



HASSENFELD  
**CHILDREN'S  
HOSPITAL**  
AT NYU LANGONE

# Atopic Dermatitis Topicals to Biologicals

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NYU School of Medicine

July 21, 2022

## DISCLOSURE OF RELATIONSHIPS WITH INDUSTRY

Vikash S. Oza MD

### DISCLOSURES

Dove: Consultant – Honoraria

Pfizer: Grant recipient: Consultant-Honoraria

Visual Dx: Consultant-Honoraria

Practicing at the cusp



# Pediatric Atopic Dermatitis Treatment Timeline

Marion Sulzberger MD

Compound F



Tacrolimus 0.03% >2yo  
Tacrolimus 0.1% >16yo



Pimecrolimus 1% >2yo



Eucrisa >2yo



Dupilumab 12-18yo



Dupi 6-12yo

Ruxolitinib 1.5% cream (>12yo) Dupi 6mo-6yo  
Upadacitinib >12yo



1952

2000 2001

2016

2018

2020

2021

2022

Hey doc, the eczema  
came back – now  
what?

Steroids for my baby

It's the d

When wi  
away

We on  
natu



the

Education

Topical Management

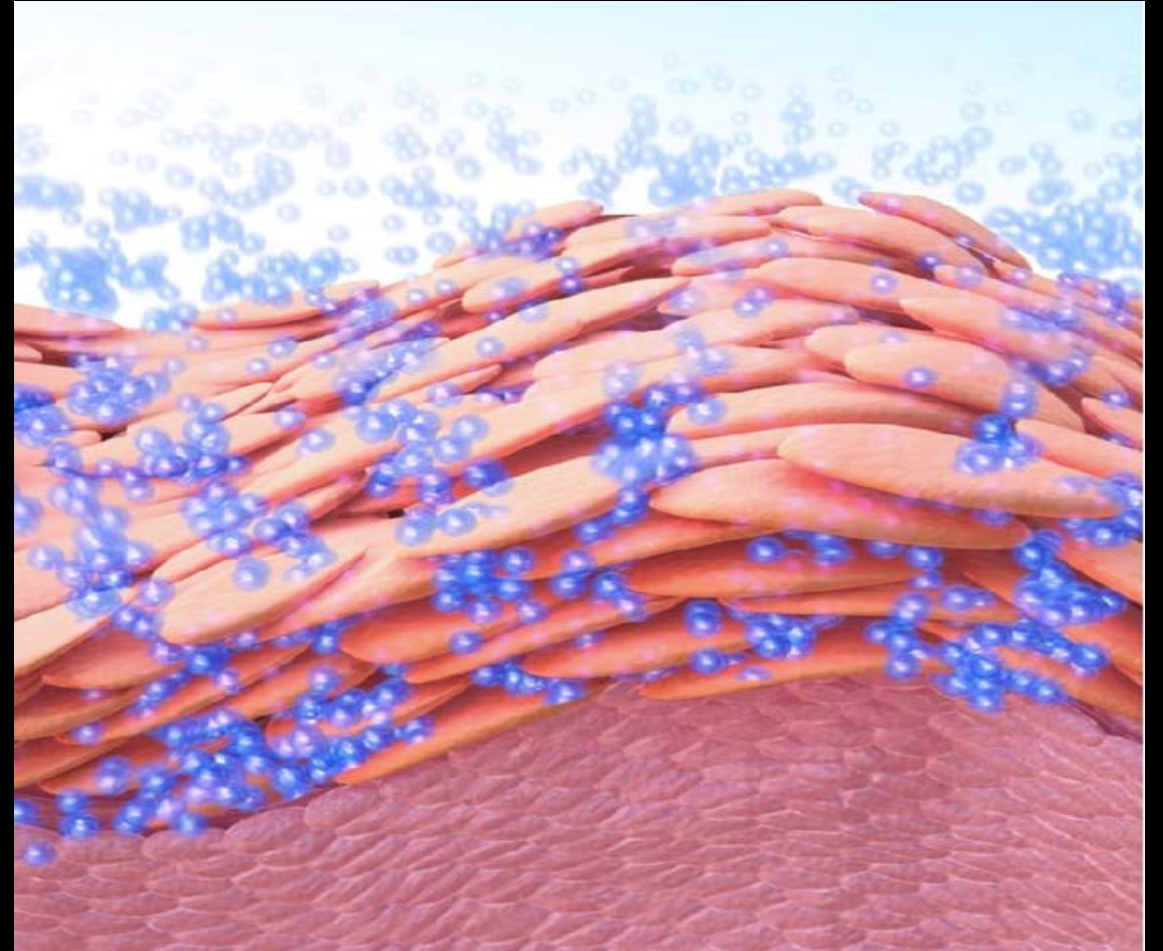
Severe Disease





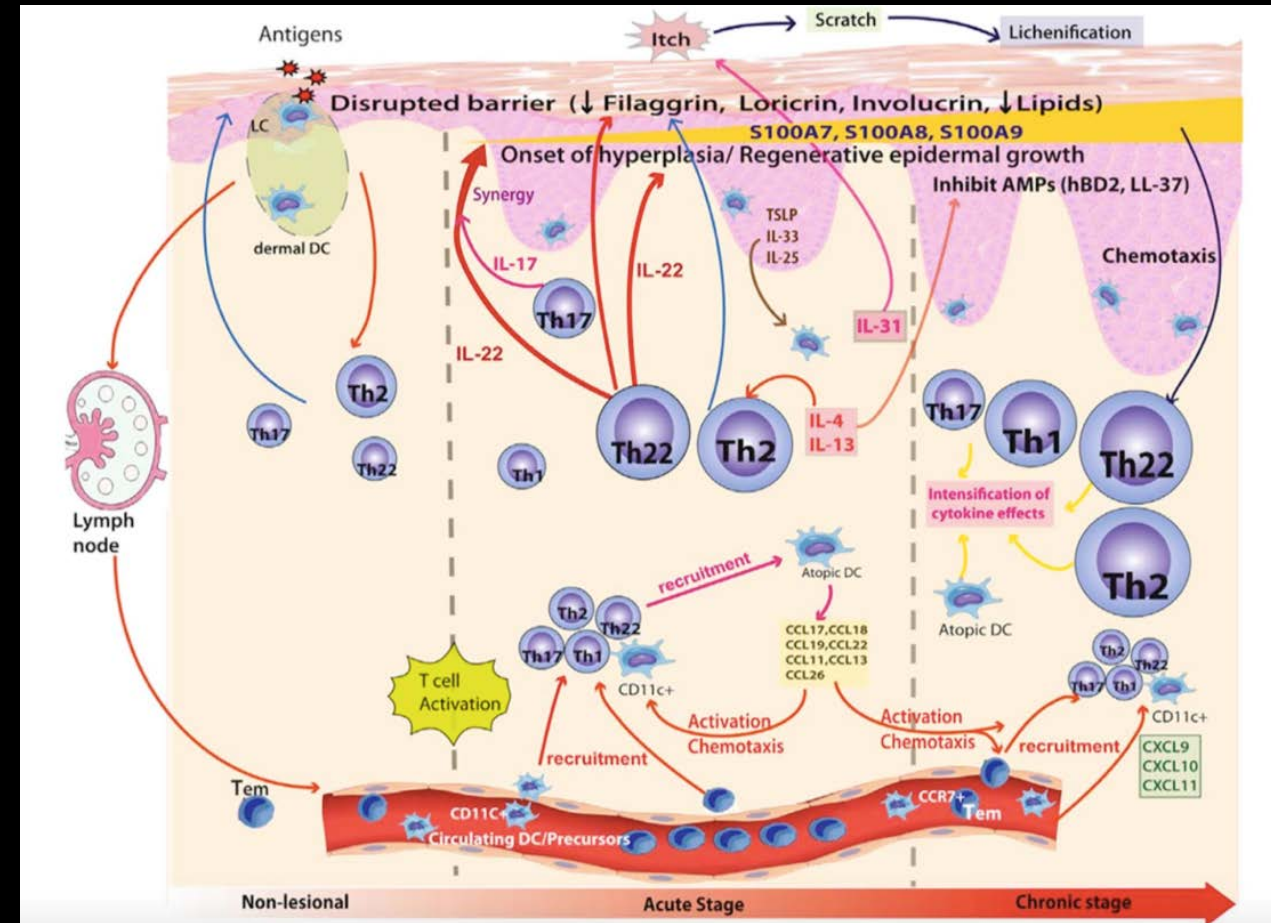


# Why? The Origin Story





## A photograph of a dense forest. A path, heavily covered with fallen tree roots and moss, leads into the distance. The trees are tall and slender, with thick green foliage forming a dense canopy overhead. The ground is covered in a layer of brown leaves and moss. The overall scene is lush and green, with sunlight filtering through the leaves.



# Skin barrier dysfunction measured by transepidermal water loss at 2 days and 2 months predates and predicts atopic dermatitis at 1 year

Maeve Kelleher, MB,<sup>a</sup> Audrey Dunn-Galvin, PhD,<sup>a</sup> Jonathan O'B. Hourihane, DM,<sup>a,b</sup> Deirdre Murray, MD,<sup>a,b</sup>  
Linda E. Campbell, BSc,<sup>c</sup> W. H. Irwin McLean, DSc, FRS,<sup>c</sup> and Alan D. Irvine, MD<sup>b,d,e</sup> *Cork and Dublin, Ireland, and Dundee, United Kingdom*

Journal of Allergy and Clinical Immunology

Volume 135, Issue 4, April 2015, Pages 930–935.e1

1903 infants



2 days old

2 months old





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Clinically Evaluate for Atopic Dermatitis  
at...

6 months old 12 months old

1903 infants



# Skin barrier dysfunction measured by transepidermal water loss at 2 days and 2 months predates and predicts atopic dermatitis at 1 year

Maeve Kelleher, MB,<sup>a</sup> Audrey Dunn-Galvin, PhD,<sup>a</sup> Jonathan O'B. Hourihane, DM,<sup>a,b</sup> Deirdre Murray, MD,<sup>a,b</sup> Linda E. Campbell, BSc,<sup>c</sup> W. H. Irwin McLean, DSc, FRS,<sup>c</sup> and Alan D. Irvine, MD<sup>b,d,e</sup> *Cork and Dublin, Ireland, and Dundee, United Kingdom*

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High TEWL at 2 days old → 7 times greater risk of AD at 1yo

*Controlling for filagrin status, parental h/o AD*

**TABLE V.** LR model for factors at birth influencing AD at 12 months

		OR, CI (P value)
TEWL birth percentiles		
25th (5.0 g <sub>water</sub> /m <sup>2</sup> /h)	—	—
50th (7.0 g <sub>water</sub> /m <sup>2</sup> /h)	—	3.2; 0.9-15.0 (.07)
75th (9.0 g <sub>water</sub> /m <sup>2</sup> /h)	—	7.1; 1.8-12.9 (.001)



When... will this be over?



# Will my infant outgrow their eczema?

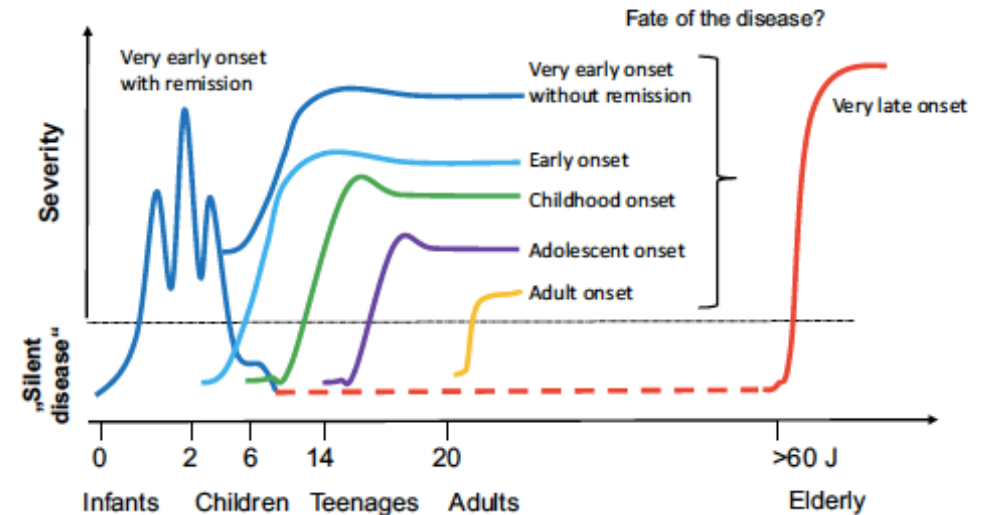
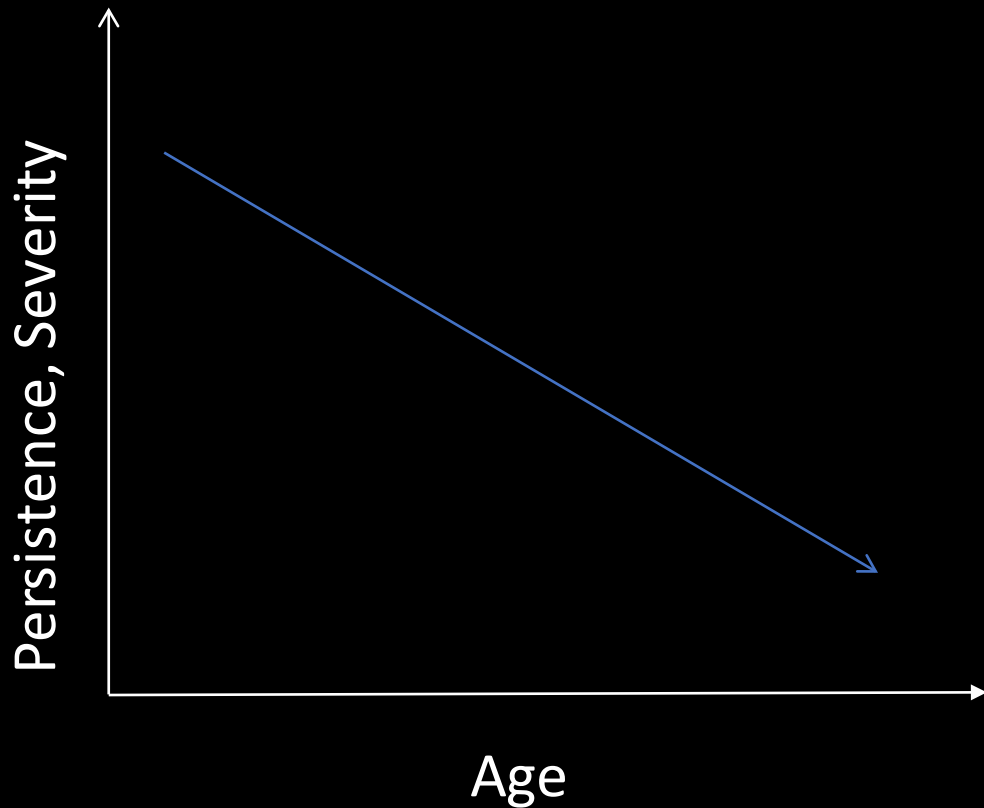


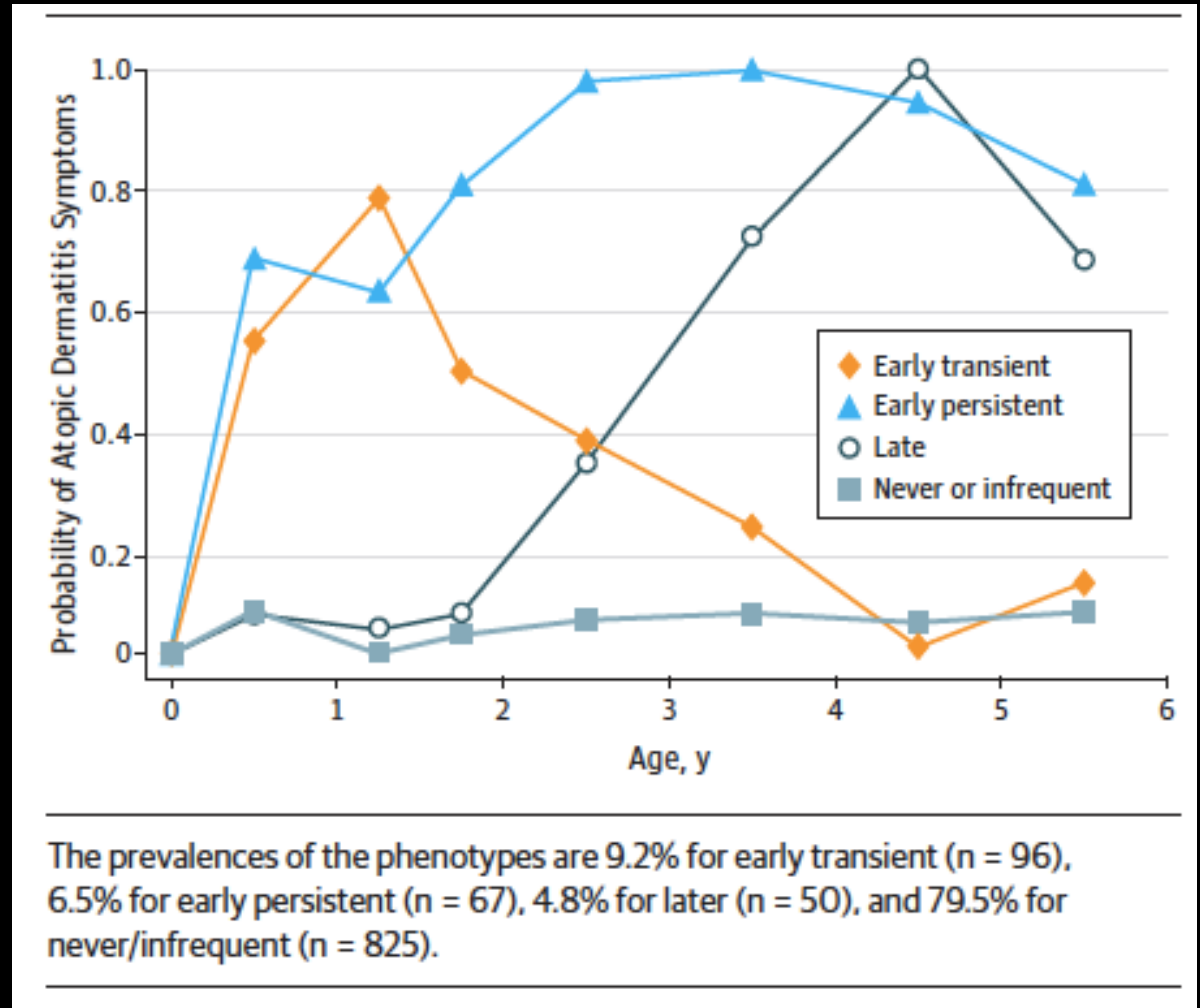
FIG 2. Clinical phenotype: stratification according to age of onset. *Curves indicate age of onset and possible natural histories (based on Garmhausen et al<sup>9</sup>).*

# Atopic Dermatitis Childhood Phenotypes

Onset < 2 year old

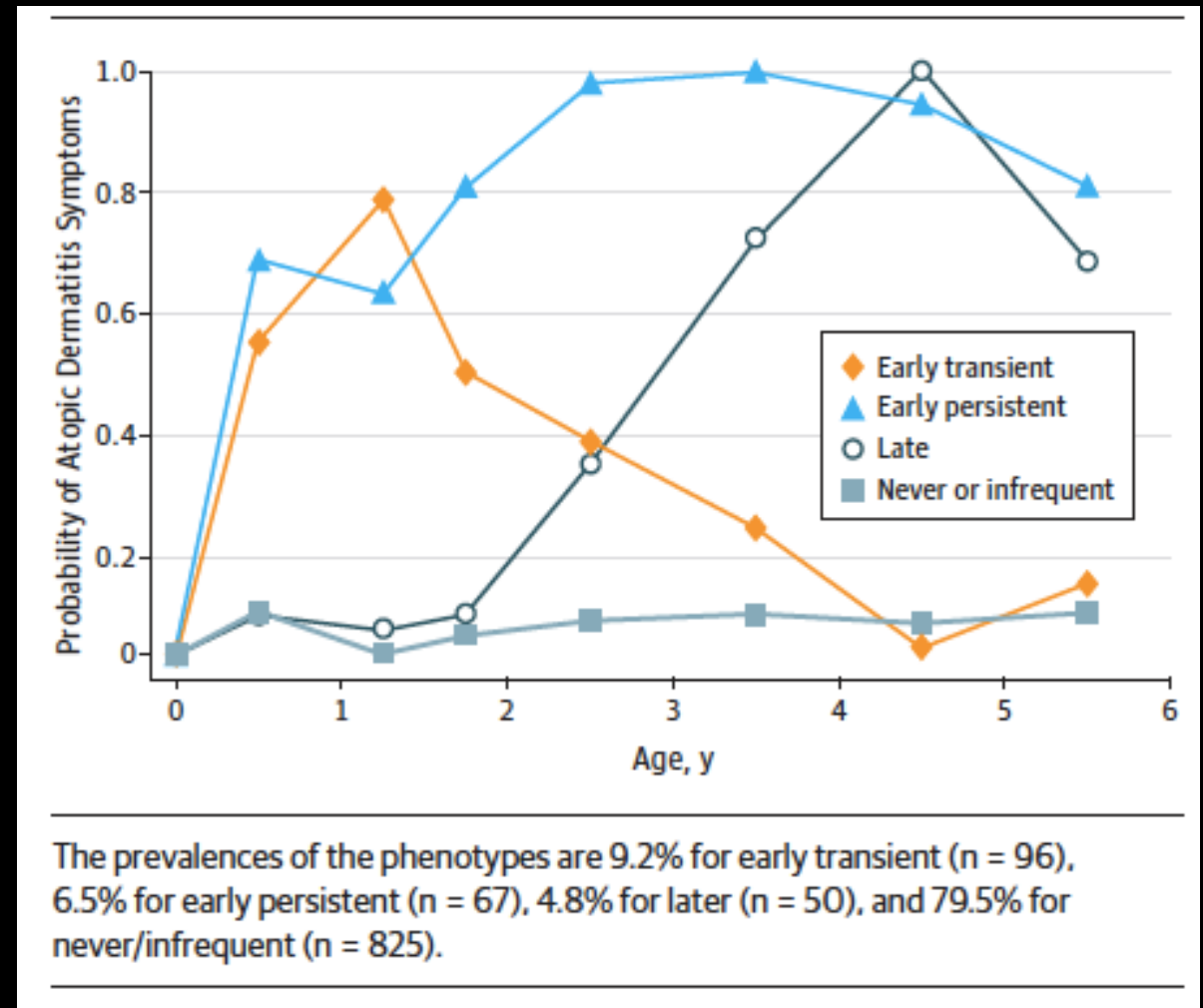
- Early transient (AD gone by 4 year)
- Early persistent

Late onset: > 2yo



# Atopic Dermatitis Childhood Phenotypes

- Early onset associated with asthma, food allergy
- Early persistent phenotype
  - Both parents with atopy
  - Disease severity





# Risk factors for persistence

- Older than 4 years old and had onset in infancy
- Parental history of atopy
- Disease severity



So... what foods do I avoid?



# “He is allergic to everything”



ALLERGENS		
ALLERGEN ALMONDS	0.80 *	▲
ALLERGEN BLUE MUSS...	<0.10 *	
ALLERGEN BRAZIL NUT	0.24 *	▲
ALLERGEN CODFISH IGE	<0.10 *	
ALLERGEN CRAB IGE	3.40 *	▲
ALLERGEN EGG WHITE...	5.98 *	▲
ALLERGEN HAZELNUT/...	1.60 *	▲
ALLERGEN OYSTER	<0.10 *	
ALLERGEN PEANUT	10.6 *	▲
ALLERGEN PISTACHIO	2.85 *	▲
ALLERGEN SCALLOP	0.32 *	▲
ALLERGEN SHRIMP IGE	3.88 *	▲
ALLERGEN SOYBEAN IGE	0.51 *	▲
ALLERGEN WALNUT	<0.10 *	
ALLERGEN WHEAT	0.37 *	▲
PECAN NUT, IGE	<0.10 *	
ALLERGEN CORN IGE	0.20 *	▲
ALLERGEN SESAME SE...	0.40 *	▲
ALLERGEN LOBSTER IGE	3.77 *	▲
ALLERGEN MILK IGE	6.56 *	▲
ALLERGEN SALMON IGE	<0.10 *	
ALLERGEN TUNA IGE	<0.10 *	
ALLERGEN CLAMS IGE	<0.10 *	
IMMUNOGLOBULIN E	419 *	▲

## American Academy of Dermatology

[View all recommendations from this society](#)

Released August 19, 2015

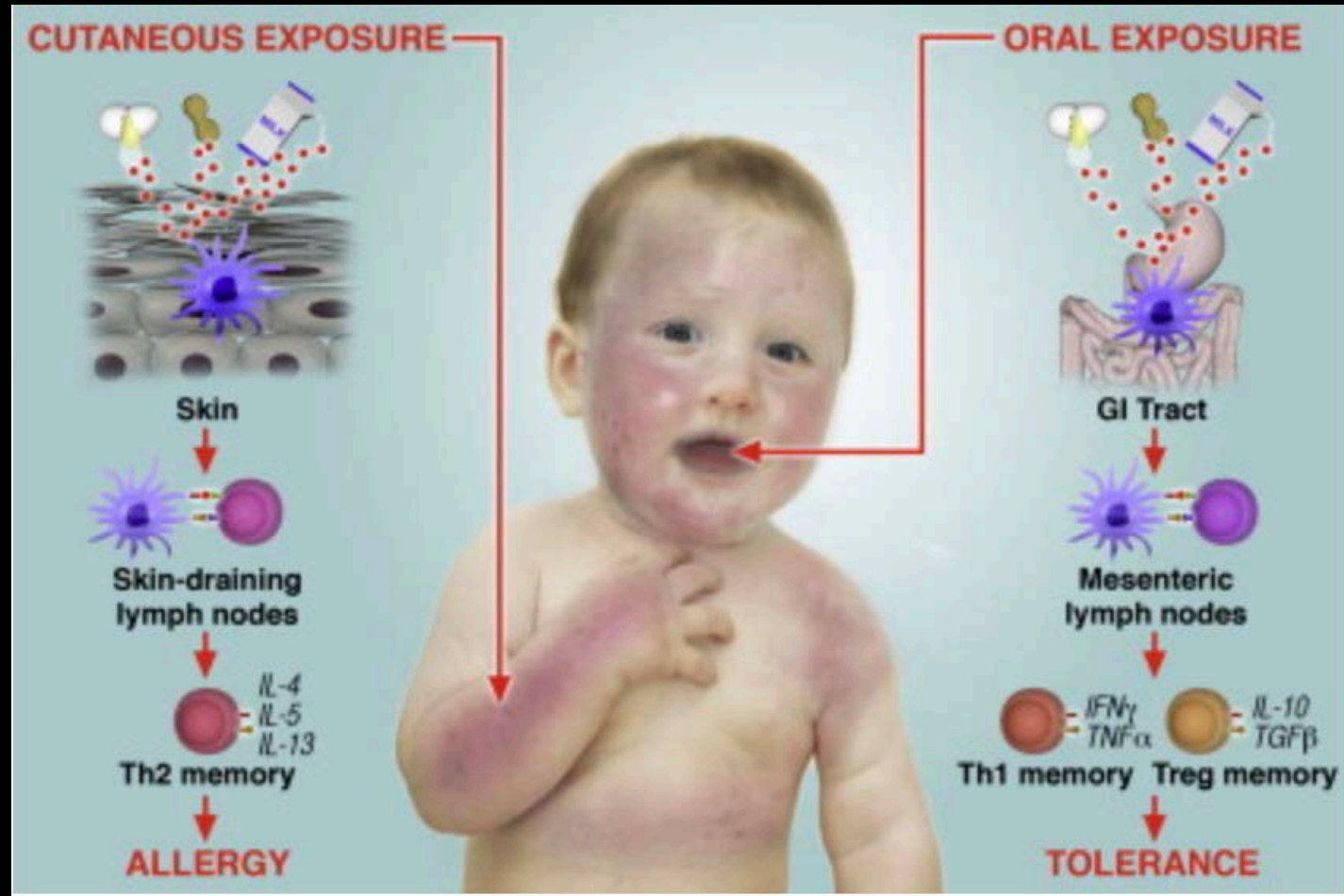
**Don't use skin prick tests or blood tests such as the radioallergosorbent test (RAST) for the routine evaluation of eczema.**

## American Academy of Allergy, Asthma & Immunology

Ten Things Physicians and Patients Should Question

**Don't perform food IgE testing without a history consistent with potential IgE-mediated food allergy.**

# Dual-Allergen-Exposure Hypothesis





# Risk of Elimination Diets

## Original Article

### Natural History of Food-Triggered Atopic Dermatitis and Development of Immediate Reactions in Children

Angela Chang, MD<sup>a</sup>, Rachel Robison, MD<sup>a,b</sup>, Miao Cai, MS<sup>a</sup>, and Anne Marie Singh, MD<sup>a,b,c</sup> *Chicago, Ill*

Retrospective review of 298 children with concerns for food triggered AD

19% of children with no prior reactions developed a type I reaction after elimination

**TABLE VI.** Twenty-five patients with food-triggered atopic dermatitis (AD) without a history of immediate reactions at the initial visit developed 31 new immediate reactions during follow-up

N	Food causing immediate reaction	Reaction severity	Average length of time to reaction	Percent food triggering AD
9	Cow's milk	4 Anaphylaxis 5 Cutaneous	1.0 y (SD 0.4 y)	7/9 (78%)
7	Egg	2 Anaphylaxis 5 Cutaneous	1.1 y (SD 0.8 y)	5/7 (71%)
5	Peanut	2 Anaphylaxis 3 Cutaneous	2.4 y (SD 1.4 y)	2/5 (40%)
10	Other	1 Anaphylaxis 9 Cutaneous	1.7 y (SD 0.6 y)	2/10 (20%)

# Diet and Atopic Dermatitis

- “Eat, eat, eat...”
  - Goal is to keep food in the diet
- No role for empiric elimination diets
- DO NOT send “screening” RAS allergy panels

Education

Topical Management

Severe Disease

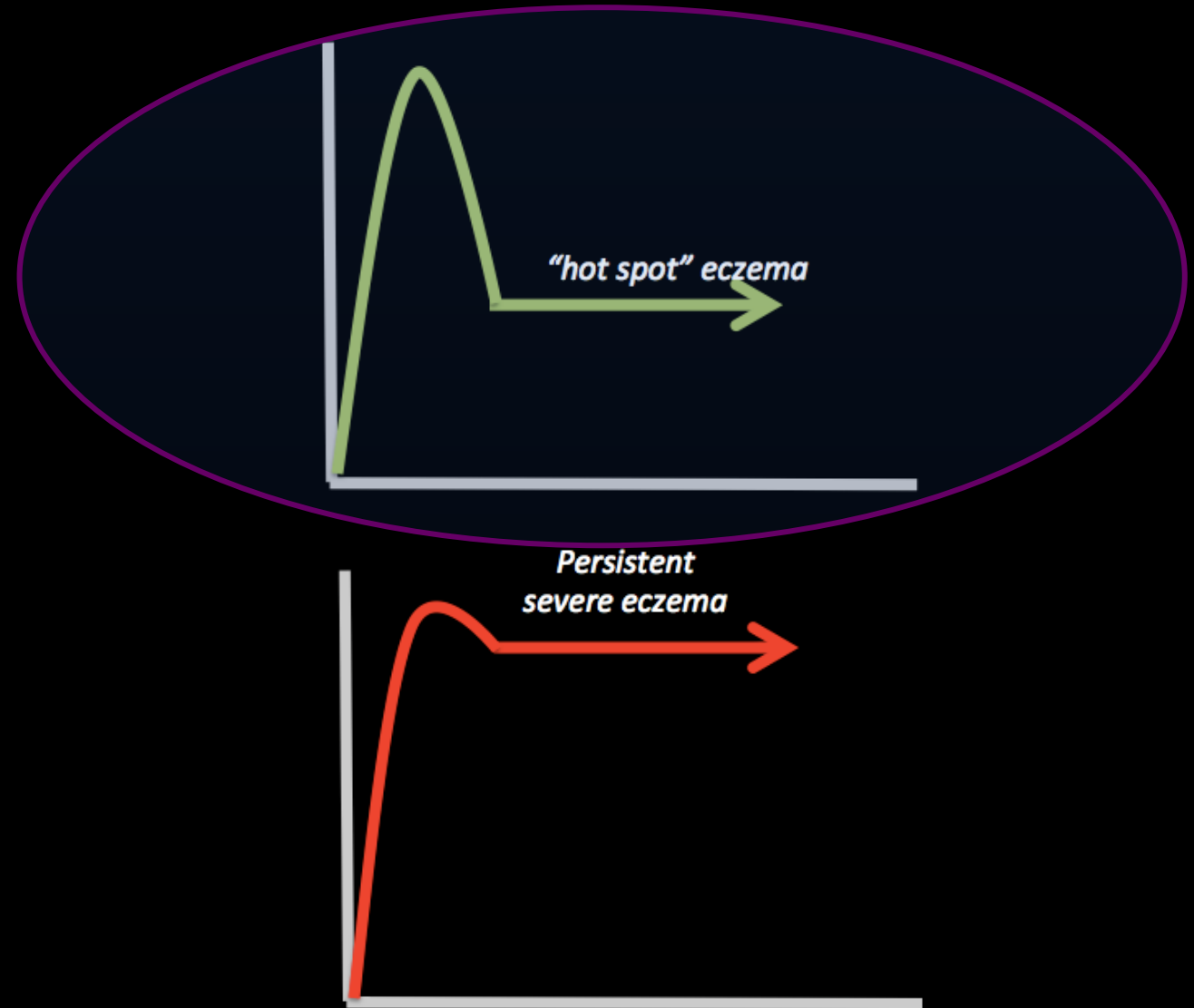


# Apply sparingly up to 5 days

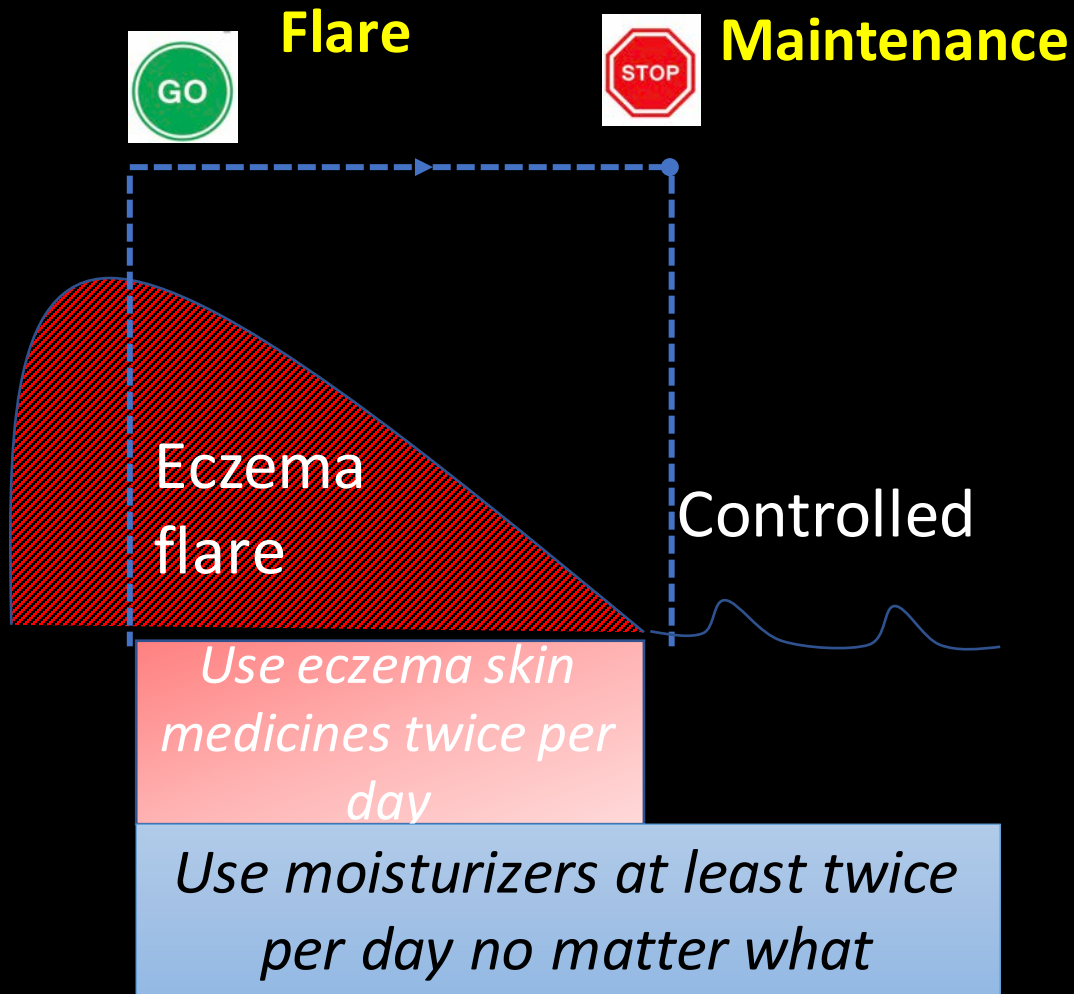




# Intermittent versus Persistent Atopic Dermatitis



# Getting over the “hump”



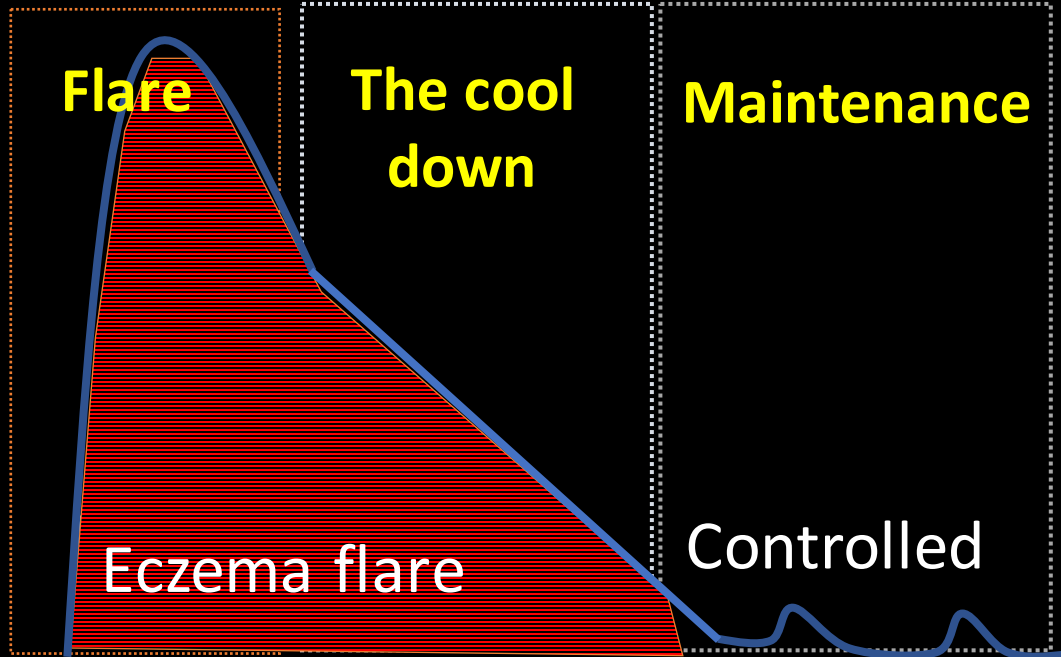
Phase 1: Flare – till clear + 2-3 days

- < 2yo: Triamcinolone 0.025% oint
- > 2yo: Triamcinolone 0.1% oint

Phase 2: Maintenance

- Aggressive emollient use
- Avoidance of triggers

# Getting over the “hump” 2.0



*Use moisturizers at least twice per day no matter what*

Phase 1: x 1-2 weeks

- < 2yo: Triamcinolone 0.025% oint
- > 2yo: Triamcinolone 0.1% oint

Phase 2: The cool down

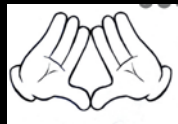
- Use above medicines every other day

Phase 3: Maintenance to “Hot spots”

- Medium TCS on weekends
- Eucrisa daily
- Tacrolimus or Pimecrolimus daily → 2-3 times per week

# Topical Steroid Strengths

Severe Hands +  
Feet



1

Clobetasol

Trunk

2

Fluocinonide (Lidex);  
Mometasone ointment

3

Triamcinolone 0.1% ointment  
Fluticasone ointment

4-5

Triamcinolone 0.025% ointment

6

Desonide; Fluocinolone (Dermasmooth) oil

7

Hydrocortisone 2.5%, 1%

Ruxolitinib 1.5% cream

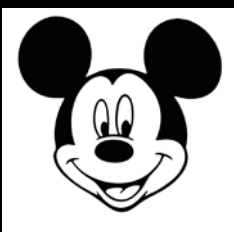
Protopic 0.1% ointment

Protopic 0.03% ointment

Pimecrolimus 1% cream  
Eucrisa

Therapeutics

Face + Groin





# Steroid Phobia



Topical Steroids as “Restorative”

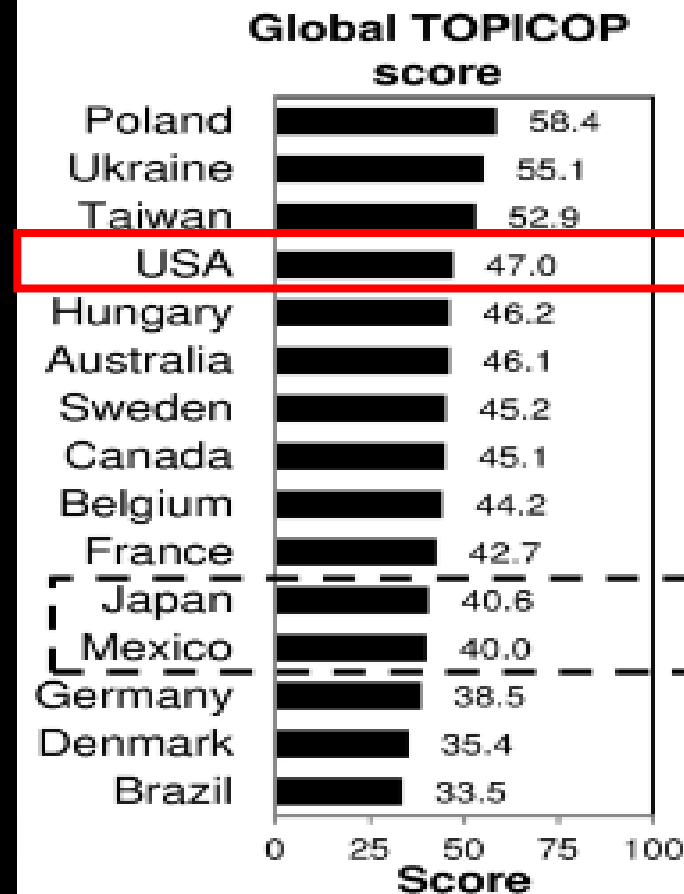


# Topical corticosteroid phobia in atopic dermatitis: International feasibility study of the TOPICOP score

TOPICOP: 1<sup>st</sup> validated TCS phobia survey

- 12 item questionnaire
- Assessed in 17 countries
- 80% of responders for patients <18yo

44% of patients endorse corticophobia



# The Effect of Topical Steroids on Growth and the Immune System

## Safety and Efficacy of Pimecrolimus in Atopic Dermatitis: A 5-Year Randomized Trial

Bardur Sigurgeirsson, Andrzej Boznanski, Gail Todd, André Vertruyen, Marie-Louise A. Schuttelaar, Xuejun Zhu, Uwe Schauer, Paul Qaqundah, Yves Poulin, Sigurdur Kristjansson, Andrea von Berg, Antonio Nieto, Mark Boguniewicz, Amy S. Paller, Rada Dakovic, Johannes Ring, Thomas Luger

**PEDIATRICS**  
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

## PETITE Study over a 5 year period

Pimecrolimus

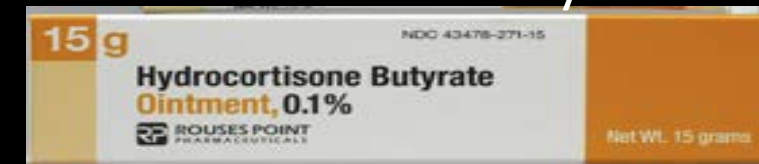
Topical Steroid

Medium Potency

Sample: 2418 infants 3-12 month



VS

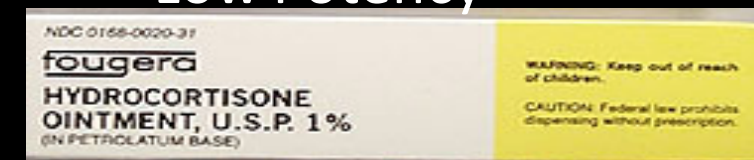


+

Topical steroid for  
breakthrough flares

or

Low Potency



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## PETITE Study over a 5 year period

Immune development measured:

- B cell (Immunoglobulins; Antibody titers to vaccine)
- T cell (Lymphocyte subset, T cell function testing)

	Growth Parameters	Immune development
Pimecrolimus	Normal	Normal
Topical Steroid	Normal	Normal



# Skin Atrophy and Topical Steroids?

Trial	Sample Size	AD Severity	Duration (wk)	Medication	Plan	Atrophy
Low Potency (Class 6-7)						
Thomas 2002	104	Mild-Mod	18	Hydrortisone ointment 1%	7 day bursts "when required"	4 cases
Jorizzo 1995	36	Mild-Mod	25	Hydrortisone ointment 1% vs Desonide ointment	BID	No cases
Mid Potency (3-5)						
Thomas 2002	103	Mild-Mod	18	Betamethasone valerate 0.1%	BID x 3 days alternate with vehicle BID x 4 days	7 cases
Hanifin 2002	154	Mod-Severe	44	Fluticasone cream	Flare: BID x 4 wks Maintenance: QD x 2 days per wk	No cases

# Molecular signatures order the potency of topically applied anti-inflammatory drugs in patients with atopic dermatitis

Emma Guttman-Yassky, MD, PhD,<sup>a,b,c</sup> Benjamin Ungar, BA,<sup>a</sup> Kunal Malik, BA,<sup>a</sup> Daniel Dickstein, BA,<sup>a</sup> Maria Suprun, MPH,<sup>d</sup> Yeriel D. Estrada, BS,<sup>a</sup> Hui Xu, MSc,<sup>a</sup> Xiangyu Peng, MSc,<sup>a</sup> Margeaux Oliva, BA,<sup>a</sup> Dan Todd, MSc,<sup>e</sup> Tord Labuda, PhD,<sup>e</sup> Mayte Suarez-Farinas, PhD,<sup>d,f,g</sup> and Robert Bissonnette, MD<sup>h</sup> *New York, NY, Ballerup, Denmark, and Montreal, Quebec, Canada*

Journal of Allergy and Clinical Immunology

Sample: 30 adult patients with atopic dermatitis

Vehicle



Pimecrolimus 1%



Betamethasone

dipropionate 0.05%



Clobetasol oint



Daily Application  
x 14 days



Day 15

TEWL

+

Skin Bx Lesional  
+Non-Lesional

# Molecular signatures order the potency of topically applied anti-inflammatory drugs in patients with atopic dermatitis

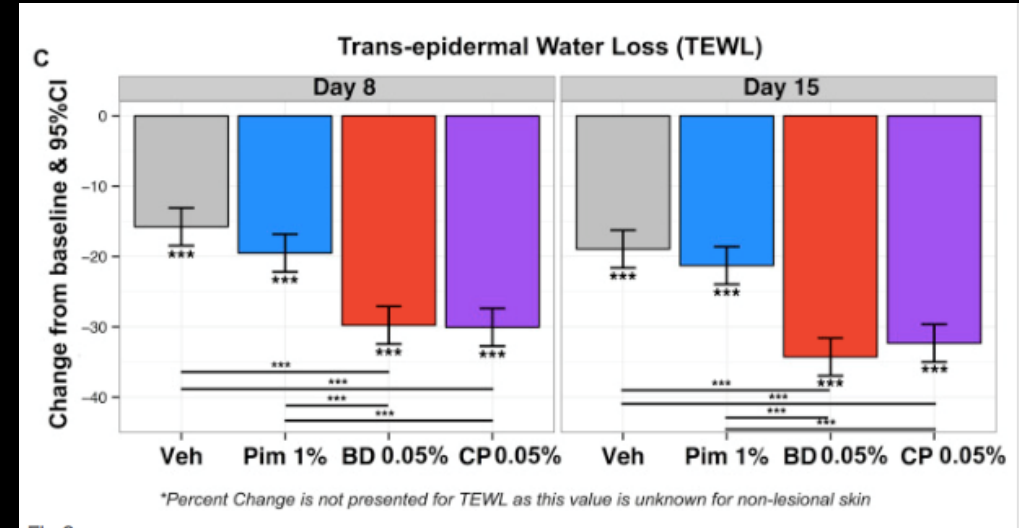
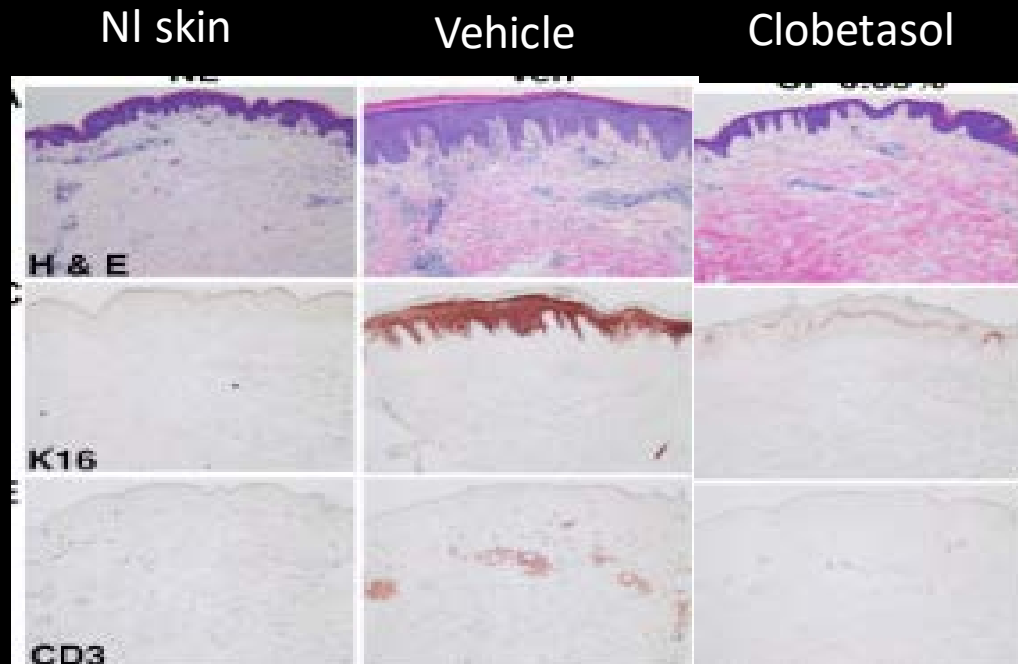
Emma Guttman-Yassky, MD, PhD,<sup>a,b,c</sup> Benjamin Ungar, BA,<sup>a</sup> Kunal Malik, BA,<sup>a</sup> Daniel Dickstein, BA,<sup>a</sup> Maria Suprun, MPH,<sup>d</sup> Yeriel D. Estrada, BS,<sup>a</sup> Hui Xu, MSc,<sup>a</sup> Xiangyu Peng, MSc,<sup>a</sup> Margeaux Oliva, BA,<sup>a</sup> Dan Todd, MSc,<sup>e</sup> Tord Labuda, PhD,<sup>e</sup> Mayte Suarez-Farinas, PhD,<sup>d,f,g</sup> and Robert Bissonnette, MD<sup>h</sup> *New York, NY, Ballerup, Denmark, and Montreal, Quebec, Canada*

Journal of Allergy and Clinical Immunology

Day 15: epidermal hyperplasia and infiltrates normalize with steroids

Significant improvement in skin barrier with steroids

- Increased production of loricrin, periplakin, filaggrin

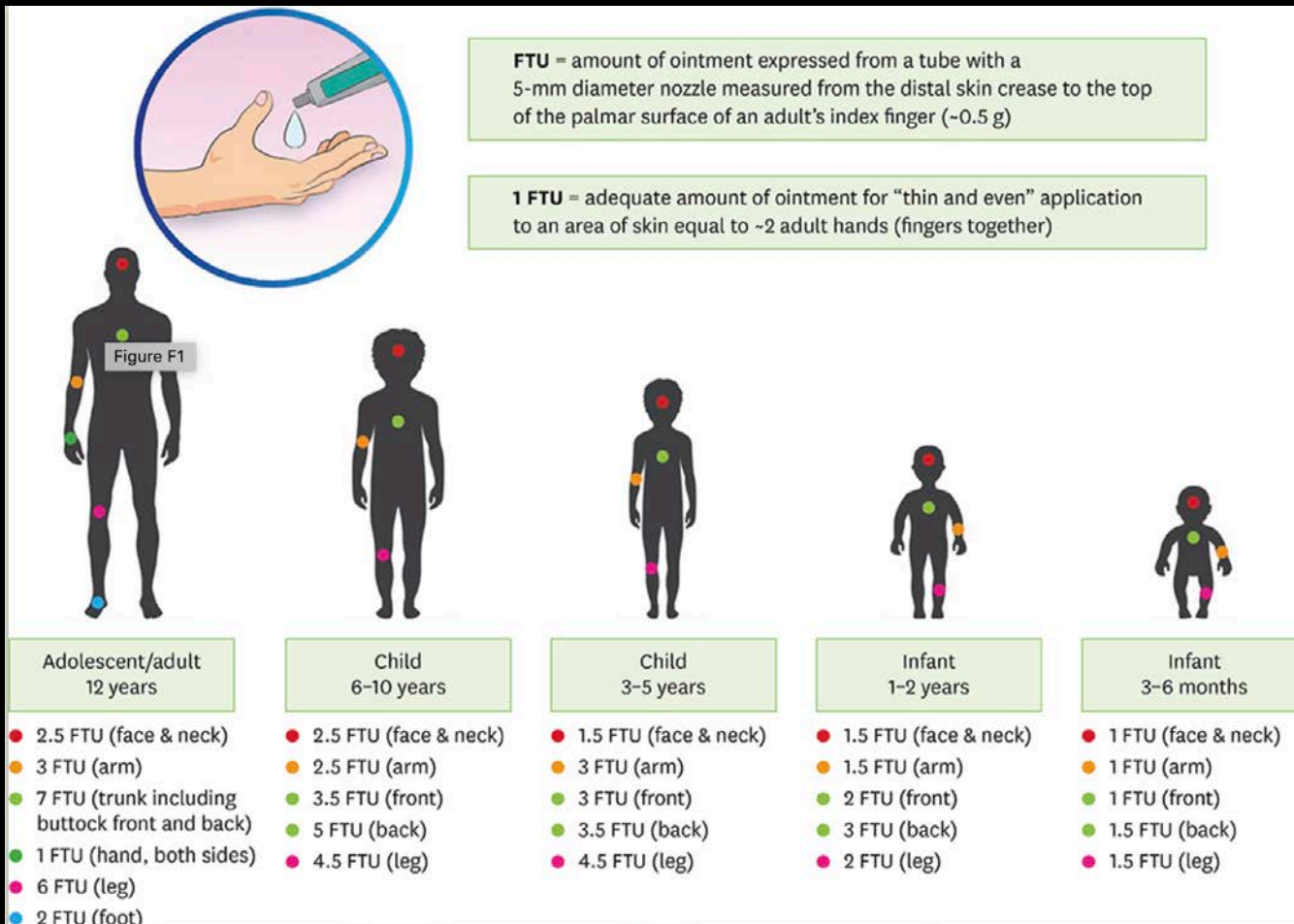


# “Not getting better” checklist

- ☐ Review possible triggers and eczema safe skin care products
- ☐ Review gentle skin care fundamentals
- ☐ How much are they actually applying
- ☐ Consider a possible allergic contact dermatitis



# Prescription Quantity



## Grams need for BID use for 1 week

Age	100% BSA	10% BSA
3-6mo	60g	6g
1-2yo	95g	9g
3-5yo	125g	13g
6-10yo	170g	17g
>12yo	235g	24g

# Atopic topical medication pointers

- Treat till clear and then for 3-5 days more
- Once daily application may be as effective as twice daily
- Set an expectation of maintenance
- Prescribe a sufficient amount

Education

Topical Management

Severe Disease



# How many children have moderate-severe atopic dermatitis?

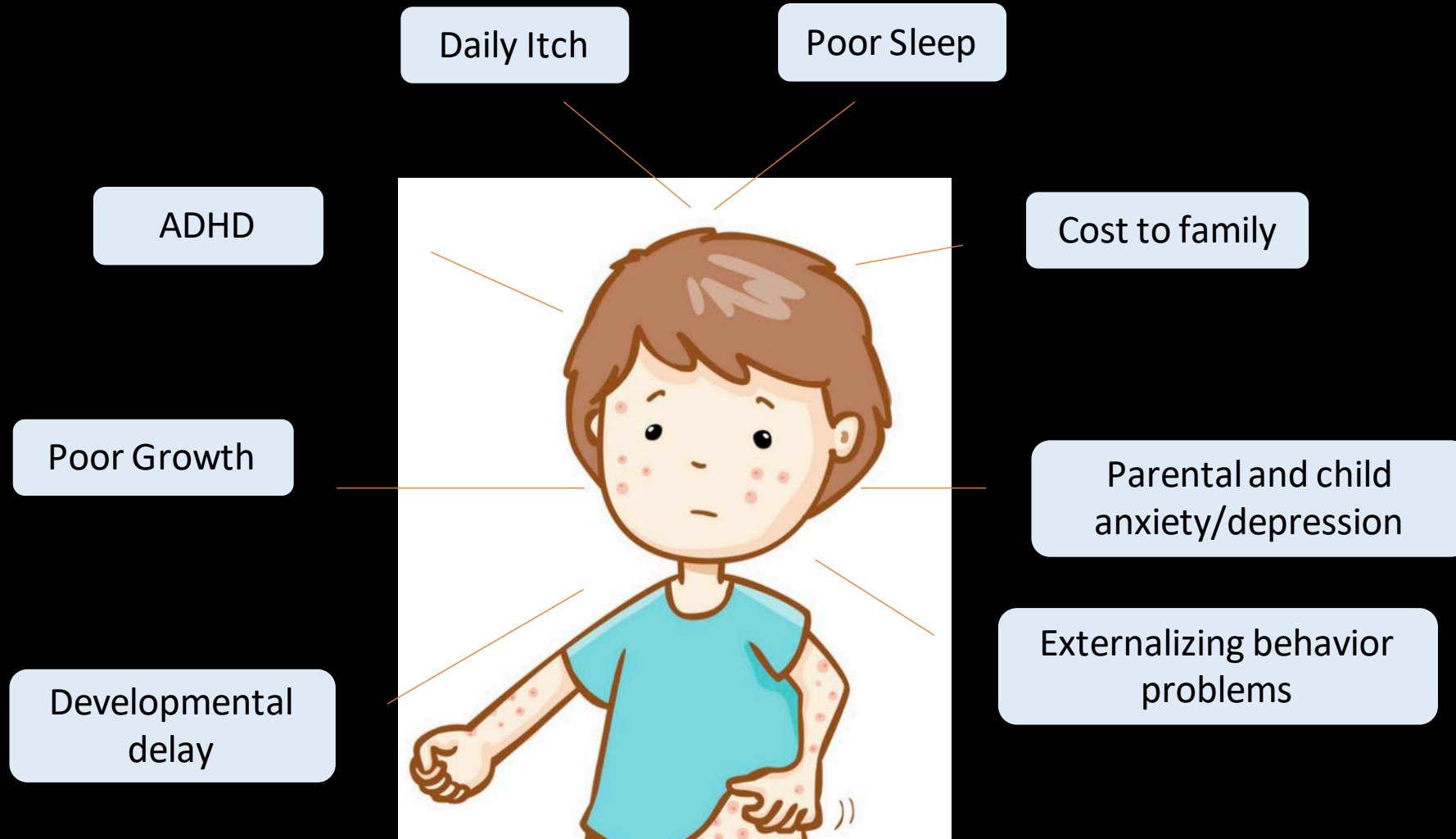
Moderate atopic dermatitis: 26%  
Severe atopic dermatitis: 7%



5 million children with at least severe disease



# Uncontrolled eczema effects a child's quality of life

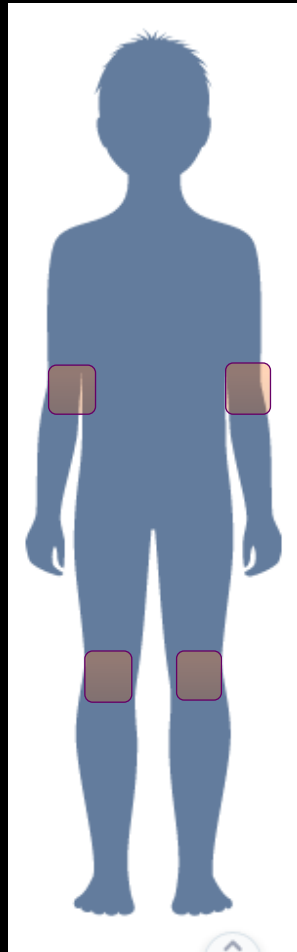


# Nonlesional skin in atopic dermatitis is not normal

Staph aureus  
colonization

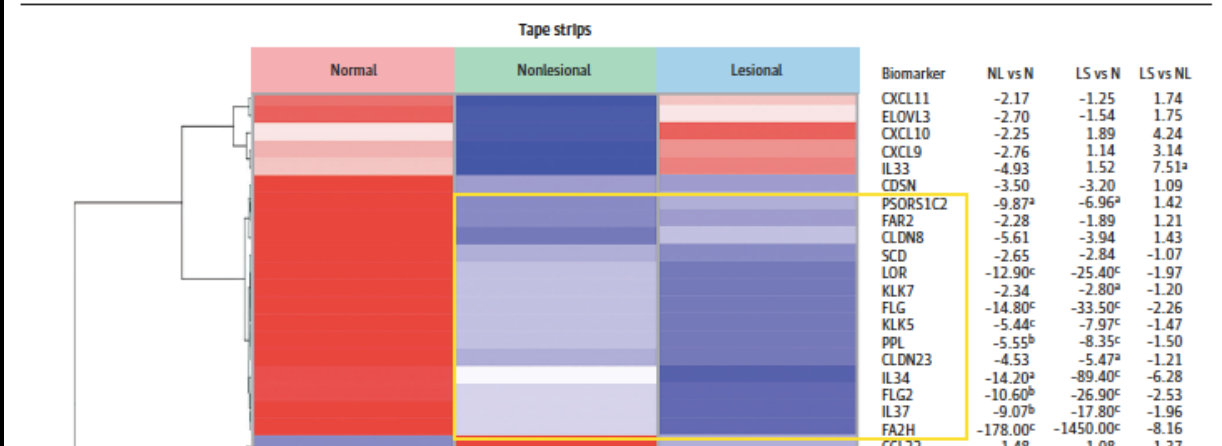
Lesional: 70-  
90%

Nonlesional:  
40%

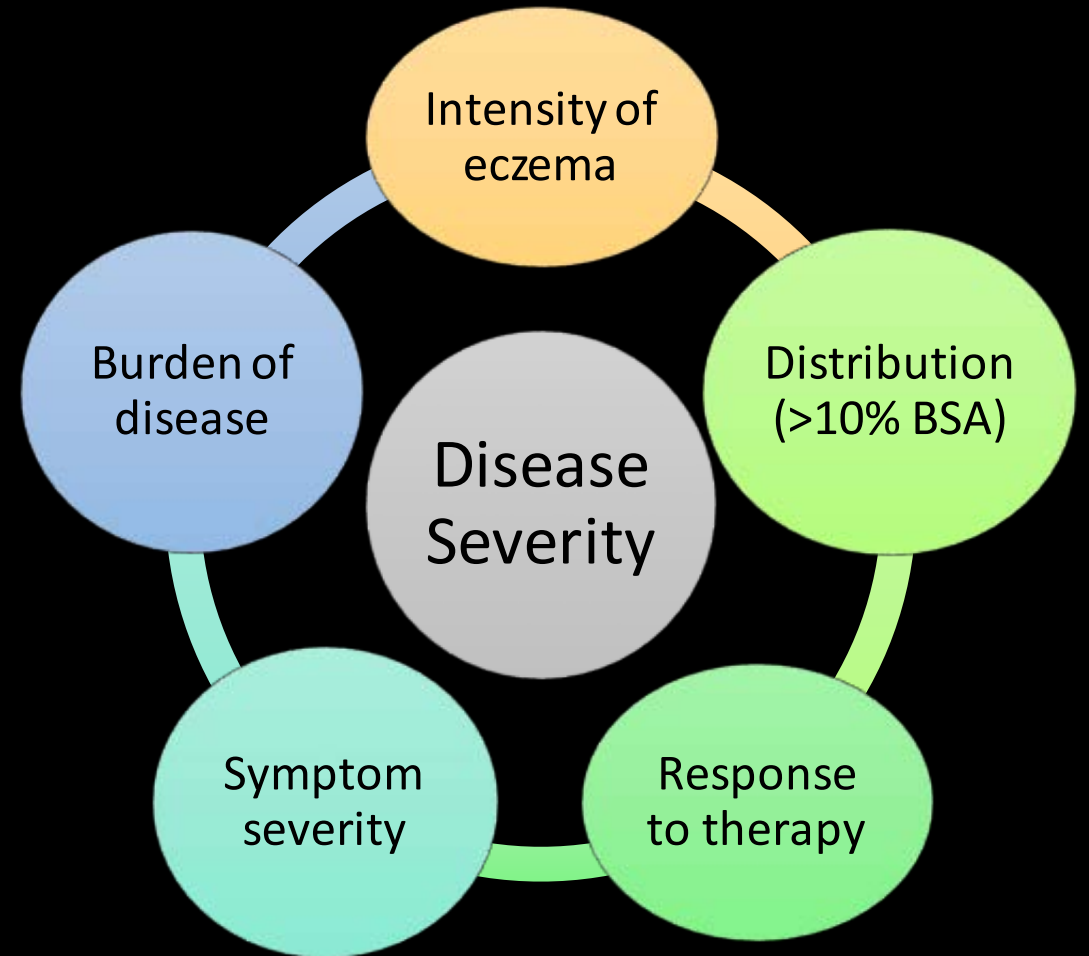


Abnormal inflammatory and barrier  
biomarkers in nonlesional skin in young  
children with atopic dermatitis

Figure 3. Heat Map of Immune and Barrier Atopic Dermatitis (AD) Biomarkers Detected in Tape Strips



# Assessing Disease Severity



# Systemic Therapies for Childhood Atopic Dermatitis

## Old School

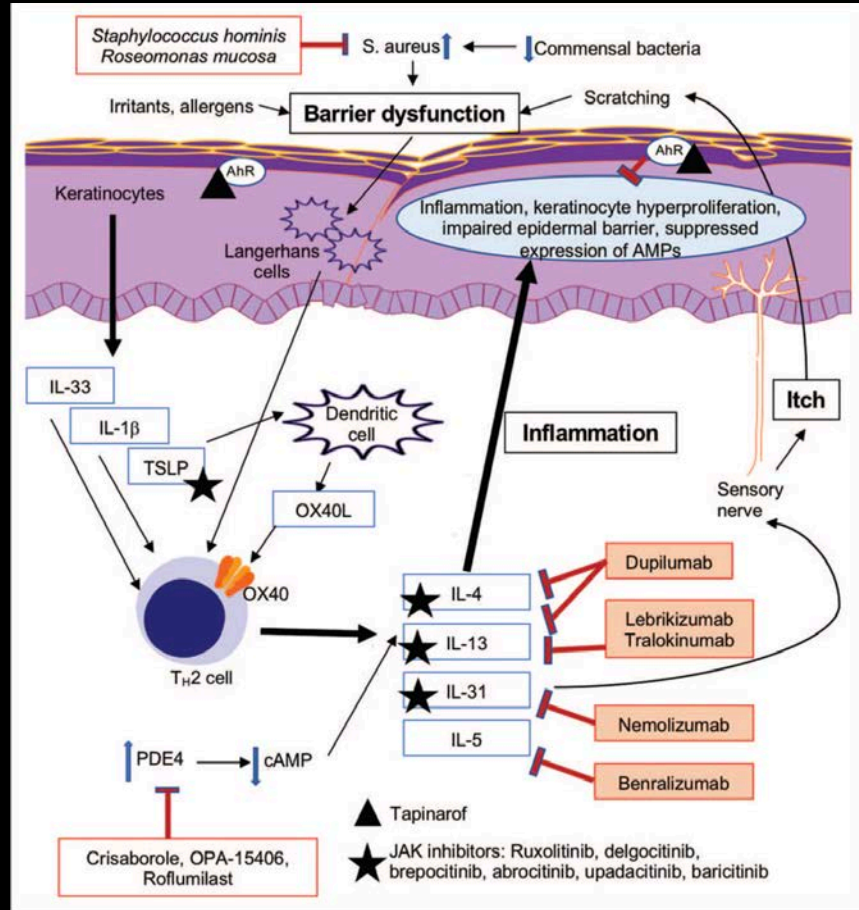
- Narrow Band UV-B therapy
- Cyclosporine
- Methotrexate
  
- Mycophenolate mofetil

## New School

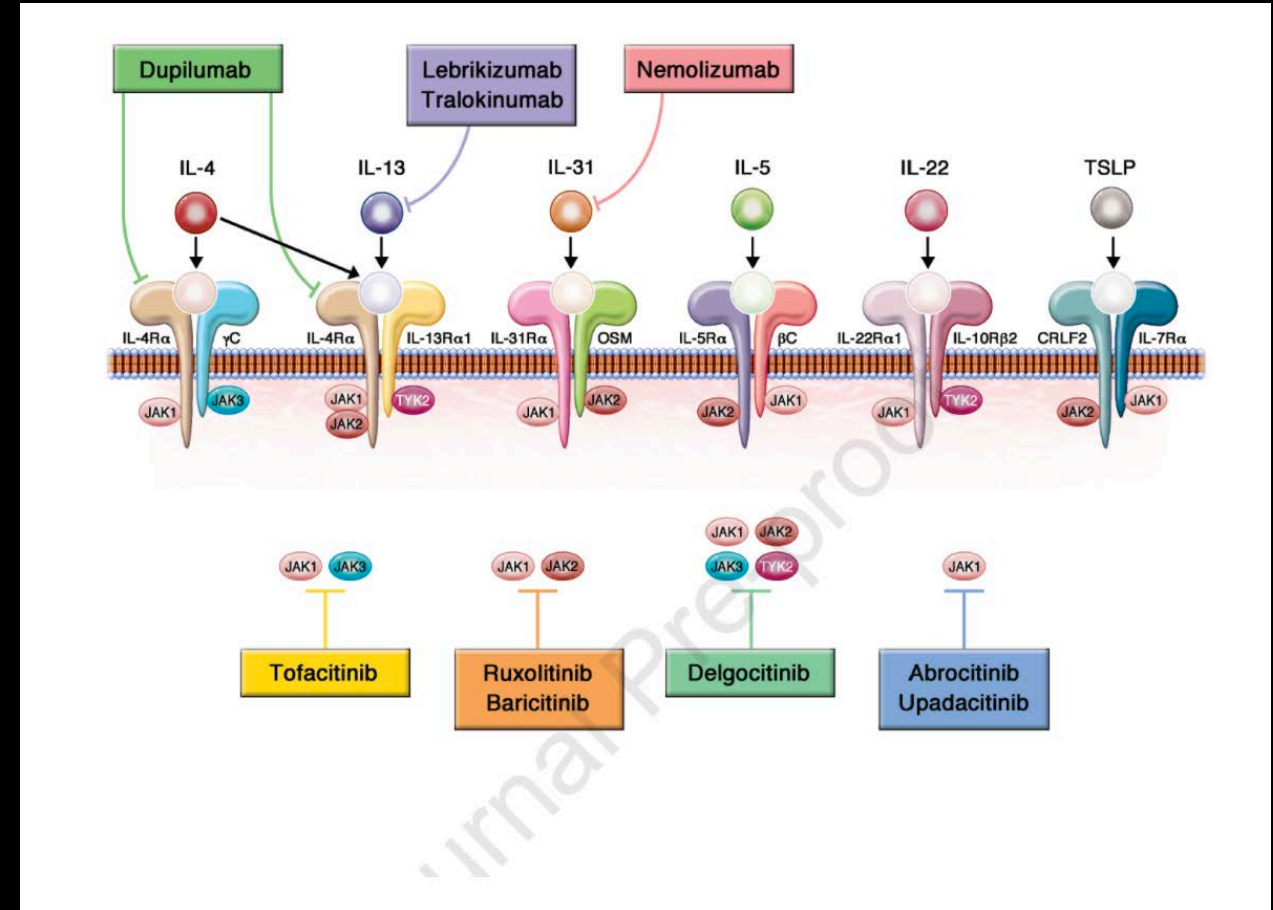
- Dupilumab
- Systemic JAK inhibitors
  - Upadactinib

# Atopic Dermatitis Drug Targets

## Cytokine Targets



## Downstream JAK/Stat Blockade





# Dupilumab Pediatric Indications

**Atopic dermatitis (mod-severe)**  
6 mo+

**Asthma (mod-severe)**  
12yo+

**Eosinophilic Esophagitis**  
12yo+



# Dupilumab Efficacy: 30-40% are clear to almost clear

Before



In 2 months

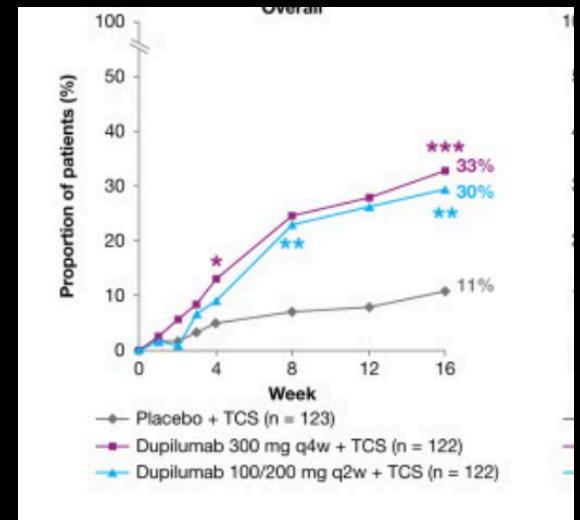
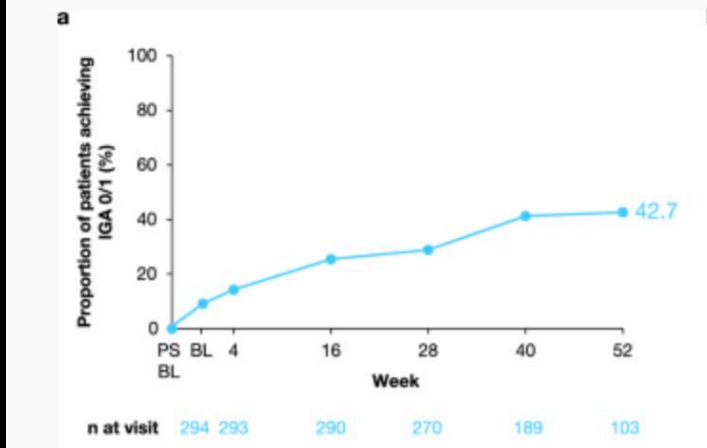


12-18 year olds

6-12 year olds

43% clear to almost clear at 1 year 33% clear to almost clear at 4

**Fig. 3**



# Dupilumab: What Pediatricians Should Know

- No routine lab monitoring is needed
- Side effects
- No live virus vaccines

Conjunctivitis  
5-10%



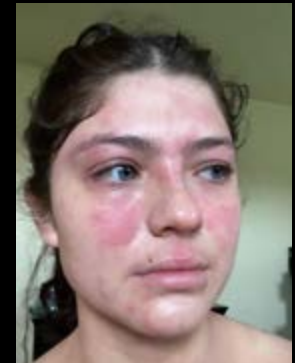
Needle  
phobia/anxiety



Injection site reaction  
5-10%



Head and neck dermatitis  
?



# Upadacitinib approved for >12yo moderate-severe AD

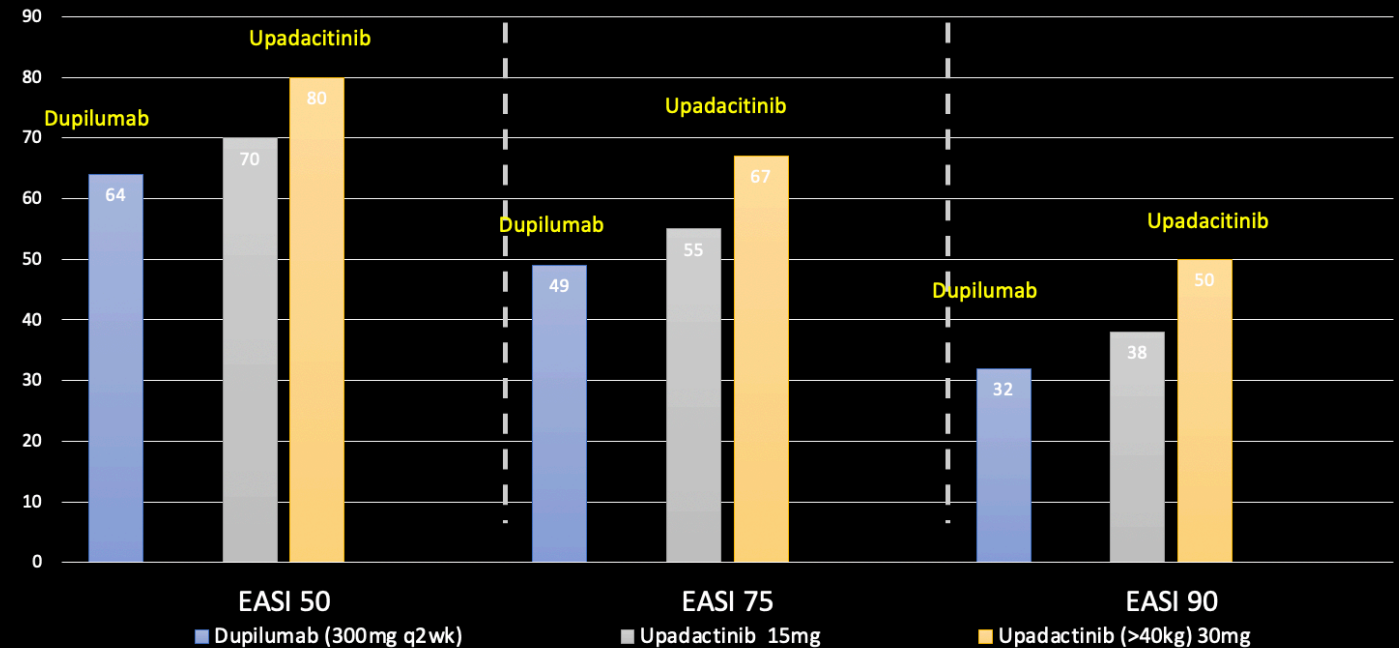
## DISRUPT

**the itch and rash of eczema with  
a once-daily pill**

Available in 15 mg or 30 mg tablets. Your doctor will  
prescribe the right dose.



*Upadacitinib achieve slightly higher improvement*



## Upadacitinib black box warning



### **WARNING: SERIOUS INFECTIONS, MALIGNANCY, AND THROMBOSIS**

*See full prescribing information for complete boxed warning.*

- Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving RINVOQ. (5.1)
- If a serious infection develops, interrupt RINVOQ until the infection is controlled. (5.1)
- Prior to starting RINVOQ, perform a test for latent tuberculosis; if it is positive, start treatment for tuberculosis prior to starting RINVOQ. (5.1)
- Monitor all patients for active tuberculosis during treatment, even if the initial latent tuberculosis test is negative. (5.1)
- Lymphoma and other malignancies have been observed in patients treated with RINVOQ. (5.2)
- Thrombosis, including deep vein thrombosis, pulmonary embolism, and arterial thrombosis, have occurred in patients treated with Janus kinase inhibitors used to treat inflammatory conditions. (5.3)



# Weighing the risks of systemic JAK inhibitors

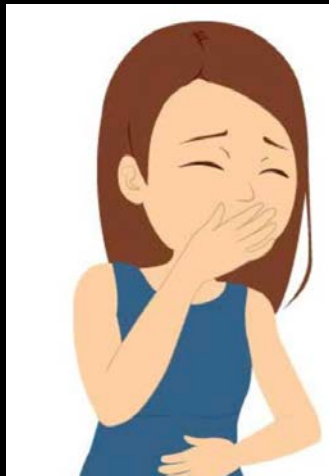
Acne  
~ 5-18%



Herpetic infections  
~5%



Nausea  
~5-20%



The NEW ENGLAND  
JOURNAL of MEDICINE

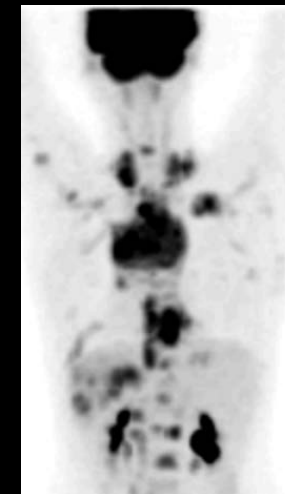
## Cardiovascular and Cancer Risk with Tofacitinib in Rheumatoid Arthritis

Steven R. Ytterberg, M.D., Deepak L. Bhatt, M.D., M.P.H., Ted R. Mikuls, M.D., M.S.P.H., Gary G. Koch, Ph.D., Roy Fleischmann, M.D., Jose L. Rivas, M.D., Rebecca Germino, Ph.D., Sujatha Menon, Ph.D., Yanhui Sun, Ph.D., Cunshan Wang, Ph.D., Andrea B. Shapiro, M.D., Keith S. Kanik, M.D., [et al.](#), for the ORAL Surveillance Investigators\*

Venous  
thromboembolism  
1.67



Cancer  
1.5



Major Cardiac  
Event  
1.2



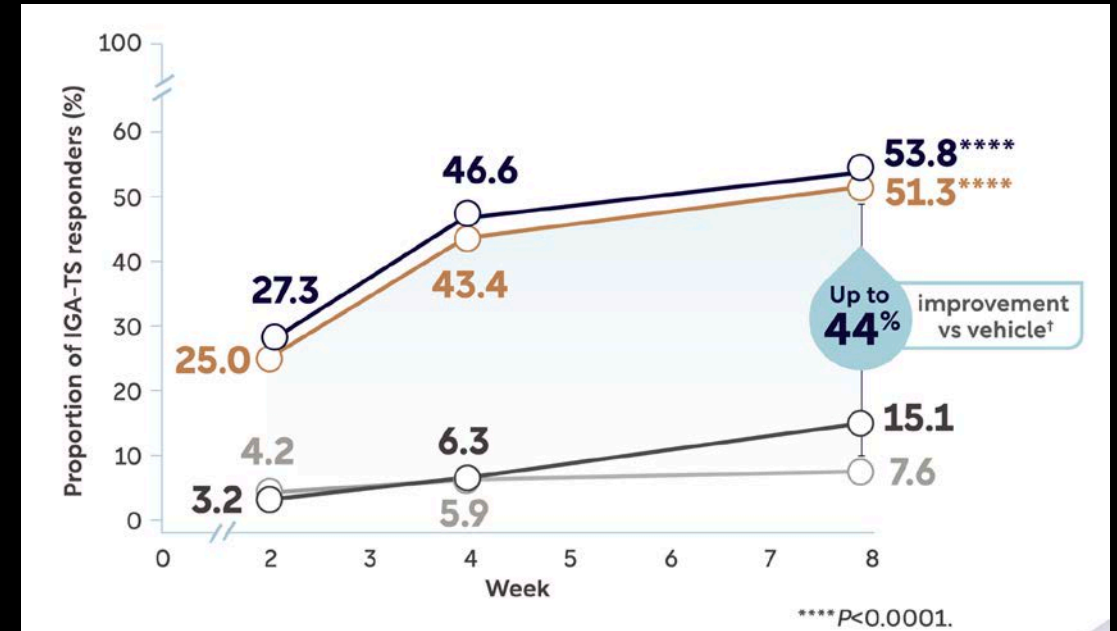
# Ruxolitinib 1.5% cream for >12 yo mild to moderate AD

Can't use on >20% body surface area

~ Half of patients were clear to almost clear by 8 weeks



60gram tube = \$2,000



# Conclusions

- Education is the foundation of atopic care
- Prescribe with confidence – make use of “controller” treatment plans
- Treatment for moderate to severe disease has been revolutionized

Thank you!





# Severe Eczema Flare Control with Wet Wraps



<2yo: Triamcinolone 0.025%  
>2yo: Triamcinolone 0.1%

## Wet Wraps

These steps will help your child's skin get better if they are having a bad "flare."



### 1. Wet Pajamas

- Put long sleeve pajamas (or other clothing you are using for a wet wrap) in a sink and fill with warm water.
- Get pajamas wet all over.



### 2. Twist Water Out

- Twist pajamas to get rid of as much water as you can. The pajamas should be damp, not wet.



### 3. Put on Damp Pajamas

- Help your child put on damp pajamas.
- Be gentle. You do not want to bother the skin.



### 4. Put Dry Pajamas on Top

- Put dry pajamas on top of the damp pajamas. This will help keep your child's skin damp — and the sheets dry!



### 5. Go to Bed

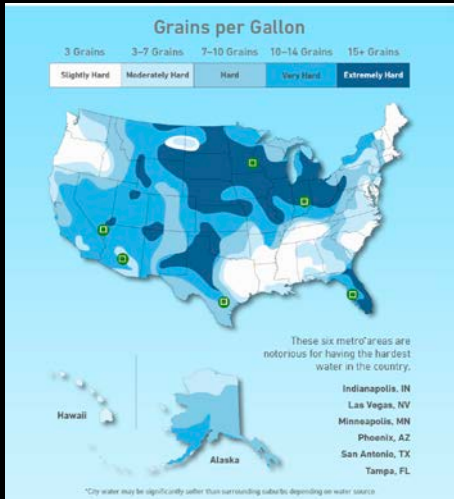
- Go to bed with wet wraps on.
- In the morning, follow your morning steps of bathing and using medicine.



Do not do for more than 1 week. Talk to your doctor right away if wet wraps do not work for your child.



# Prevention of atopic dermatitis



## Water Hardness

- Hard water strong correlation with AD
- No RCT on water softeners

Jabbar-Lopez ZK, et al Br J Dermatol. 2020 Aug;183(2):285-293.



## Breast feeding

- Exclusive BF in first 3-4 months → reduced AD prior to 2yo
- Recommended by AAP

Kramer MS, et al. BMJ 2007;335:815.



## Probiotic use

- Prenatal + postnatal may reduce AD
- *Lactobacillus rhamnosus* and *paracasei*
- Not recommended by AAP

Li L et al . Am J Clin Dermatol 2019



## Dog ownership

- No to AD
- Yes to food allergy

Marrs T, et al; EAT Study Team. Allergy. 2019 Nov;74(11):2212-2219



40% of children with moderate-severe  
atopic dermatitis have food allergies

75% of parents endorse manipulating  
their child's diet to control AD

Johnston GA et al. Br J Dermatol. 2004