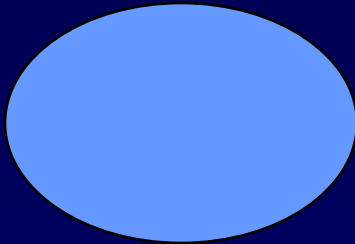
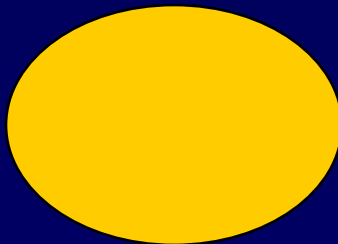
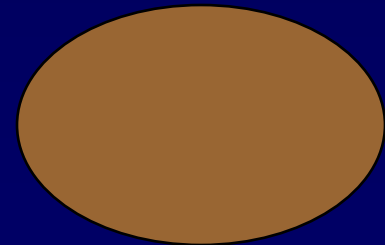
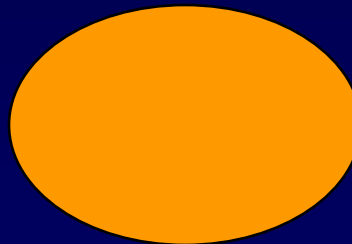
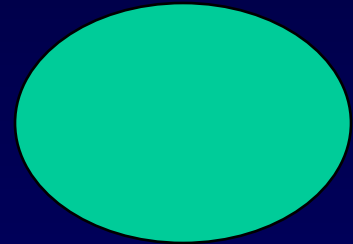
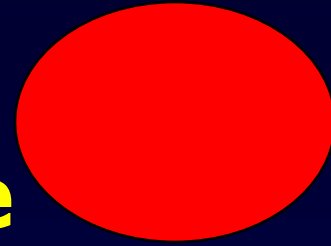


Can Atopic Dermatitis Be Prevented?

Eric Simpson, MD, MCR
Associate Professor, Dermatology
Oregon Health & Science University



RELEVANT DISCLOSURES

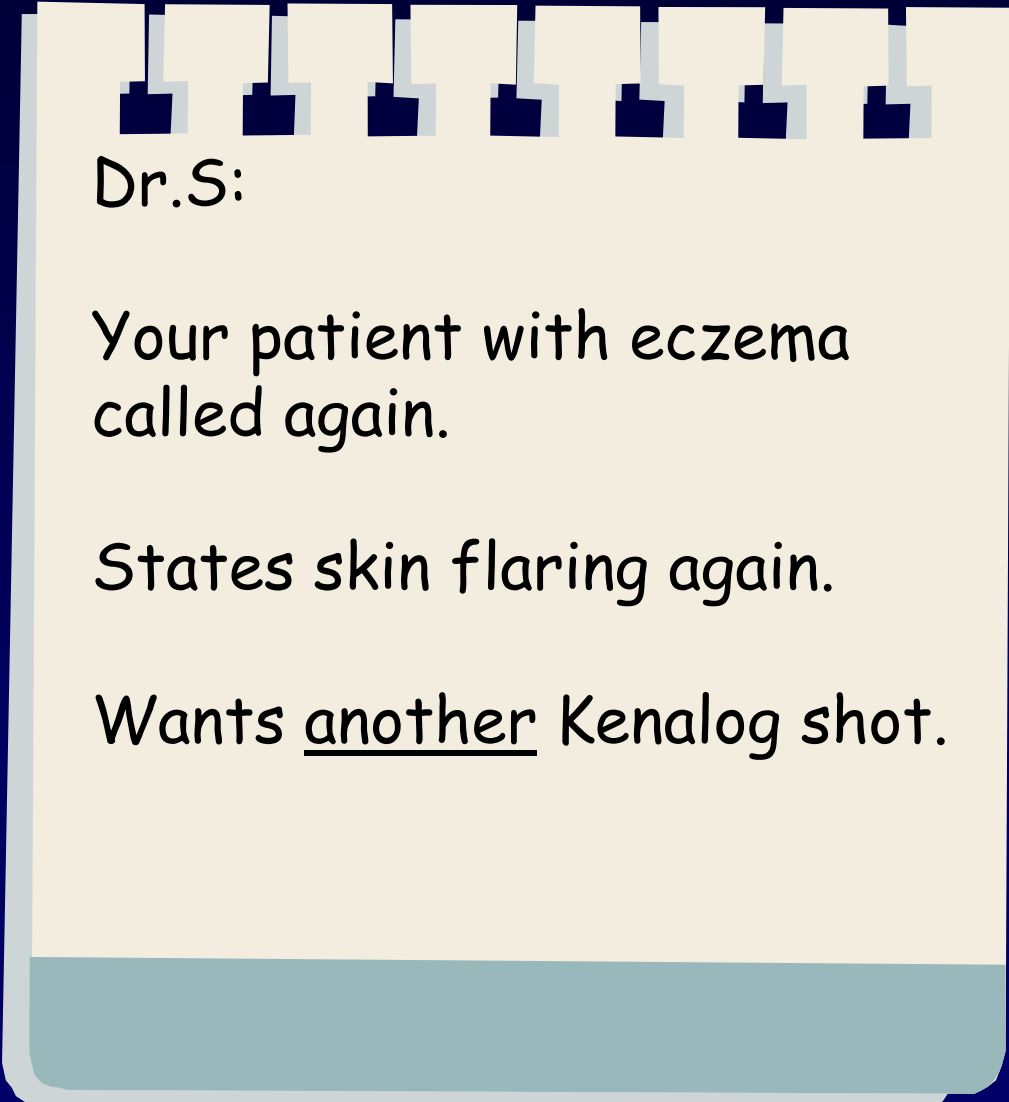
- Consultant for Galderma
- Research grant from Ceragenix

PREVENTION RESEARCH DEFINITIONS

- Primary- prevent the onset of the disease
- Secondary- early detection and reduce morbidity from the disease once diagnosed [FLARE PREVENTION]
- Tertiary- reducing the negative impact of the disease and reducing disease-related complications

OBJECTIVES

1. Improve Long-term Control of AD



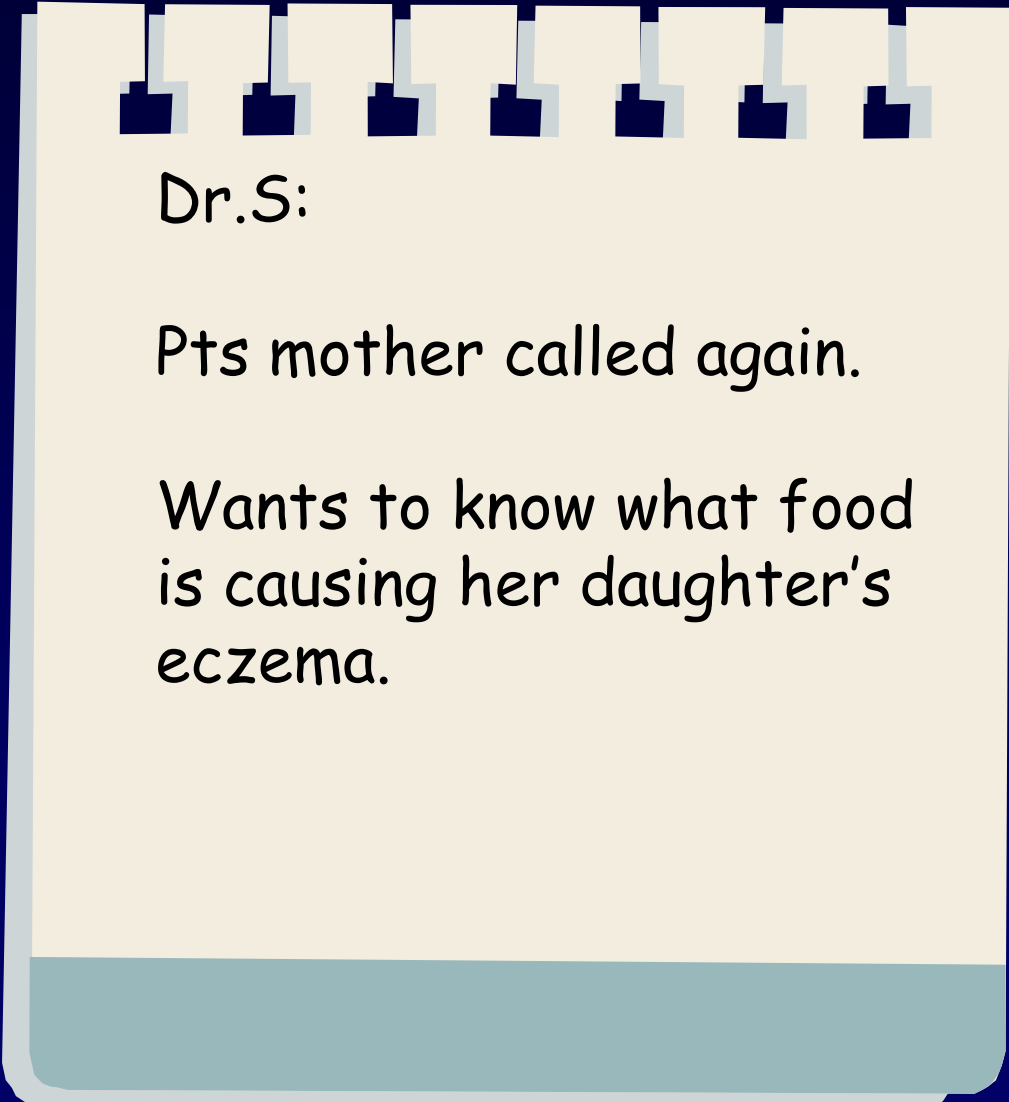
Dr.S:

Your patient with eczema
called again.

States skin flaring again.

Wants another Kenalog shot.

2. Understand the role of allergen avoidance



Dr.S:

Pts mother called again.

Wants to know what food is causing her daughter's eczema.

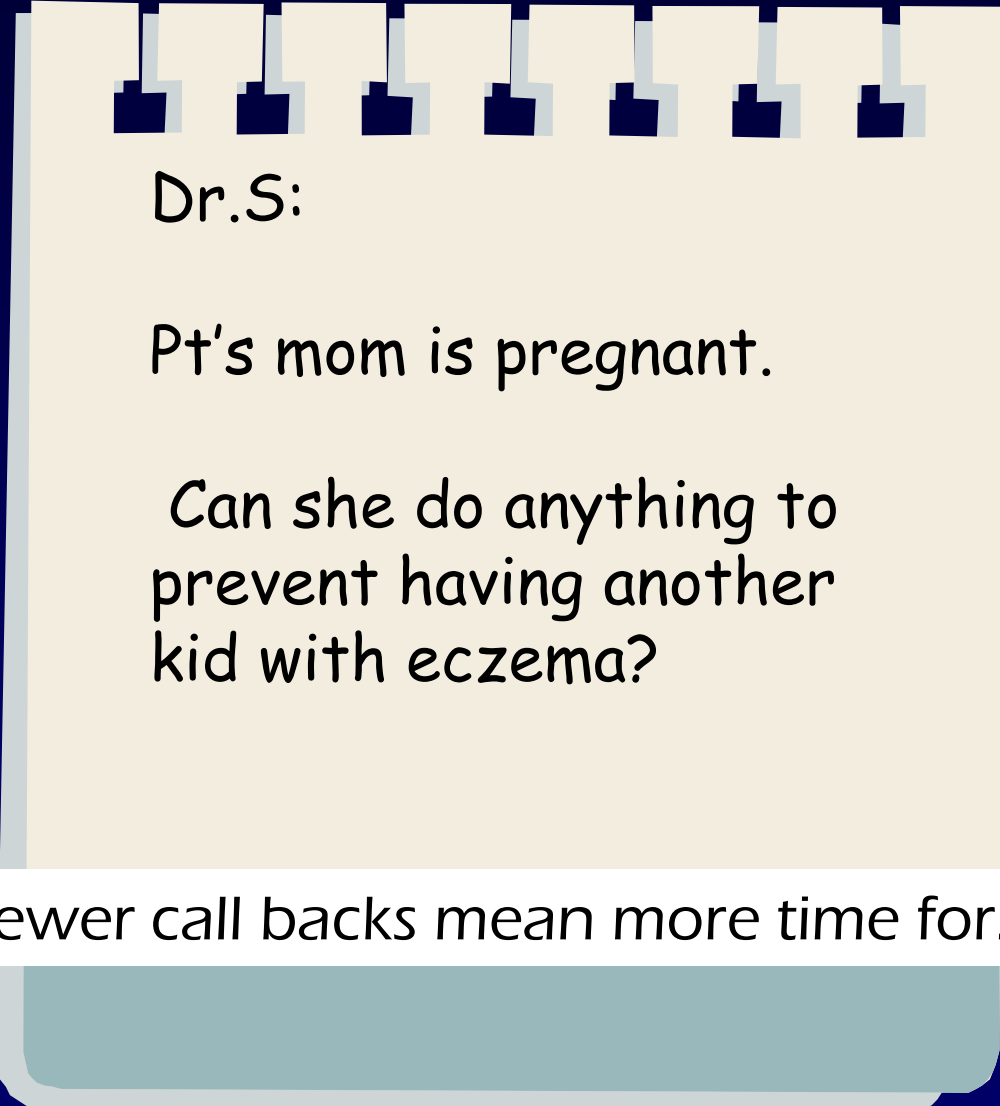
3. Prevent Staphylococcal infections

Dr.S:

Pts father called.
States he is getting pus
bumps and yellow
crusting.

Skin starting to flare.

4. Can eczema onset be prevented?



Dr.S:

Pt's mom is pregnant.

Can she do anything to
prevent having another
kid with eczema?

Fewer call backs mean more time for...







BEFORE FLARE PREVENTION....

INDUCING CLEARANCE

Initial Visit is Education

- STEROID PHOBIA
 - Discuss risk of not treating
- CAUSATION AND FOOD ALLERGY
 - Skin barrier disease
 - Allergy associated but not the cause
- WRITE OUT CLEARANCE PROTOCOL-Hanifin
- SCHEDULE 1 WEEK FOLLOW-UP

1 WEEK LATER...

NOW WHAT?



FLARE PREVENTION STRATEGIES

- Emollients
- Barrier Devices
- Intermittent Anti-inflammatory Therapy
- Antimicrobial therapy
- Probiotics
- Allergen Avoidance

FLARE PREVENTION

Mild Disease

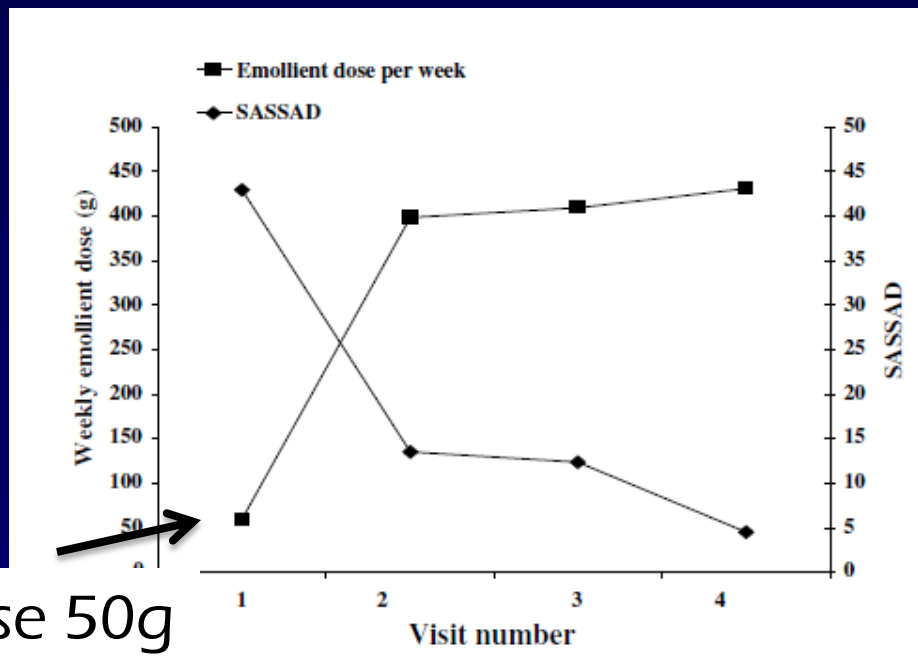
- Bathe as often as they want
- Mild cleansers to diaper area and scalp
- Moisturize! Moisturize! Moisturize!
- Do emollients really work?

Epidemiology and Health Services Research

Comparison of parent knowledge, therapy utilization and severity of atopic eczema before and after explanation and demonstration of topical therapies by a specialist dermatology nurse

M.J.CORK,*†‡ J.BRITTON,§ L.BUTLER,‡ S.YOUNG,* R.MURPHY¶
AND S.G.KEOHANE**

reduction in the severity of the eczema. The main change in therapy utilization was an 800% increase in the use of emollients (to 426 g weekly of emollient cream/ointment) and no overall increase in the use of topical steroids, accounting for potency and quantity used.



Baseline Use 50g

Moisturizers I Use

Few allergens, good oil content

- Cetaphil Cream
- CeraVe Cream
- Plain petrolatum
- Plastibase
- Aquaphor

FLARE PREVENTION STRATEGIES

- Emollients
- Role of Devices
- Intermittent Anti-inflammatory Therapy
- Antimicrobial therapy
- Probiotics
- Allergen Avoidance



- Sinclair Pharmaceuticals (UK)
- Hyaluronic acid
- Extract of *Vitis vinifera*
- Studies in mild-mod disease
 - 70% clear or almost clear
 - Better than vehicle
 - Vehicle an irritant?



EPICERAM

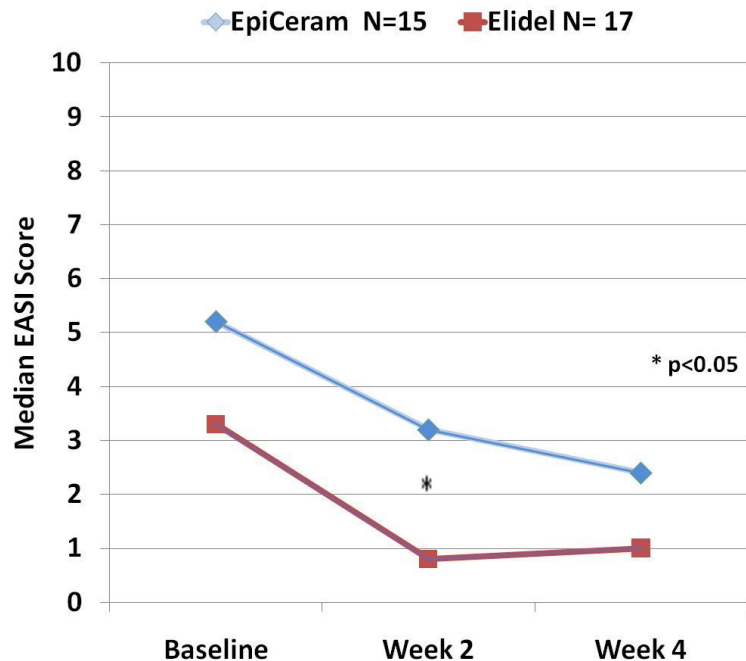


- Ceramides, cholesterol and fatty acids
- Marketed late 2008
- Compete with calcineurin inhibitors as steroid-sparing agent

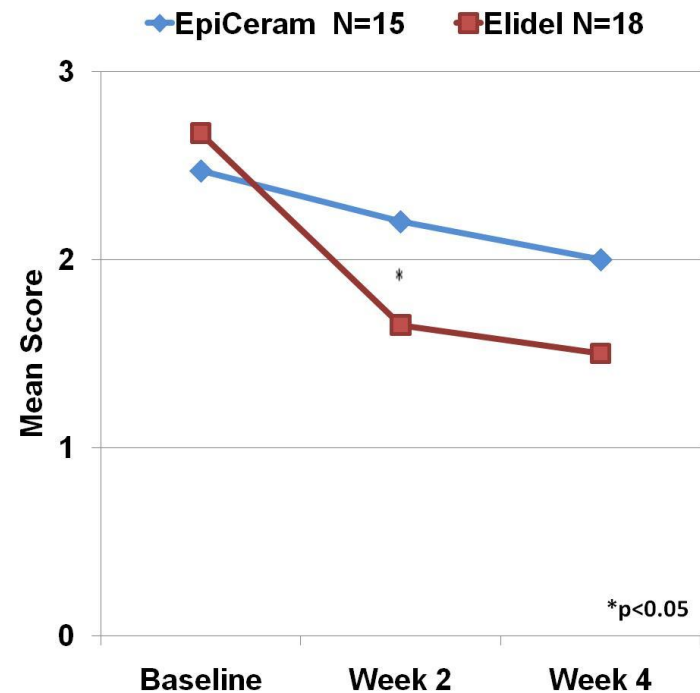
EPICERAM

International Symposium of Atopic Dermatitis, 2008

Median EASI Scores Over Time



Investigator Global Assessment



MimyX

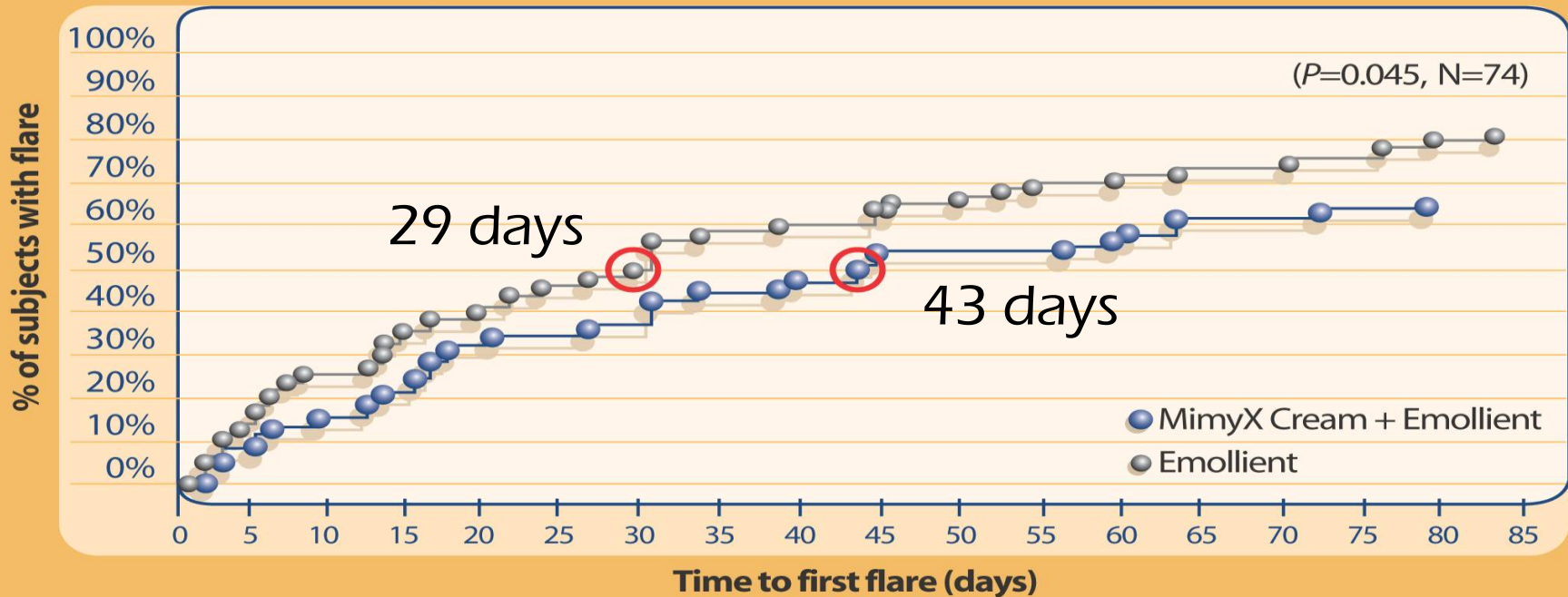
- Stiefel
- Palmitamide MEA
 - Fatty acid
 - Binds to cannabinoid receptors
- Equivalent to 1% hydrocortisone but with purported barrier repair abilities

Eucerin alone

Mimyx + Eucerin



Summary of Time to First Flare (ITT Population)



- Median time to first flare:
 - Mimyx Cream + emollient **48% longer remission**
- **25% greater incidence** of flare with emollient only vs skin treated with Mimyx Cream ($P<0.051$).

DEVICES

Summary

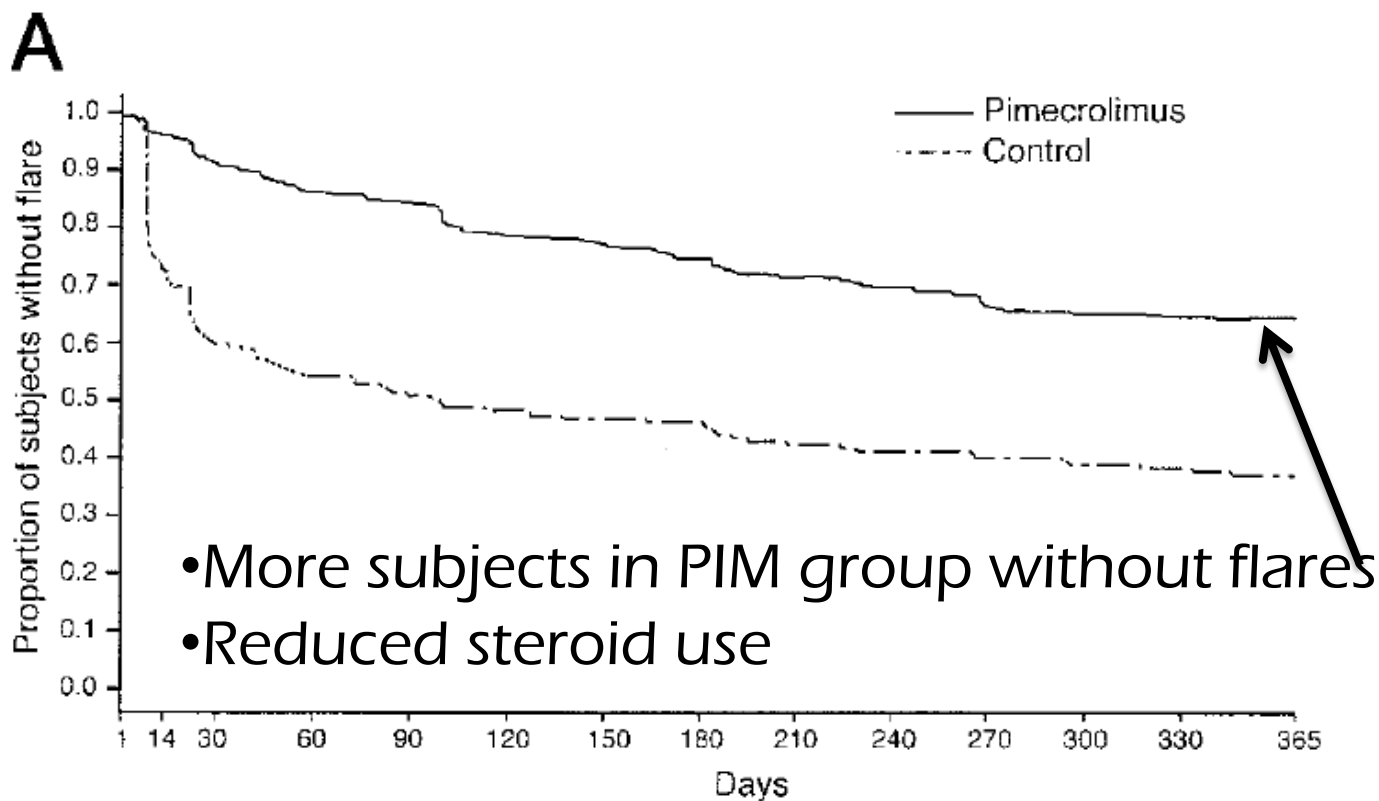
- May have modest anti-inflammatory properties
- Could use to treat mild disease, but why?
- Too expensive for use as moisturizer
- If interested or scared patient, use one instead of TCI for steroid-sparing agent

FLARE PREVENTION STRATEGIES

- Emollients
- Role of Devices
- Intermittent Anti-inflammatory Therapy
- Antimicrobial therapy
- Probiotics
- Allergen Avoidance

Pimecrolimus used for early disease vs vehicle Steroid used for flares

Proportion of Subjects Without Flare



Wahn, U. et al. Pediatrics 2002;110:e2

FLARE PREVENTION

Topical Steroids

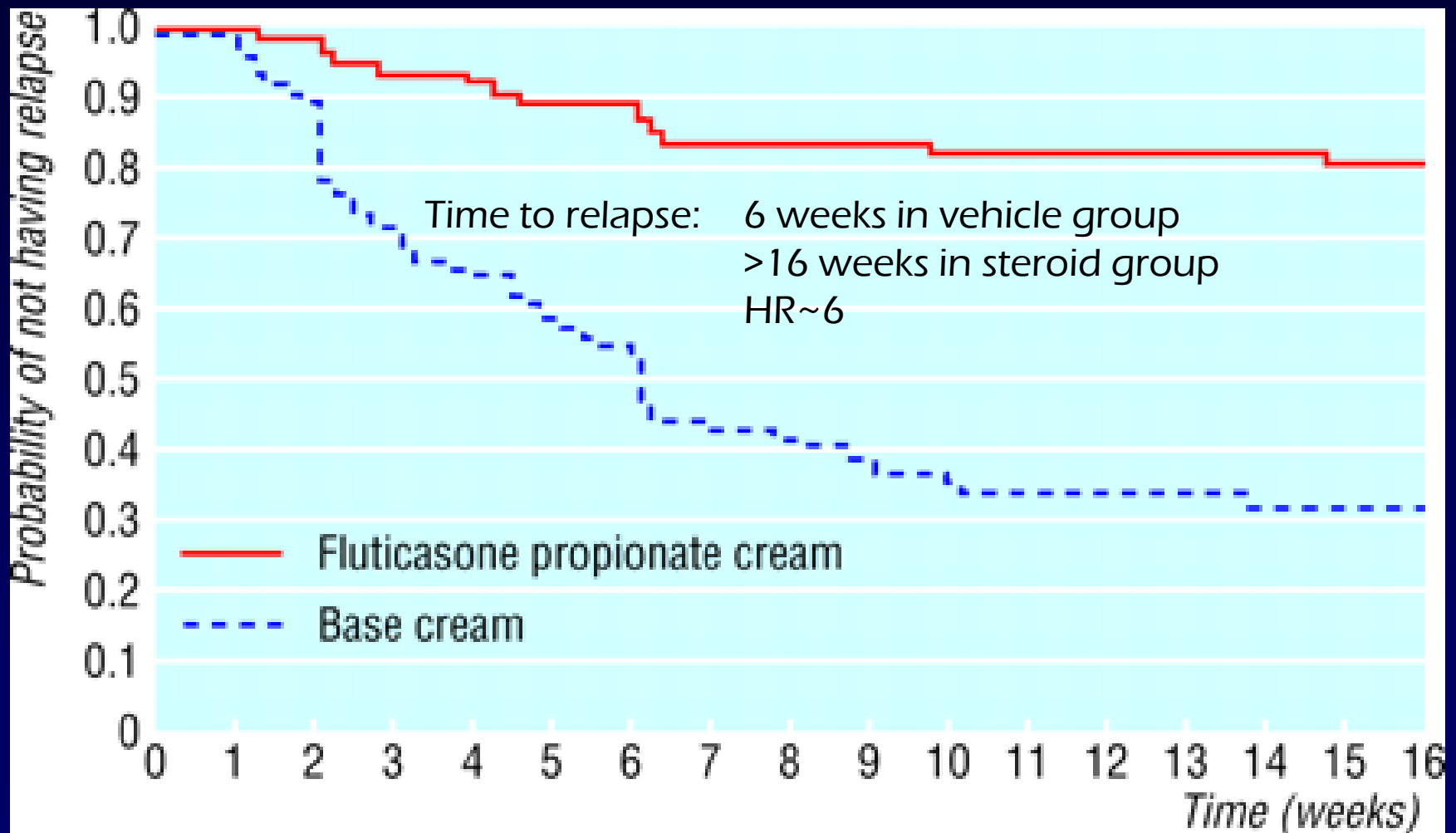
- 3 studies including pediatric and adult patients evaluating topical fluticasone to prevent relapses
- Used on healed sites and early disease
- All 3 studies with same conclusions

Twice weekly fluticasone propionate added to emollient maintenance treatment to reduce risk of relapse in atopic dermatitis: randomised, double blind, parallel group study

John Berth-Jones, Robert J Damstra, Stefan Golsch, John K Livden, Oliver Van Hoogheem, Fulvio Allegra, Christine A Parker

- RCT of 295 patients aged 12-65 with AD
- Cleared on 1 month of fluticasone cream or ointment
- Fluticasone 2X/week to healed sites vs. placebo control

PROBABILITY OF NO RELAPSE

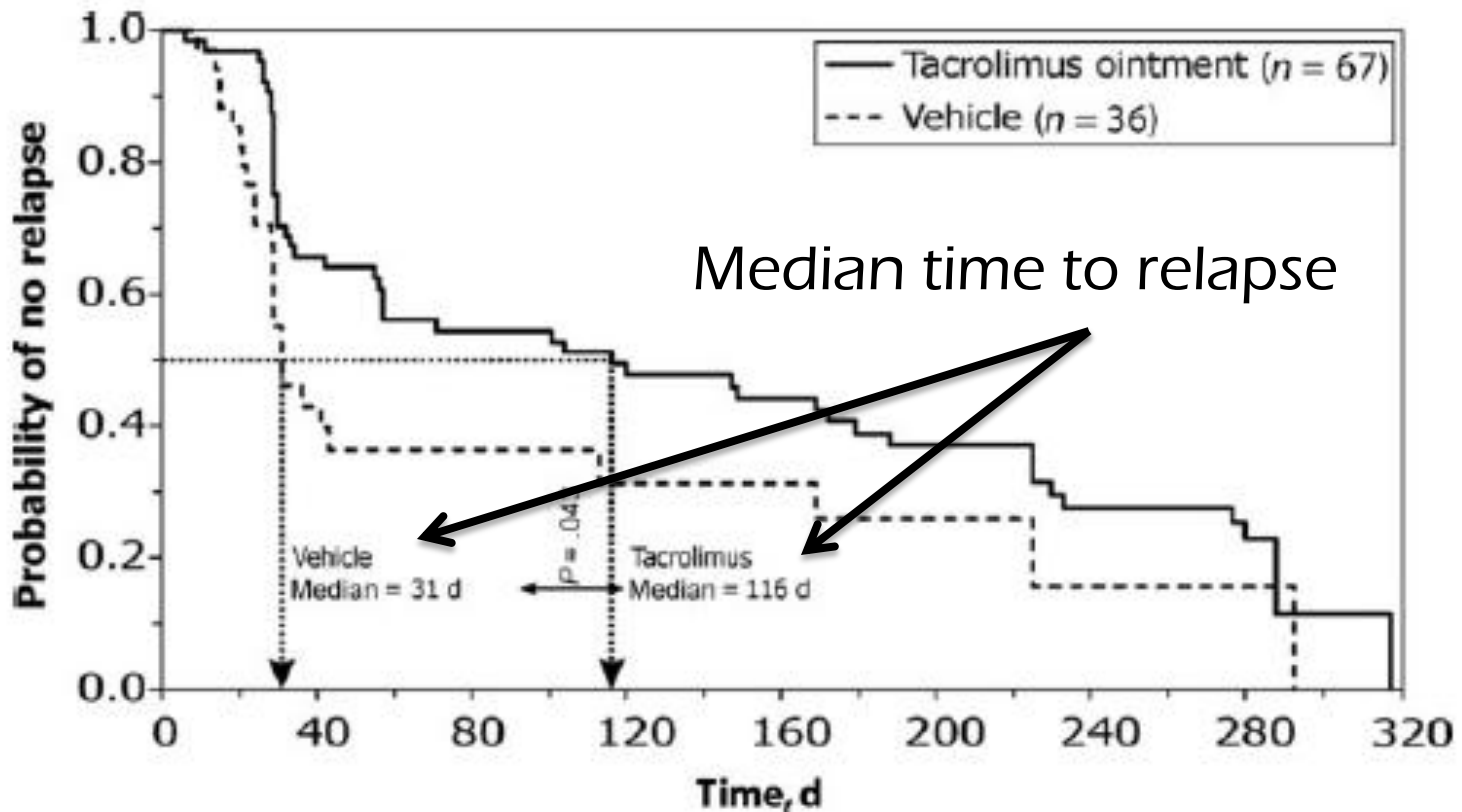


Can you do this with TCI's?

Three Times Weekly Tacrolimus Ointment Reduces Relapse in Stabilized Atopic Dermatitis: A New Paradigm for Use

Amy S. Paller, MD^a, Lawrence F. Eichenfield, MD^b, Robert S. Kirsner, MD, PhD^c, Toni Shull, RN^d, Eileen Jaracz, PharmD^d, Eric L. Simpson^e, for the US Tacrolimus Ointment Study Group

Pediatrics, 2008



Intermittent Anti-inflammatory Therapy

Summary

- If using more than 10-14 days per month topical steroid, add TCI's
- For severe disease:
 - clearance protocol,
 - then either 2X/week topical steroid OR
 - 3X/week TCI to healed sites and increase to bid to early disease
- WRITE IT OUT!

FLARE PREVENTION STRATEGIES

- Emollients
- Role of Devices
- Intermittent Anti-inflammatory Therapy
- Antimicrobial therapy
- Probiotics
- Allergen Avoidance

Interventions to reduce *Staphylococcus aureus* in the management of atopic eczema (Review)

2008

Birnie AJ, Bath-Hextall FJ, Ravenscroft JC, Williams HC



**THE COCHRANE
COLLABORATION®**

Interventions to reduce *Staphylococcus aureus* in the management of atopic eczema (Review)

Birnie AJ, Bath-Hextall FJ, Ravenscroft JC, Williams HC



THE COCHRANE
COLLABORATION®

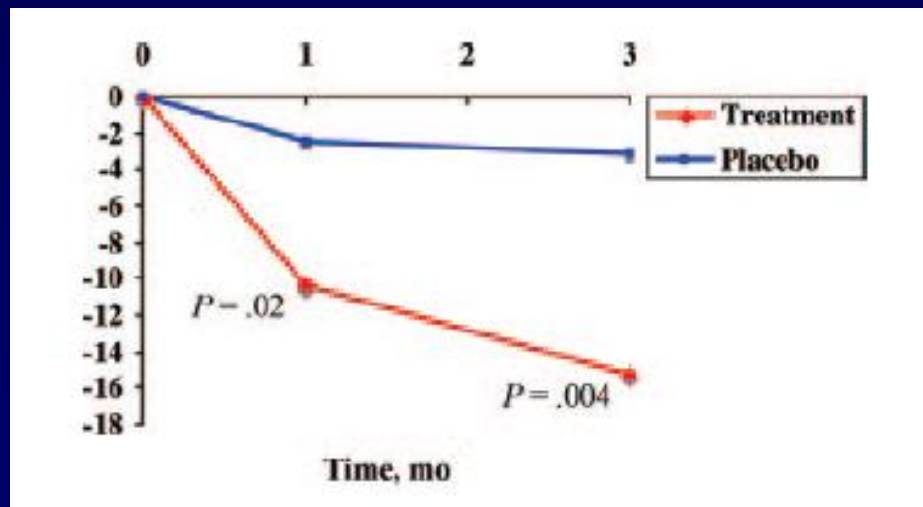
Summary

- Oral abx did not help in infected or non-infected eczema (3 studies)
- Antimicrobial soaps, creams, or bath additives did not help (7 studies)
- Antimicrobials added to topical steroids reduced staph counts but did not improve the eczema (9 studies)

Treatment of *Staphylococcus aureus* Colonization in Atopic Dermatitis Decreases Disease Severity

Jennifer T. Huang, MD^{a,b}, Melissa Abrams, MD^{a,b}, Brook Tlougan, MD^{a,b}, Alfred Rademaker, PhD^c, Amy S. Paller, MD^{a,b}

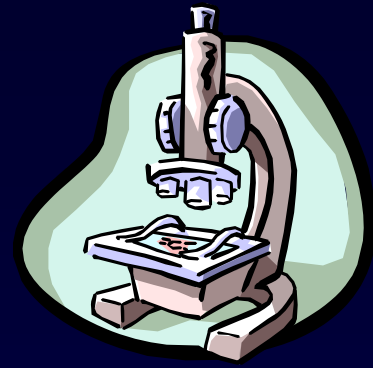
- Bleach baths 2X/week 5-10 minutes
 - 0.005% (0.5cup 6% bleach in 40 gallon tub)
 - Mupirocin nasal 5 days each month
 - Placebo controlled



FLARE PREVENTION STRATEGIES

- Emollients
- Role of Devices
- Intermittent Anti-inflammatory Therapy
- Antimicrobial therapy
- Probiotics
- Allergen Avoidance

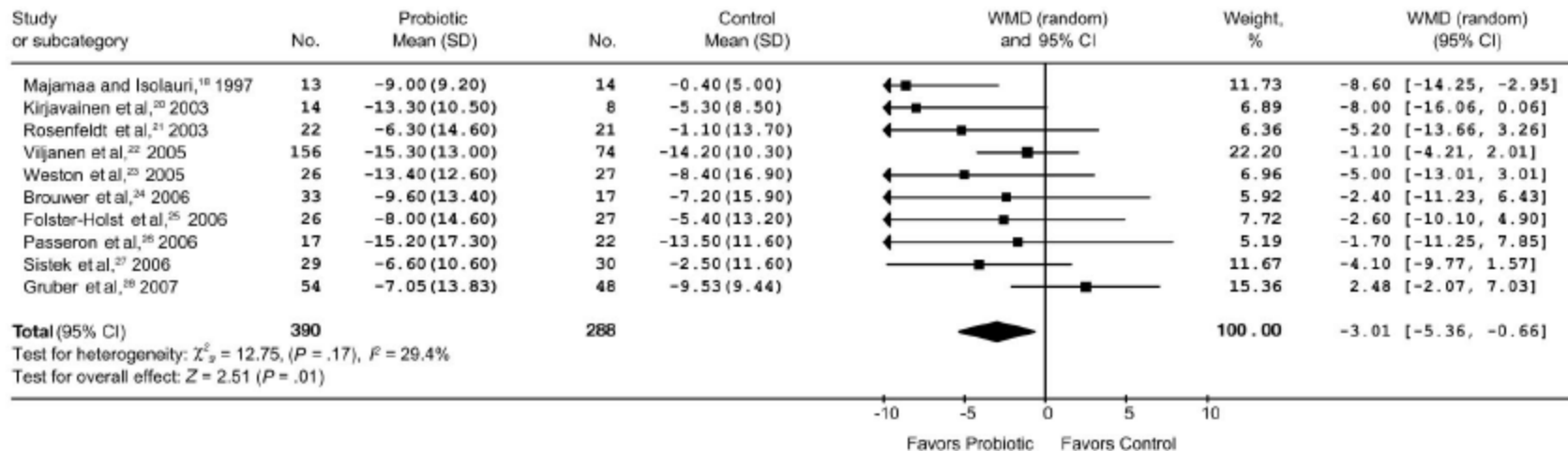
PROBIOTICS



- Cultures of bacteria that are beneficial to the gut microflora
- Normal gut microflora may be an important inhibitor of Th2 responses
- Probiotics may correct abnormal atopic microflora and promote Th1 responses

SYSTEMATIC REVIEW

Michail, 2008



- Mean change of 3.01 in SCORAD (1-102 scale)
- SCORAD for moderate AD=25
- “Doubtful clinical significance”

COCHRANE SYSTEMATIC REVIEW PROBIOTICS FOR AD TREATMENT

Boyle RJ, 2008

- Reviewed 12 studies
- Effect size of 2.46 ($P=0.33$)
- “Not effective”
- Cases of bowel ischemia and infection reported (pneumonia, sepsis, meningitis)

PROBIOTIC ORAL THERAPY FOR AD

Summary

- Inconsistent results for both treatment and prevention
- If any effect, likely small
- A role of gut flora on immune dysregulation not established
- Need further information on strain effects, potency, viability, storage

FLARE PREVENTION STRATEGIES

- Emollients
- Role of Devices
- Intermittent Anti-inflammatory Therapy
- Antimicrobial therapy
- Probiotics
- Allergen Avoidance

Review article

Dietary exclusions for improving established atopic eczema in adults and children: systematic review

- 9 RCT's
- One with some benefit
 - +IgE to egg
 - Egg avoidance group did better

**F. Bath-Hextall¹, F. M. Delamere²,
H. C. Williams³**

¹Faculty of Medicine and Health Sciences, University of Nottingham, Nottingham, UK; ²Centre of Evidence-Based Dermatology, University of Nottingham, Nottingham, UK; ³Department of Dermatology, University of Nottingham, Nottingham, UK

DUST MITE AVOIDANCE



DUST MITE AVOIDANCE STUDIES IN AD

AAD Guidelines of care for atopic dermatitis.

Hanifin, J. et.al. 2004: J. Amer. Acad. Dermatol. 50:391-404, 2004

- ✓ Tan, 1996
 - Adult and pediatric with improvement
- ✓ Ricci, 2000
 - Pediatric study showed improvement
- ✗ Gutgesell, 2001
 - Adult study, no improvement
- ✗ Holm, 2001
 - No improvement
- ✗ Koopman, 2002
 - Pediatric AD, no improvement
- ✗ Oosting, 2002
 - Adults and pediatrics, no improvement

WHEN TO ADDRESS ALLERGY

- If immediate urticarial lesions develop within 30 minutes of eating.
- Parent concerned about eczema flaring after a food despite good skin care.
- RAST for milk, egg, soy, wheat, peanut, fish
- Otherwise, redirect focus to good skin care!

VITAMIN D, of course!

- Upregulate AMP's and immunomodulatory effects
- Upregulates cathelicidins in AD (Hata, JACI, 2008)
- Slight improvement in AD (Sidbury, BJD 2008)
- More Vit D as infant, more atopy (Back, Acta 2009)

FLARE PREVENTION STRATEGIES

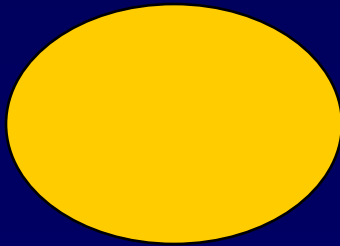
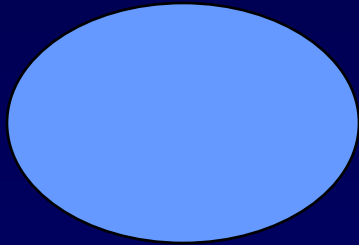
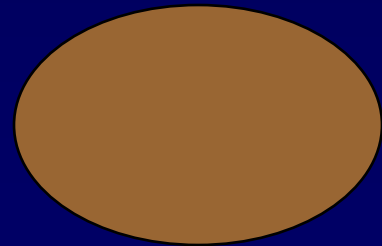
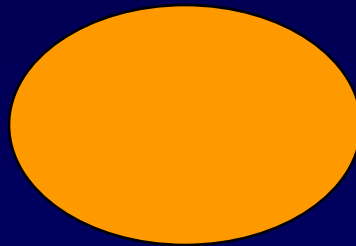
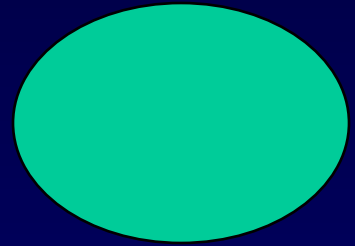
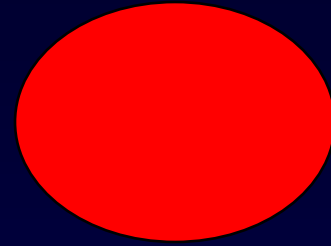
- Emollients
- Role of Devices
- Intermittent Anti-inflammatory Therapy
- Antimicrobial therapy
- Probiotics
- Allergen Avoidance
- Vitamin D

SUMMARY

Eczema Flare Prevention

- Simple soak and smear works.
- Education and follow-up in a week.
- Incorporate TCI's to early recurrence for moderate disease.
- Use twice weekly steroid or three times weekly tacrolimus oint to NORMAL skin to prevent flares in moderate-severe patients.
- Replace low levels of vitamin D

Can Atopic Dermatitis Be Prevented?



Primary Prevention of Atopic Dermatitis

Why?

- World-wide, common disease
- Economic, social, patient QOL burden
- Co-morbid allergic diseases
- Research focused on allergen avoidance
- Genetic studies reveal skin barrier important

ECZEMA PREVENTION

Update JACI 2005;116:49-55

- Canadian intervention study of 5000 children
- No prevention of AD with a combination:
 - breast feeding
 - delayed intro of foods
 - and dust mite avoidance
- **No studies focused on the skin barrier for prevention**

Evidence Barrier Protection from Birth can Prevent AD

- Early use of petrolatum protective in one study (Macharia, 1991)
- Aquaphor prevents “dermatitis” in prematures
- Emollients prevent flares of AD
- What are current guidelines for skin care of newborn?

Skin Care in the Well Term Newborn: Two Systematic Reviews

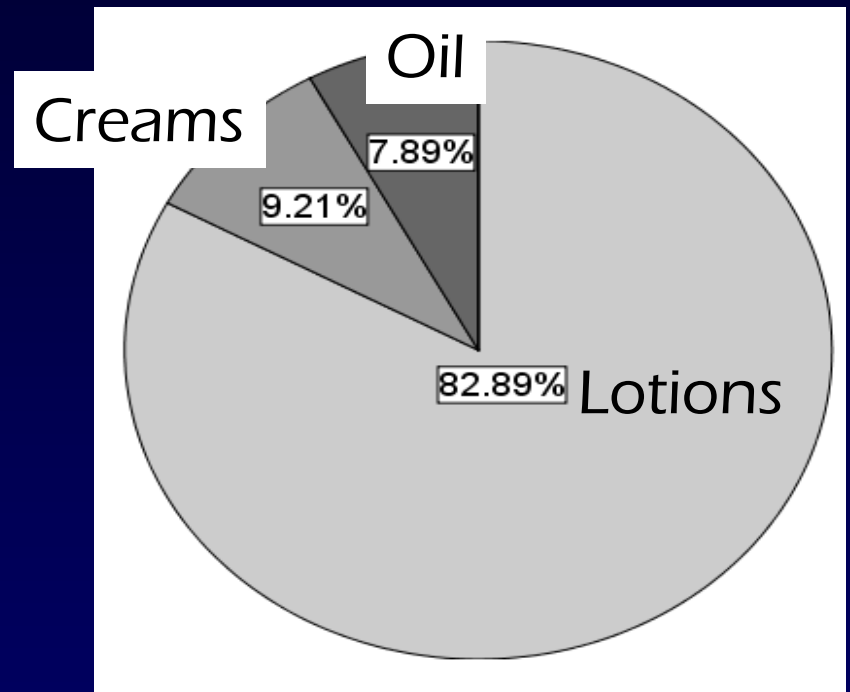
Birth, September 2005

*Lynne Walker, BSc(Hons), MA, RM, RGN, Soo Downe, BA(Hons), RM, MSc, PhD, and
Liz Gomez, BA(Hons), MA, RM*

- Two research questions
 - How does the use of soap and detergents affect newborn skin?
 - Consequences of moisturizer use?
- No studies identified examining skin care of the term newborn
- Guidelines say no emollient needed unless dry skin apparent

OHSU INFANT SKIN CARE SURVEY

	Cases (%)	Controls (%)	OR	P
Bathing >3 times per week	72.0	73.3	0.94	.641
Use of soap during bathing	90.0	92.0	0.78	.214
Regular use of any moisturizer	76.0	74.7	1.07	.913
Regular use of watery lotion	63.0	61.3	1.07	.562



- Frequent bathing and moisturizer use is very common prior to AD development
- These skin care practices may be detrimental to the skin barrier and may promote AD development

OHSU AD PREVENTION STUDY

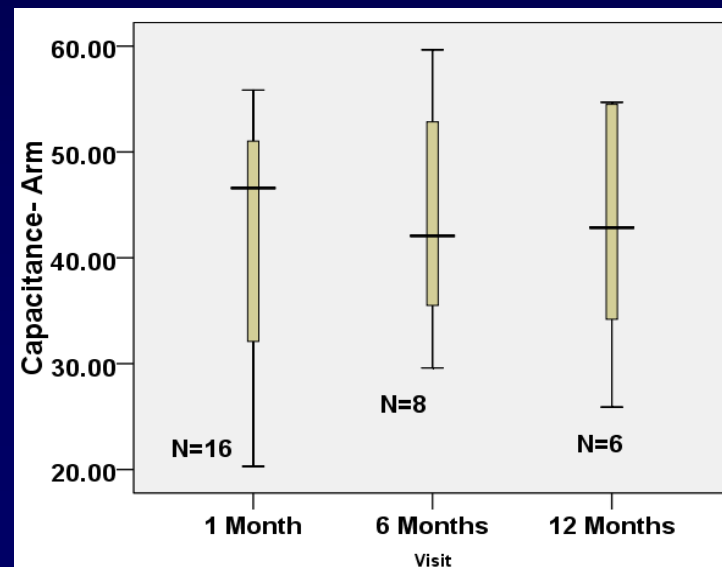
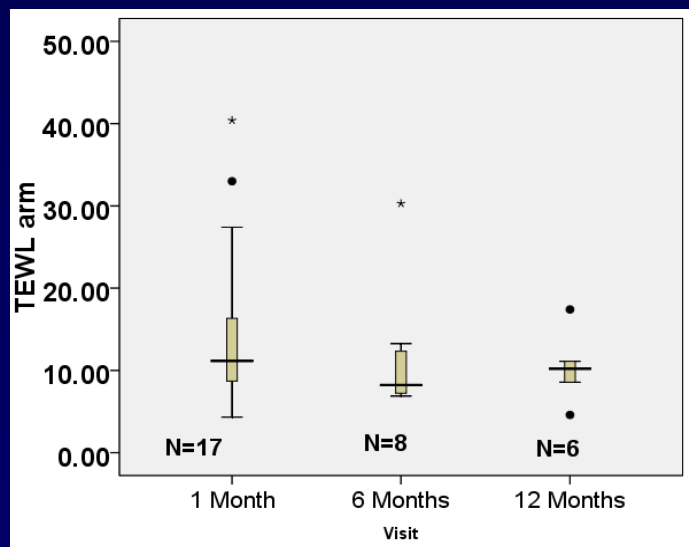
Methods

- Hypothesis: Emollient therapy from birth is a safe and feasible approach to AD prevention
- 22 neonates enrolled
- Cetaphil cream daily to all body surfaces from day 7
- Examine for AD development and barrier function

OHSU AD PREVENTION PILOT STUDY

Results

Subjects enrolled	Mean Follow-up (days)	Median Follow-up (days)	Follow-up Range (days)	Number meeting criteria for AD	Adverse events	Compliance with intervention
22	447	397	30-759	2 (9%)	None	85%



AD PRIMARY PREVENTION

Summary

- Barrier protection from birth is safe and a feasible approach to AD prevention
- Barrier protection may reduce IgE sensitization that occurs through the skin
- Can it prevent AD? Can it prevent allergic asthma?
- What is the best barrier protectant?

ACKNOWLEDGEMENTS

- Dermatology Foundation
- National Eczema Association
- Jon Hanifin
- Mickey Simpson