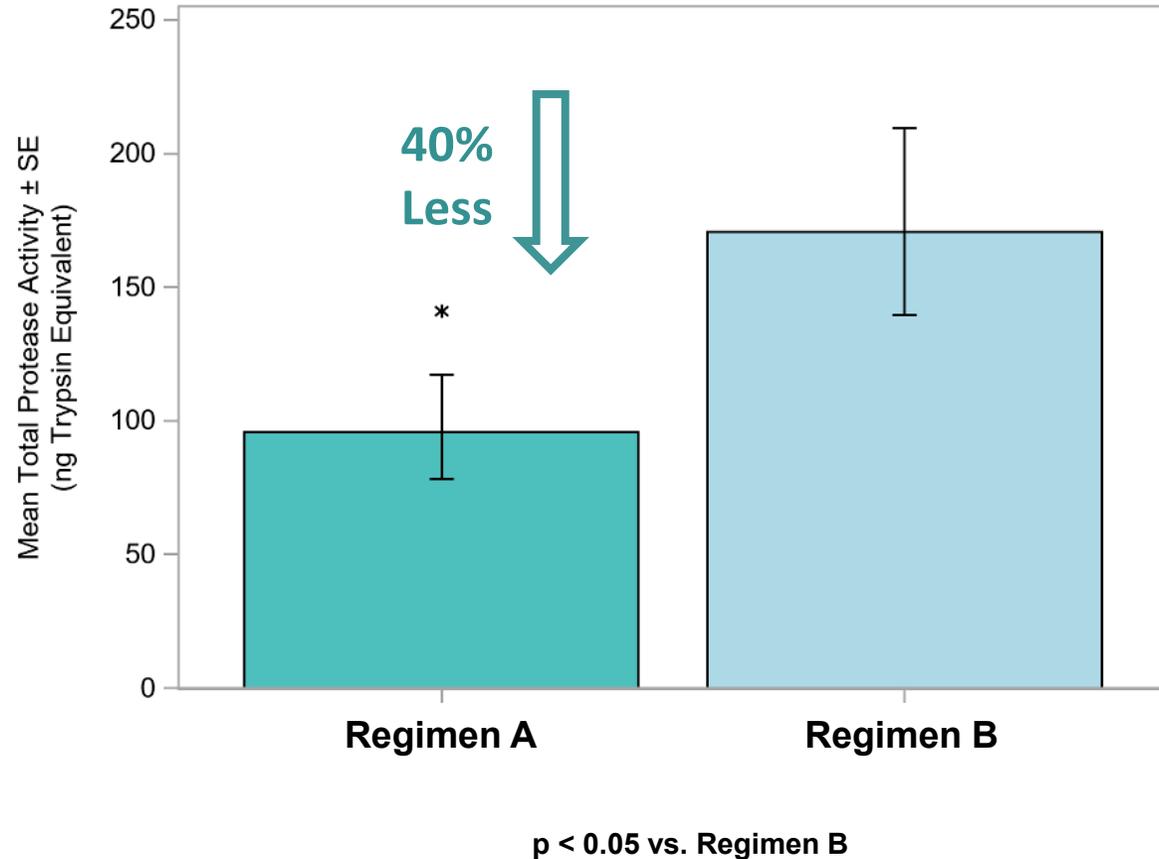
Elevated diaper area skin pH



## Regimen A:

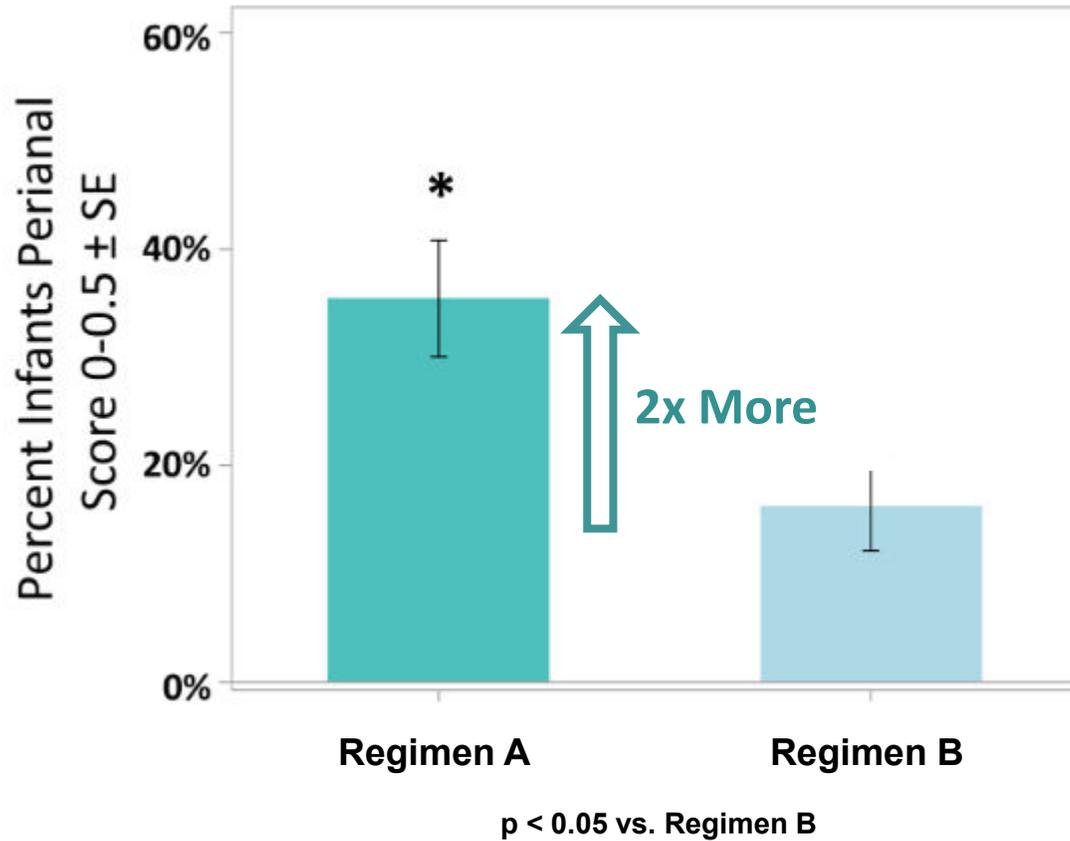
✓ Normalized diapered skin pH vs. Regimen B & Washout

# Removing Feces From Skin: Residual Enzyme Activity

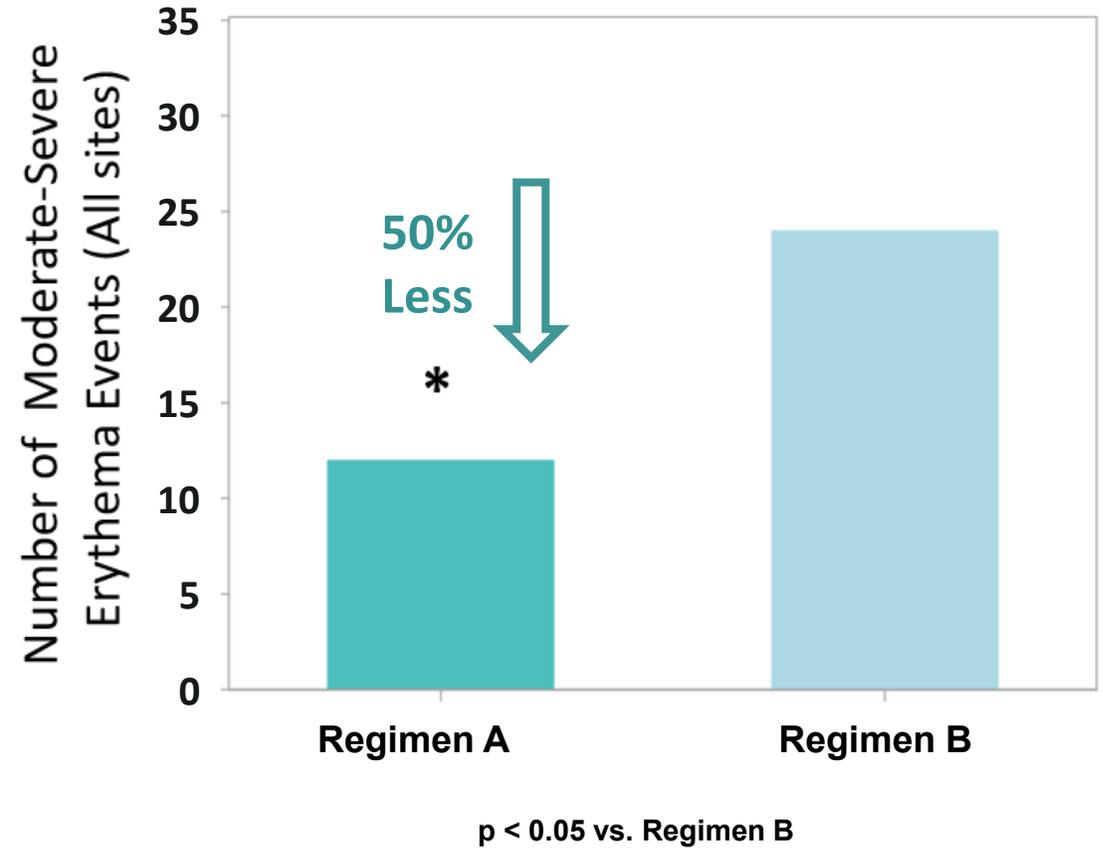


- Regimen A *reduced residual fecal enzyme* activity at the PBI by 40% compared to Regimen B post-stool cleaning.
- An estimated *80% reduction in Trypsin enzyme activity*.

**Regimen A:  
2X More Erythema-Free  
Infants at Perianal Site**



**Regimen A:  
Fewer More  
Severe Erythema Events**



# Summary

- Baby's skin is dynamic and “balance” is needed to care for it
- Retaining vernix has skin benefits
- Avoid overbathing/underbathing
- DDA Prevention is critical to baby health and wellness: superabsorbent products, hygiene/cleanliness (not scrubbing), support acidic pH, frequent changing to avoid skin overhydration, proactive care may include a thin layer of a topical cream
- Skin and diapering product impact the frequency and severity of DDA



Pampers®

