MASTERS OF PEDIATRIC DERMATOLOGY

Infants and Atopic Dermatitis

PEER TO PEER TOOLKIT

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POWERED BY LivDerm

MASTERS OF PEDIATRIC DERMATOLOGY

ATOPIC DERMATITIS (AD)

1. A disease of the whole family
2. No patient should leave the office without an instructional handout with the therapeutic ladder
3. If your stable atopic patient is flaring, think:
   - STAPH
   - STAPH
   - STAPH
4. Be aware of racial and cultural diversity

INFANTS AND ATOPIC DERMATITIS

CLINICAL WORK UP

SCORAD

Signs:
- Redness
- Swelling
- Oozing/Crusting
- Excoriations
- Skin thickness/lichenification
- Dryness

Symptoms:
- Pruritus
- Sleep disturbances

Patient History:
- Family and personal history of AD with diatheses
- Chronic and relapsing dermatitis
- NB pigmentary and follicular issues in SOC
- Pruritus

AAD GUIDELINES: Journal American Academy of Dermatology 2020

SCHACHNER'S TIPS AND TRICKS IN DIAGNOSING AD

A chronic or chronically relapsing pruritic dermatoses in patient and family

History

- Milk and food sensitivity
- Insect bite sensitivity – papular urticaria
- Pigmentary changes
- Diaper dermatitis

Physical Exam

- Follicular accentuation – sub-keratosis pilaris and lichen spinulosum
- Hyperlinear palms
- Check behind ears for potato chips

INFANTS AND ATOPIC DERMATITIS

CHALLENGES - MINDING YOUR P'S, BUT NO Q'S

- Inflammation is often under-diagnosed
- Inflammation is often over-diagnosed
- You have to "lay on the hands"
- Pigment alteration is often a major concern

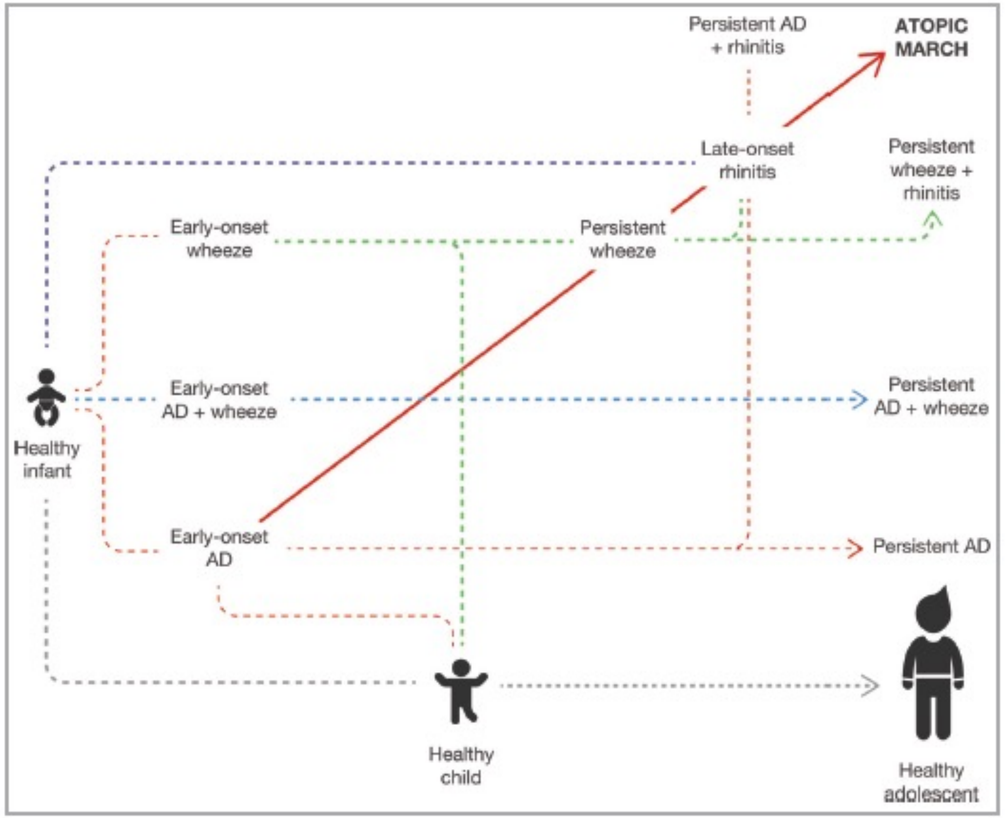
1. Prevalence
2. Persistence
3. Pigment
4. Perplexed doctors
5. Palpation
6. Pruritus
7. Prurigo Nodularis
8. Perceptions that are culturally stigmatizing

THE ATOPIC MARCH

- The complex pathophysiology of AD translates into a heterogeneous clinical presentation and trajectories of disease progression.
  - A significant proportion will develop persistent AD and/or other atopic conditions.

↑ Atopic march:

- **<u>Younger onset of AD</u>**
- Family history of AD
- **<u>Greater early severe AD</u>**
- Filaggrin mutation
- **<u>Urban environment*</u>**
- Polysensitization



Could early use of emollients attenuate the Atopic march? LS

Irvine AD. Br J Dermatol 2019; ;181(5):895-906. doi: 10.1111/bjd.17766. Atopic dermatitis (AD)

OVERVIEW

Currently Available Treatments for Young Children

Topical

- Corticosteroids
- Corticosteroid-Sparing Prescription Products
- Alternative Options
- Pipeline

Treatment considerations for topical therapy in young children

> High BSA: weight
> Increased risk of significant percutaneous absorption
> Impact of age-specific data and labelled indication

Systemic

- Methotrexate
- Dupilumab

TOPICAL CORTICOSTEROIDS (TCS)

- First-line Rx for AD not controlled with skin care/emollients
- Most products are labelled for BID use, but data supports efficacy of QD application, with better safety.
- Intermittent use is effective for mild AD.
- Comparative TCS trials are lacking.
- Anticipatory guidance/medication monitoring can improve adherence.

TOPICAL CORTICOSTEROID VARIABLES - *BEYOND POTENCY*

RELATIVE POTENCIES OF TOPICAL CORTICOSTEROIDS

Class, Potency	Drug, Strength
I, Very High	Augmented betamethasone dipropionate, 0.05% Clobetasol propionate, 0.05% Diflorasone diacetate, 0.05% Halobetasol propionate, 0.05%
II, High	Amcinonide, 0.1% Augmented betamethasone dipropionate, 0.05% Betamethasone dipropionate, 0.05% Desoximetasone, 0.05% and 0.25% Diflorasone diacetate, 0.05% Fluocinonide, 0.05% Halcinonide, 0.1% Mometasone furoate, 0.1% Triamcinolone acetonide, 0.5%
III-IV, Medium	Betamethasone valerate, 0.1% Clocortolone pivalate, 0.1% Desoximetasone, 0.05% Fluocinolone acetonide, 0.025% Flurandrenolide, 0.05% Fluticasone propionate, 0.005% and 0.05% Mometasone furoate, 0.1% Triamcinolone acetonide, 0.1%
V, Lower-Medium	Hydrocortisone butyrate, 0.1% Hydrocortisone probutate, 0.1% Hydrocortisone valerate, 0.2% Prednicarbate, 0.1%
VI, Low	Alclometasone dipropionate, 0.05% Desonide, 0.05% Fluocinolone acetonide, 0.01%
VII, Lowest	Dexamethasone, 0.1% Hydrocortisone, 0.25%, 0.5% and 1% Hydrocortisone acetate, 0.5-1%

Adapted from Paller AS, Mancini AJ. Eczematous eruptions in childhood. In: Paller AS, Mancini AJ. Hurwitz Clinical Pediatric Dermatology. St. Louis, MO: Elsevier Inc; 2011 chapter 3, p.49.

> Vehicle
- Tactile acceptance
- Percutaneous absorption

> Allergenicity

> Application
- Site
- Frequency
- Quantity
- Occlusion
- Duration

> Cost/access

TCS LABELLED FOR SHORT-TERM PEDIATRIC USE

Product	Potency	Age	Frequency	Duration (wk)
Clobetasol propionate 0.05% foam	1	> 12 yr	BID	2
Betamethasone dipropionate	1	>13 yr	QD-BID	3
Fluocinonide 0.1% cr	1	>12 yr	QD-BID	2
Mometasone 0.1% cr/oint	2/4	> 2 yr	QD	3
Fluticasone 0.05% lotion/cr	5	> 1 yr	QD-BID	4
Prednicarbate 0.1% cr/oint	5	> 1 yr	QD-BID	3
Aclometasone 0.05% cr/oint	6	> 1 yr	BID-TID	2
Fluocinolone acetonide 0.01% oil	6	>2 yr	BID	4
Desonide 0.05% foam/gel	6	> 3 mo	BID-TID	4
Hydrocortisone butyrate 0.1% cr	6	> 3 mo	BID-QID	4

TCS ADVERSE EFFECTS

> Insidious, dose-dependent, unclear incidence

> Cutaneous: barrier dysfunction, atrophy, perioral dermatitis/acne, telangiectasia, striae, hypopigmentation, rebound

> Extracutaneous: HTN, hyperglycemia, glaucoma, adrenal suppression, poor growth

> Risk factors:
- Long-term use (especially potent products)
- Occlusion
- Use on face/folds

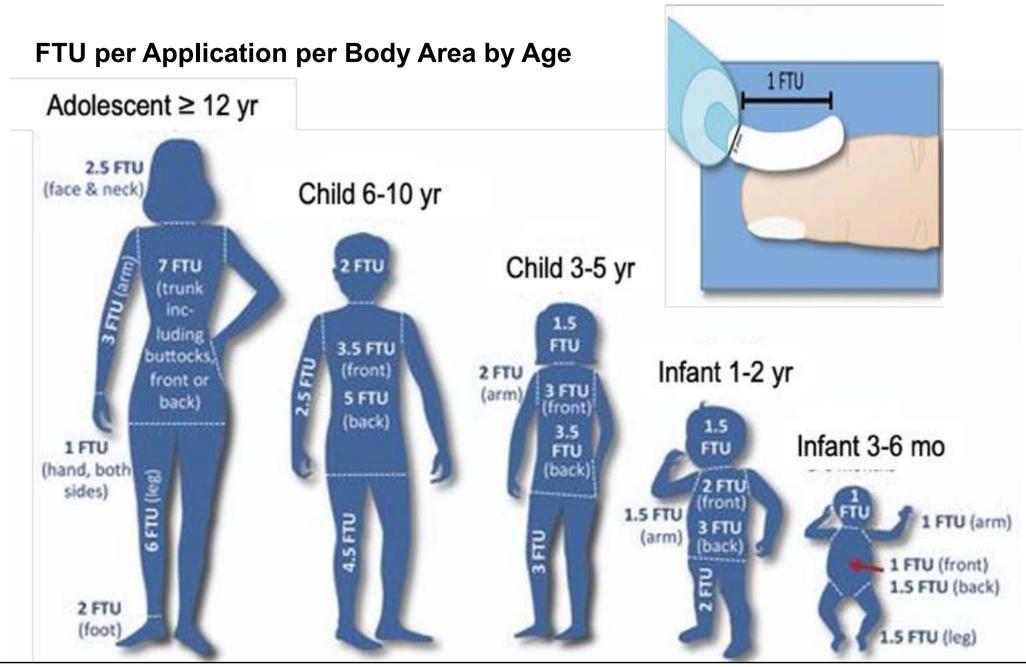
> Consider AM cortisol screening for excessive exposure.

ESTIMATED EFFECTIVE APPLICATION AMOUNTS

Finger Tip Unit (FTU) = amount of ointment expressed from a tube with a 5mm diameter nozzle measured from the distal skin crease to the tip of the palmar surface of an adult's index finger [~0.5g]

1 FTU = adequate amount of ointment for "thin and even" application to an area of skin equal to ~2 adult hands (fingers together)

FTU per Application per Body Area by Age



Quantity by Age (Whole Body Application per wk/mo)

	Emollient (g/wk)
Infant	100
Child	150-200
Adol/Adult	500

Ointment	Acute BID Treatment (g/wk)	Maintenance Treatment (g/mo)		
		1-2X/wk	2-3X/wk	1-2X/wk
Infant	60-100	10	15	**75**
Child	125-250	20	30	**150**
Adol/Adult	260-300	40-60	60-90	**350-450**

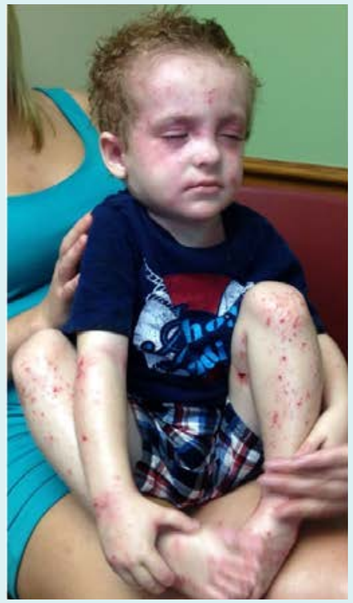
Cream	Acute BID Treatment (g/wk)	Maintenance Treatment (g/mo)		
		1-2X/wk	2-3X/wk	1-2X/wk
Infant	66-110	15	20	**100**
Child	140-275	25	35	**175**

Eichenfield, L et al. Pediatrics. 2015;136:554-565.

REASONS FOR TOPICAL TREATMENT FAILURE

> Inability to use effectively
- Access
- Acceptance
- Comprehension
- Time requirement

> Excessive amounts needed to control disease



Consider systemic treatment for patients with skin disease that cannot be controlled with topical medication, especially in the setting of other atopic morbidities

Sidbury R, et al. J Am Acad Dermatol. 2014;71:327. Beattie PE, Lewis-Jones MS. Clin Exp Dermatol. 2003;28:549.
National Eczema Association: Educational announcement: use of topical steroids for eczema. 2020 (https://nationaleczema.org/warnings-for-topical-steroids-eczema/)

INFANTS AND ATOPIC DERMATITIS

PRACTICAL STRATEGIES FOR DISCUSSING SYSTEMIC THERAPY

- High level overview of mechanism: this is a different approach to control of a chronic disease

- When to consider
  - Optimized topical treatments and still frequently flaring
  - Constantly itchy or uncomfortable
  - Interfering with school or sports activities
  - Interferes with family planning
  - The treatment regimen itself has become burdensome
  - Frequently missing school of work because of skin
  - Comorbidities – asthma or allergies – “high Type 2 inflammation burden”

INFANTS AND ATOPIC DERMATITIS

SYSTEMIC OPTIONS

> Off-label/limited data: methotrexate, immunosuppressants

> On-label

- Corticosteroids
- Dupilumab
  - Completed ph 3, 16 wk trial; age 6 mo-5 yr; N=162 (6.8% ≤2yr); 77% IGA4; concomitant TCS
  - Ongoing long-term extension
- Lebrikizumab ph 3, 16 wk trial; age 6 mo-17 yr; recruiting

https://www.clinicaltrials.gov/ct2/show/NCT03346434?term=dupilumab&cond=atopic+dermatitis&age_v=1&draw=2&rank=2
https://www.clinicaltrials.gov/ct2/show/NCT05559359?recrs=abd&type=Intr&cond=Atopic+Dermatitis&age_v=1&draw=3&rank=13
Paller AS et al. Dupilumab in children aged 6 months to younger than 6 years with uncontrolled atopic dermatitis: a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2022;400(10356):908-919.
Cork MJ, et al. Dupilumab provides favourable long-term safety and efficacy in children aged ≥ 6 to < 12 years with uncontrolled severe atopic dermatitis: results from an open-label phase IIa study and subsequent phase III open-label extension study. Br J Dermatol. 2021;184(5):857-870.

INFANTS AND ATOPIC DERMATITIS

METHOTREXATE

- Onset of efficacy: 12-16 wk after initiation
- Typical starting dose: 0.3–0.5 mg/kg/wk, (max 1 mg/kg and 25 mg/wk)
- Relative contraindications: child-bearing potential, persistent transaminase elevation, fatty liver, hx frequent extracutaneous infections, obesity, renal disease
- Folic acid suppl (starting at 1 mg/day regardless of wt) can minimize assoc GI AEs
- Routine surveillance labs (CBC, hepatic enzymes, Cr) at baseline, 1mo then Q3-4 mo
- Can be discontinued abruptly without AEs other than gradual disease worsening.

Siegfried EC et al. Methotrexate for Inflammatory Skin Disease in Pediatric Patients: Consensus Treatment Guidelines. Pediatric Dermatology, accepted for publication Feb 2023.

ENLARGED TOOLBOX FOR PEDIATRIC AD

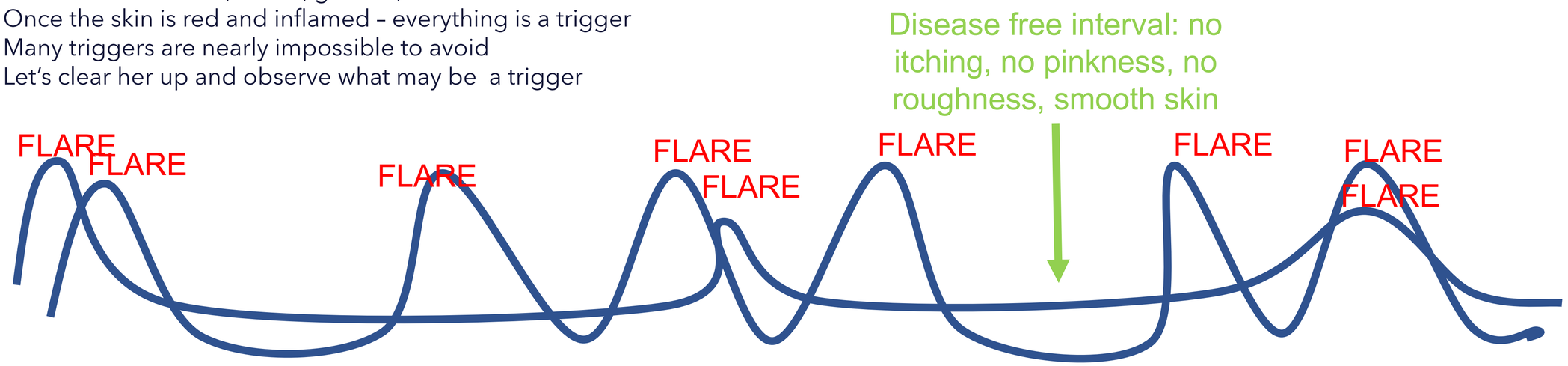
- Crisaborole ointment (Mild-moderate AD > 3months of age)
- Ruxolitinib cream (mild-moderate AD > 12 years)
- Dupilumab (moderate to severe AD > 6 months)
- Upadacitinib (AD > 12 yrs)
- Abrocitinib (AD > 18 yrs)
- Tralokinumab (AD > 18 yrs)
- Forthcoming soon: Tapinarof, Roflumilast, Lebrikizumab
- Many others….

Siegfried EC et al. Methotrexate for Inflammatory Skin Disease in Pediatric Patients: Consensus Treatment Guidelines. Pediatric Dermatology, accepted for publication Feb 2023.

OPTIMIZING TREATMENT IN AD

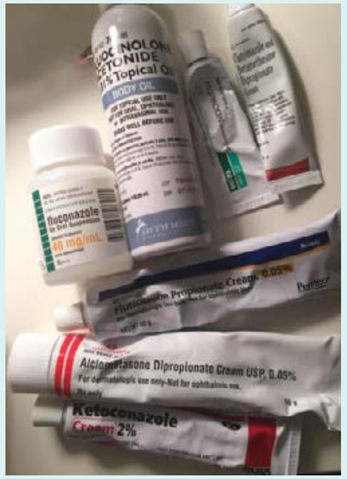
- Education is key
  - Establish relationship w patient & family
  - One main key – we can clear her and AD is inherited and chronic
  - Communicate goals:
    - Control flare and clear her skin
      - Optimize topical treatment regimen
  - Prolong disease free time
  - Minimize risk of infection
  - Relieve pruritus and improve sleep

- High level discussion of underlying cause of AD to debunk myth that food elimination will clear the eczema
  - Discuss the genetic component/skin barrier defect underlying AD
  - There is not one trigger…. (unfortunately) there are numerous triggers!
  - Most common: Heat, Sweat, grasses, viral illnesses
  - Once the skin is red and inflamed – everything is a trigger
  - Many triggers are nearly impossible to avoid
  - Let's clear her up and observe what may be a trigger



OPTIMIZING TREATMENT IN AD: THE PLAN

- Address steroid phobia
- Maximize the benefit of the TCS
  - Choose the right strength
  - Long enough duration
    - Skin needs to be smooth, no longer rough and no longer itchy
- High level maintenance
  - Twice weekly lower potency TCS
  - Twice weekly TCI
- Dry skin care
  - Give specific recommendations for specific products
  - Ask what they are using
- Practice cultural sensitivity
  - Many recommendations given by family and friends
  - Culturally appropriate
- Help sleep with anti-histamines if necessary
- Keep it simple & write it out
- Close follow up is key



CHALLENGES – SOCIAL DETERMINANTS OF HEALTH

- Patients with **low income** may not be able to access healthcare and/or health insurance
- Living in more **populated and urban areas** or in substandard housing can be exposed to more eczema triggers, such as tobacco smoke and dust mites
- Patients with **low health literacy** may not understand their health condition, potentially leading to issues with medication use or following through with treatments
- Patients who speak **different languages** may not fully understand treatment plans or obtain appropriate health services
- A study of 201 pediatric AD patients found that African-American children were more likely to be in lower income families, be exposed to tobacco smoke, have caregivers with lower educational attainment, and live in rented homes
- Additionally, a recent study of 841 adults within the USA found that there was greater eczema symptom burden in patients with low income (less than $15,000/year) vs patients with high income (at least $15,000/year)

Tackett KJ, Jenkins F, Morrell DS, McShane DB, Burkhart CN. Structural racism and its influence on the severity of atopic dermatitis in African American children. Pediatr Dermatol. 2020 Jan;37(1):142-146. doi: 10.1111/pde.14058. Epub 2019 Dec 18. PMID: 31854003.
Bukstein DA, Friedman A, Reyes EG, Hart M, Jones BL, Winders T. Impact of social determinants on the burden of asthma and eczema: results from a US patient survey. Adv Ther. Published online January 24, 2022. doi:10.1007/s12325-021-02021-0
https://eczemainskinofcolor.org/social-and-economic-factors/

DIFFERENCES IN RACIAL SKIN

	Transepidermal Water Loss	Water Content	Ceramide Level	Skin Reactivity
Black skin	++	+	+	+
Caucasian skin	+	++	++	++
Asian skin	+++	+++	+++	+++

Derived from: Wan DC, Wong VW, Longaker MT, Yang GP, Wei FC. Moisturizing different racial skin types. J Clin Aesthet Dermatol. 2014 Jun;7(6):25-32. PMID: 25013536; PMCID: PMC4086530.

RECOGNIZE CULTURAL DIVERSITY

- **Hispanic and Black** children are more likely than white children to present with poorly controlled and persistent AD[1]
- AD can be a lifelong issue with implications on **performance in occupational and academic settings**[2]
- Children with **skin of color (SOC) and AD were absent more often from school** than white children with AD[3]
  - As compared to white children, black children had a 1.5-fold higher chance of being absent 6 days over a 6-month school period[3]

Additional considerations:

- Fragrance and cologne use
- Antibiotic/steroid/antifungal compounds commonly used
- Corn starch & talcum powder
- Concern for fungal infection and vitiligo
- Use of homeopathic remedies

1. Kim Y, Blomberg M, Rifas-Shiman SL, Camargo CA Jr, Gold DR, Thyssen JP, Litonjua AA, Oken E, Asgari MM. Racial/Ethnic Differences in Incidence and Persistence of Childhood Atopic Dermatitis. J Invest Dermatol. 2019 Apr;139(4):827-834. doi: 10.1016/j.jid.2018.10.029. Epub 2018 Nov 8. PMID: 30414911; PMCID: PMC6431568.
2. Vivar KL, Kruse L. The impact of pediatric skin disease on self-esteem. Int J Womens Dermatol. 2017 Dec 12;4(1):27-31. doi: 10.1016/j.ijwd.2017.11.002. PMID: 29872673; PMCID: PMC5986112.
3. Wan J, Margolis DJ, Mitra N, Hoffstad OJ, Takeshita J. Racial and Ethnic Differences in Atopic Dermatitis-Related School Absences Among US Children. JAMA Dermatol. 2019 Aug 1;155(8):973-975. doi: 10.1001/jamadermatol.2019.0597. PMID: 31116350; PMCID: PMC6537763.

INFANTS AND ATOPIC DERMATITIS

SUMMARY

- Education is key at every visit – emphasize one thing
- Involve the patient/family at every step including extended family
- Make culturally appropriate specific recommendations
- Discuss option of systemic therapies early
- Written action plan
- Topical treatment is standard-of-care, first-line treatment for AD.
- Cost and access support initial use of generic TCS.
- Optimize topical therapy right strength and duration
- TCS-sparing products are most often used first-line for face/folds and long-term maintenance.
- Active maintenance with non TCS and dry skin care
- Methotrexate or dupilumab should be considered for young children who fail topical treatment.
- The risk of systemic absorption is underappreciated for all topical products; monitor quantity use, especially in infants.
- Keep abreast of emerging therapies