Updates in Pediatric Dermatology

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Disclosures

- None
  - except a large amount of gratitude to the dermatology and pediatric residents I have the opportunity to work beside

Common Pediatric Dermatology Diagnoses

- Psoriasis
- Infantile Hemangiomas
- Atopic Dermatitis

- Goals – that you leave today with:
  - a new clinical skill for each diagnosis
  - a new therapeutic modality for each diagnosis
  - a new way to communicate to parents to help increase their health knowledge

Psoriasis

Psoriasis has arrived

Psoriasis has arrived

- A multitude of new medicines, which are having a trickle down affect on how we treat childhood psoriasis
- A country wide understanding of the emotional impact psoriasis has had on patients for years
- The rich and famous admitting to their struggles with psoriasis

Epidemiology

- All ages 2 – 3 % of population
- 31- 45% of adults report an onset during first two decades of life

Genetics

- 70% of patients have a family history
- Major genetic determinant is PSORI(30-50%) and is the major histocompatibility complex on chromosome 6
- Early onset psoriasis is linked to HLA Cw6
- 73% of guttate psoriasis is linked to HLA Cw6

Psoriasis

- Can or can not be pruritic, not a criteria
- Distribution in infancy – diffuse eruption or scalp, diaper area and skin folds
  - Difficult to separate from seborrheic dermatitis
- Distribution in toddlers and up
  - Extensor surface extremities, scalp and skin folds
- Commonly a more adherent scale than atopic dermatitis
- Usually well demarcated lesions
- May have guttate form presenting with a strept trigger
- More common to have facial lesions in childhood psoriasis than adult psoriasis

Presentation

- Congenital
  - neonatal pustular
- Facial
  - 4 – 5 % (periocular)
- Plaque/Inverse
  - Typical presentation
- Guttate
  - 44% of pediatric patients(40% progress to plaque type)
- Scalp
  - 20 – 40% it is the initial site of involvement
- Diaper area
  - 4% present with this alone, 13% with this and other sites
- Nail
  - 25-50% more common in second decade
- Pustular
- Extracutaneous
- Drug induced

Pediatric Psoriasis

Understanding psoriasis as the tip of the iceberg

- Comorbidities
- Therapeutics

Pediatric Psoriasis

Time to be Brave

- Asking the uncomfortable questions
- Pointing out the obvious
- Giving the bad news
- Finding out the unspoken obstacles
- Therapeutics

Pediatric Psoriasis

Comorbidities

- Emotional Impact
- Psoriatic arthritis
- Cardiovascular disease
- Obesity

Pediatric Psoriasis

- Yes we are on the *frontline fighting the war* on childhood obesity
- In our favor is the emotional impact of psoriasis
  - We have the attention of our patients due to the "outward sign" of this quiet health issue

Quality of Life Concerns

- Anxiety and depression are common among patients and caregivers
- Compounding these emotional disorders
  - the patients' developmental needs
  - Family dynamics
  - Social acceptance

- Dermatol Clin. 2013 Apr;31(2):211-21
- An Bras Dermatol. 2013 Nov-Dec;88(6):894-9

Ask the Questions

- Have you been teased or has someone pointed out your psoriasis and it hurt your feelings? And how do you respond?
- Ask the parents their perception and then give them time to express their own concerns
  - At times, depending on the age of the child, you may need to have the child occupied or speak to parents by phone call(time to get sticker or a drink in the hall)

Be ready for the fall out

- Greatly variable responses
  - Some families have already discussed and are very open to the emotional concerns
  - Some have never spoken about it and still do not want to express these emotions
  - Some have been waiting for someone to open up the flood gates – here is where the BRAVE part comes in

Pediatric Psoriatic Arthritis

- Juvenile idiopathic arthritis(JIA) and oligoarticular JIA will comprise a number of children that will be better classified as psoriatic arthritis
- Typical onset was before 5 years of age
- Common joint involvement was wrist and small joints
- Psoriatic lesions, nail pits and family history of psoriasis help to separate these patients from JIA patients
    - Clin Exp Rheumatol. 2011 May-Jun;29(3):582-8

Pediatric Psoriatic Arthritis

- Looking at this diagnosis throughout childhood
  - there seems to be evidence that when we see older children pre teens and teens present with arthritis their severity should be less than younger children
    - Curr Opin Rheumatol. 2011 Sep;23(5):437-43

Plant the seed

- Many parents do not know of the association of arthritis with psoriasis
- Thorough review of symptoms and education parents is the best first step

Looking Beyond the Psoriasis

- When presented with the obese pediatric patient that has psoriasis consider consults from pediatric subspecialist
  - Endocrinology, psychology, rheumatology, dietician
  - hopefully we have time to make a difference

Childhood Obesity

Childhood Obesity

- JAMA Dermatol.Feb 2013:149(2):166-176.

Speak the Obvious

- Fewer than one-quarter of parents of overweight children report having been told that their child was overweight

Arch Pediatr Adolesc Med. 2012;166(4):317-322

Pediatric Psoriasis Clinical Pearls

- Thorough review of systems may flush out the co-morbidities
  - Why is the knee injury not resolving, joint stiffness
- We must get the patient in a gown/skin exams are invasive
  - Many doctors do not require children to get into a gown can be uncomfortable
- Must examined from scalp to toes the patient and family may not know where psoriasis lesions are commonly located – i.e. scalp, genitalia
- Document BSA - will help with insurance coverage of medications and best method to monitor efficacy of therapeutics

Pediatric Psoriasis Clinical Pearls

- When unsure of diagnosis there are some clues
- History of infantile seborrheic dermatitis, severe diaper rashes
- Family history of psoriasis or psoriatic arthritis
- Nail pitting, geographic tongue, perianal pinkening, facial lesions
- Strept Pharyngitis associated with onset or flares of lesions

Pediatric Psoriasis Severity

- Concerns for arthritis
- BSA
- Scalp
- Palmoplantar
- Genitalia
- Depression/anxiety

Therapeutics

- Topicals
  - range from topical steroids, calcipotriene, retinoids, tar, calcineuron inhibitors, keratolytics
- NBUVB, natural sunlight
- Systemic medications
  - Methotrexate
  - Cyclosporine
  - Oral retinoids
  - Biologics –
    - Enbrel – etanercept - 4 and above
    - Stelara – ustekinumab – 12 and above

Simple Steps to Help Lighten the Load

- Let them know they are not alone
- Special time
- Simplify treatment
- Discuss the master plan
- Praise emotional strengths
  - Sharing feelings
  - Asking the questions
  - Answering the question

Therapeutics

- Topicals
  - Be careful using topicals that cause any burning in the younger age groups
  - Assess the family dynamics and stressers
    - Take a step into the day to day lifestyle of the family
  - Use this as a time for stress relief not exacerbating the stress
    - This can be that special time which is critical for a child's emotional development

Therapeutics

- Phototherapy
- Vitamin D
- Natural sunlight
  - Education on sunprotection
  - Caution in adolescents and over utilizing this treatment

- NBUVB
  - Will require additional effort and time
  - Caution with sunnier months in Ohio or vacation times
  - Caution with compromising education
  - Br J Dermatol, 2010;163:321-328.

Systemic Medications

- Methotrexate
  - 0.2 – 0.7 mg/kg/week
  - Folic acid supplementation
  - Comes in 2.5 mg tablets or injectable 2.5 mg/ml
  - Coming down the pike - Methotrexate polyglutamate
  - J Am Acad Dermatol. 2014 Feb;70(2):252-6

Systemic Medications

- Cyclosporine
  - 1 -4 mg/kg/day
  - Typical monitoring
  - Does come as liquid 100 mg/ml or tablets 25 mg or 100 mg

Systemic Medications

- Acitretin
  - 0.5 – 1.0 mg/kg/day
  - Typical monitoring
  - Consider bone growth

Systemic Medications

- Etanercept(Enbrel) – 4 and above
- Ustekinumab (Stelara) – 12 and above
- Thus far seems to efficacy similar to adults

- J Am Acad Dermatol 2010; 63:762–768.

The internet speaks volumes

Psoriasis

National Psoriasis Foundation	INTER REF www.psoriasis.org
The Psoriasis Association	INTER REF www.psoriasis-association.org.uk
Psoriasis Help Organization	INTER REF www.psoriasis-help.org.uk
Psoriasis and Psoriatic Arthritis Alliance	INTER REF www.papaa.org

Infantile Hemangiomas

No financial disclosures

timolol will be discussed as an off label treatment for infantile hemangiomas

We have come so far …

Infantile Hemangioma recent literature

- Pathogenesis
- Type of cells involved
  - Immature endothelial cells
  - Endothelial progenitor cells
  - Interstitial cells
  - Pericytes
  - Hemangioma derived stem cells

  - Boscolo and Bischoff. Angiogenesis. 2009:12(2):197-207.

Infantile Hemangioma recent literature

- Molecular mechanisms
  - Vasoconstriction
    - Beta receptors blocked by propanolol inhibit vasodilation by adrenaline and cause vasoconstriction
  - Inhibition of angiogenesis
    - By blocking the beta adrenoreceptors the ERK/MAPK is deactivated decreasing the release of VEGF
  - Induction of apoptosis
    - By disengaging the inhibition of apoptosis caused by beta-adrenergic agonists
    - Storch and Hoeger. Br J of Derm 2010 163,pp269-274.

Infantile Hemangioma recent literature

- Proliferative Phase
  - Much earlier than previously believed – *the Iphone camera and anxious parents can not be disputed*
  - Rapid growth is prior to 8 weeks of life
  - The time between their first pediatric appointment and the second

  - Tollefson and Frieden. Pediatrics. 2012 Aug;130(2).e314-20.

Infantile Hemangioma recent Literature

- Scoring
  - Many have been proposed and range from requiring US to clinical scores
  - Hemangioma Activity Score(HAS)
  - Simplified scoring on three clinical findings
    - Color
    - Swelling
    - Ulceration

    - Janmohamed et al. Clin and Exp Dermatol 2011,36,715-723.

What infantile hemangiomas need to be treated?

- Stratifying risks
- Prognosticating growth
- Weeks of life to evaluate

Why treat

- More than one-half of children with untreated hemangiomas experience residual changes such as scarring, atrophy, redundant skin, discoloration, and telangiectasias
- “ it will go away”

JAMA Dermatol. 2016 Nov;152(11):1239-1243

Risk Stratication

- Moderate Risk
  - lateral face, scalp, hands and feet
  - Body folds
  - Segmental > 5 cm of trunk or extremities
- Low risk
  - Nonvisible areas

  - Luu and Frieden. Br J of Derm 2013;169(1):20 – 30.

Risk Stratification

- Very High Risk
  - Segmental face or perineal
  - PHACE, PELVIS
- High Risk
  - Bulky lesions face
  - Central face
  - Periorbital, oral and nasal
  - Early white discoloration

Periocular Infantile Hemagioma

Infantile Hemangioma treatment

- Low risk
  - Observe or
  - timolol gel forming ophthalmologic drops
- Moderate risk
  - timolol gel forming ophthalmologic drops or
  - propanolol
- High risk
  - propanolol
- Very high risk
  - propanolol

Infantile Hemangioma treatment

- Propanolol 4mg/ 1 ml
  - ECG
  - Initiate as inpatient for patients less than 8 weeks
  - After 8 weeks initiate at 1 mg/kg/day
  - 1 - 2 weeks after may increase to 2 mg/kg/day
  - Treatment to one year of age and weaning of medication between 12 – 18 months
  - May have rebound regrowth from very minimal to needing to reinitiate treatment

Infantile Hemangioma Clinical Pearls

- Classify infantile hemangioma
  - Superficial, deep or combined
- Being careful to consider proliferative phase and treatment
- Knowing most concerning sites
- Treatment is to halt growth so giving correct expectations

Treatment makes the clinical diagnosis critical

- Clinical appearance within 1 – 2 months of life
- Clinical observance of growth
- Understanding the natural course with and with out treatment

Propanolol

- First designed medication completed in 1964 by James Black
- Original goal was a treatment for angina, but also proves to be an antihypertensive
- Lipophilic non selective beta antagonist
- Dr. Leaute-Labreze publishes the first report of propanolol as treatment for infantile hemangiomas
- March 2014 FDA approves Hemangiol for IH treatment being initiated in 5 week to 5 month old children

Propanolol dosing

- 0.6mg/kg/dose bid x 1 week
- Then increase to 1.1 mg/kg/dose bid x 1 week
- Then 1.7 mg/kg/dose ongoing
- Doses are 8 hours apart
- Treat for 6 months

Side Effects of Propanolol

- Nonselective β-blockers can block catecholamine-induced glycogenolysis, gluconeogenesis, and lipolysis, predisposing to hypoglycemia
- Bronchial hyperreactivity, described as wheezing, bronchospasm, or exacerbation of asthma/bronchitis, is a recognized side effect of propranolol as the result of its direct blockade of adrenergic bronchodilation

Side Effects

- Hyperkalemia (without electrocardiographic changes) was reported in 2 children on propranolol for IH postulate that it was tumor lysis from the large ulcerated IH combined with impaired potassium uptake into cells as the result of β blockade.
- Dental caries have been reported in 2 pediatric patients treated with propranolol β-adrenergic antagonism of salivary gland function resulting in decreased salivation

Complications Recorded	No. of Patients/ Total No. of Patients in Papers Reporting Complication	Frequency (%) of Complication Among Papers Reporting Said Complication	Overall Frequency (%) of Total of 1175 Patients Reviewed in 85 Papers
Asymptomatic hypotension or hypotension (unspecified)	33/228	14.5	2.8
Symptomatic hypotension	3/46	6.5	0.3
Pulmonary symptoms (bronchoconstriction, bronchiolitis, wheezing, pulmonary obstruction, apneic episode)	16/201	8.0	1.4
Hypoglycemia	10/88	11.4	0.9
Asymptomatic bradycardia or bradycardia (unknown)	11/126	8.7	0.9
Symptomatic bradycardia	1/2	50	0.1
Sleep disturbance (including nightmares)	44/326	13.5	3.7
Somnolence	26/220	11.8	2.2
Cool or mottled extremities	20/225	8.9	1.7
Diarrhea	9/53	17.0	0.8
Gastroesophageal reflux disease or gastrointestinal upset	8/133	6.0	0.7

More Common Side Effects

- hypotension
- hypoglycemia
- sleep disturbance
- somnolence
- Diarrhea

- Pediatrics. January 2013, VOLUME 131 / ISSUE 1

Treatment Successes

- Treatment questions unanswered
  - Hypotension due to beta blockers and when there an associated congenital heart defects(coarctation of aorta) and neck vessel malformations
  - Regrowth after typical treatment – past 18 months of life

Could a topical beta blocker be as effective?

- Limit side effects
- Depth of absoption
- Application to skin with increased vascular spaces
- Evaluating treatment efficacy is very difficult, especially for deep and mixed

Topical timolol

- All patients except one improved, with a mean improvement of 45 ± 29.5%. Predictors of better response were superficial type of hemangioma (p = 0.01), 0.5% timolol concentration (p = 0.01), and duration of use longer than 3 months (p = 0.04).

Pediatr Dermatol. 2012 Jan-Feb;29(1):28-31. doi: 10.1111/j.1525-1470.2011.01664.x. Epub 2011 Dec 9

Topical timolol

- Timolol seems to be a well-tolerated, safe treatment option with moderate to good effectiveness, demonstrating best response in thin, superficial IHs regardless of pretreatment size. Timolol can be recommended as an alternative to systemic β-blockers and watchful waiting for many patients.

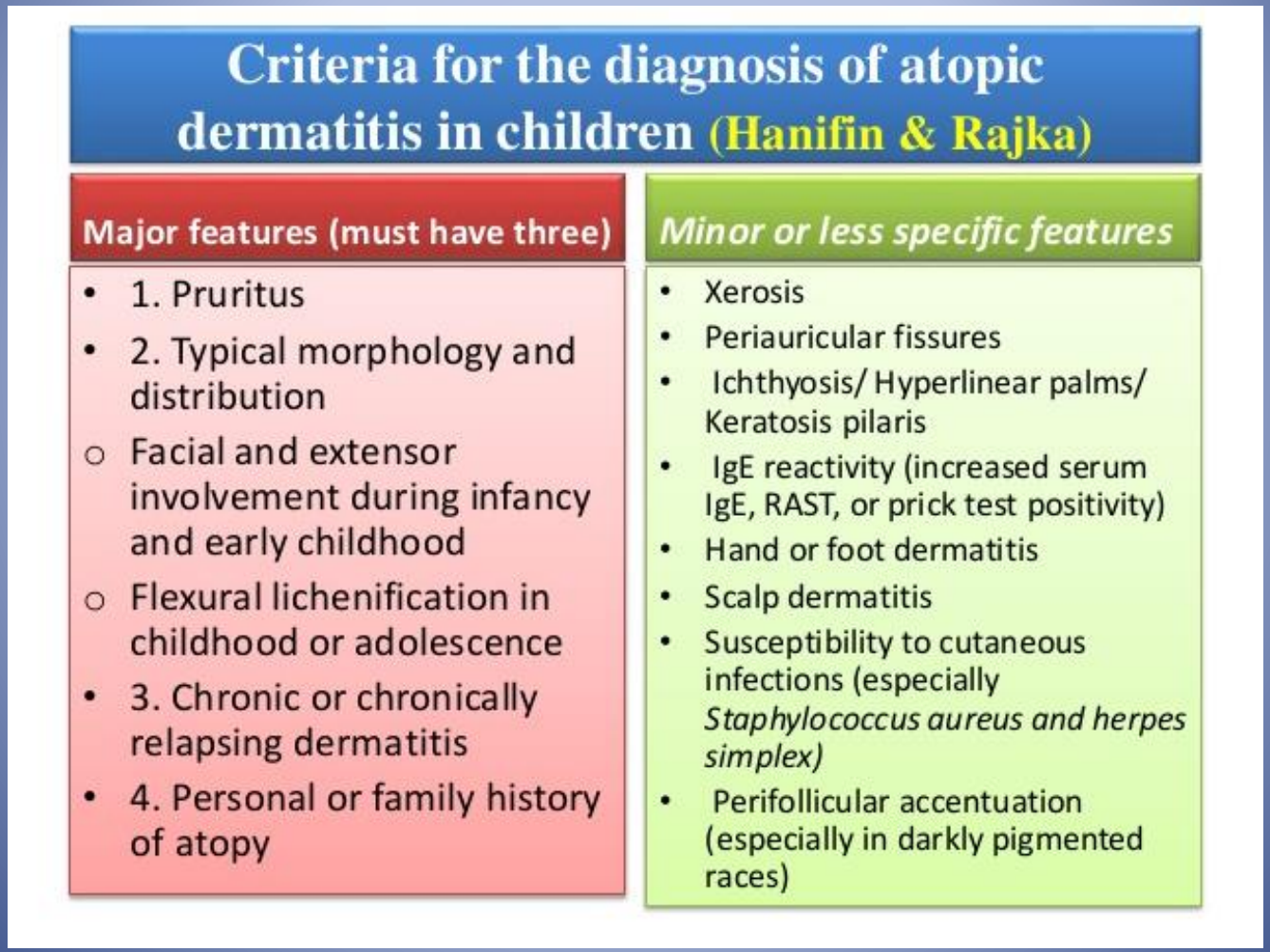
Pediatrics. 2016 Sep;138(3). pii: e20160355. doi: 10.1542/peds.2016-0355. Epub 2016 Aug 15.

Atopic Dermatitis

Atopic Dermatitis
Prototypic pediatric dermatitis diagnosis

- Primarily a disorder of childhood
- Difficult to push forward etiology and therapies due :
  - to wide phenotype
  - variation in severity
  - mostly affects children
  - lack of recognition significant morbidity

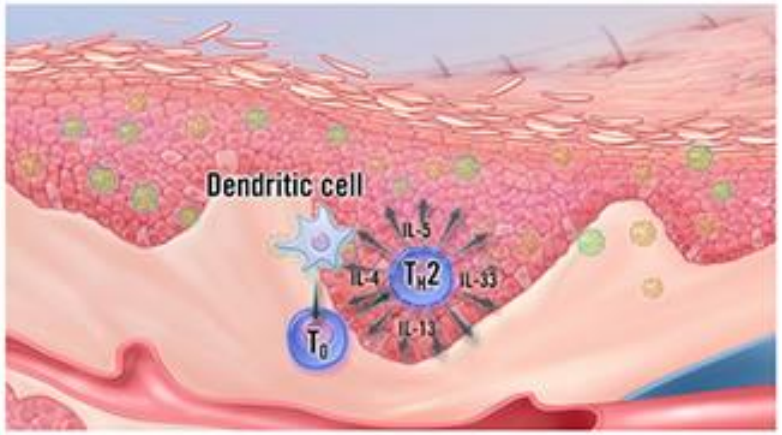
Criteria for Atopic Dermatitis



The whole inside or outside…

The Shifting Perspective on AD Pathogenesis

- AD is related to both barrier dysfunction and inflammation.
- Immunologic basis of inflammation
- JAK pathway impacts cytokine receptors.
- Driven by Th2, TSLP, and IL-4, -5, -13, -17, and -33



Bao L, et al. *JAK-STAT.* 2013;2:e24137.[7]

Moisturization

- Effectiveness of Moisturizations in the Treatment of Patients with Eczema.
- **Evidence-Based Answer**
- Moisturizers decrease the rate of eczema flare-ups by 3.7 times vs. no treatment (number needed to treat [NNT] = 4), as well as the amount of topical corticosteroids used per eczema flare-up (9.3 g less). Adverse effects are minimal.[1] (Strength of Recommendation: A, based on consistent, good-quality patient-oriented evidence.)

ARIANNA BECKER, DO, and MATTHEW RENSBERRY, MD, Florida Hospital Family Medicine Residency Program, Orlando, Florida. *Am Fam Physician.* 2018 Jan 1;97(1):18-19.

Atopic Dermatitis Treatment

- First line Topical Therapy
  - Moisturization
  - Topical steroids
  - Calcineuron inhibitors – first line for facial atopic dermatitis lesion for 2 year olds and above

Atopic Dermatitis

- Topical steroids
  - Cream vs ointment
    - Burning due to creams
    - Weighing compliance – you must ask
  - Classifications
    - Location of application
    - Trying to reach control and then wean
    - Clear expectations on amount to be used
  - Dosing schedules

Atopic Dermatitis

- Choice of potency – classification
  - Age
    - Less than 2 years – caution going above class six
    - Amount of BSA
    - Locations – folds and face
  - Lichenification
    - Needs higher potency
  - Flares
    - If you can not wean the topical steroid or multiple flares (greater than 4 – 6 in 6 months) may need to increase potency

Atopic Dermatitis

http://www.treateczema.ph/treating-eczema/

How Do I Apply It?

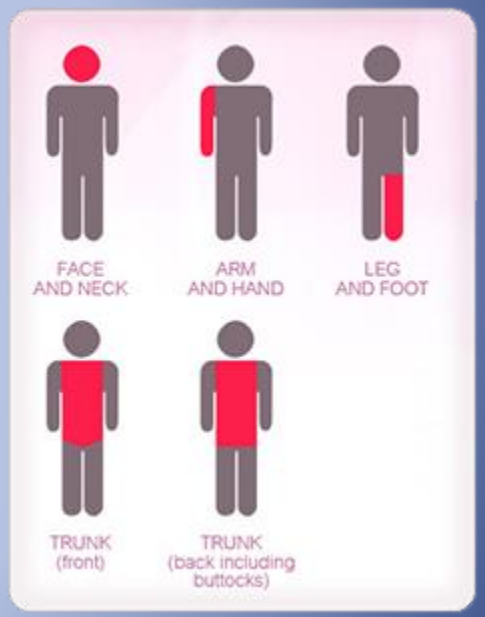
Smooth in a small amount on the affected area

Fingertip units can be a useful way to measure how much you need

- For adults, use an adult's fingertip
- For children, use a child's fingertip

With the following FTUs on these body parts:

BODY PART	FTU REQUIRED TO COVER				
	3-6 mos	1-2 yrs	3-5 yrs	6-10 yrs	Adults
FACE AND NECK	1	1.5	1.5	2	2.5
ARM AND HAND	1	1.5	2	2.5	4
LEG AND FOOT	1.5	2	3	4.5	8
TRUNK (FRONT)	1	2	3	3.5	7
TRUNK (BACK INCLUDING BUTTOCKS)	1.5	3	3.5	5	7



Atopic dermatitis

- Weaning schedule proposed in AAD standard of care for Atopic Dermatitis in 2004
  - Apply to affected areas
    - Twice a day 2 weeks
    - Once a day for 2 weeks
    - Then apply once twice a week
    - Goal: 8 applications per 4 weeks as ongoing therapy

Atopic Dermatitis

- Inability to control with standard of care weaning schedule
  - Moisturizing?
  - Steroid sparing treatment
    - Calcineuron inhibitor (Protopic(tacrolimus) or Elidel(pimecrolimus) - refrigerate
    - Phosphodiesterase(PDE) 4 inhibitor – (Eucrisa(crisaborole)
    - All above cause some stinging

Atopic Dermatitis

Methotrexate – off label

1 mg/kg/week with max 25 – 30 mg/week
Folic acid daily

- An anti-metabolite that inhibits dihydrofolate reductase,methotrexate is more anti-inflammatory than immunosuppressive at dermatological doses.
- Although its mechanism of action at atopic dermatitis is not known, it is effective on the purine pathway, amino-imido-carboxy-amidoribonucleotidetransformylase and adenosine, methionine
- synthetase and S-adenyl methionine to inhibit inflammatory cell chemotaxis and cytokine synthesis may be responsible. Commonly used for psoriasis

Atopic Dermatitis

- Cyclosporine – off label
  - inhibits T cell activation and modulates cell mediated immune response
  - promotes a Th1 cytokine profile
- typical starting dose is 2 mg/kg/day to max 5 mg/kg/day
- with therapeutic response within several days to 1 week. Some prefer a lower
- starting dose of 2–3 mg/kg/day, particularly to reduce
- nausea in the paediatric population

Atopic Dermatitis

- mycophenolate mofetil (Cellcept) – off label

1 – 2 gm/day

- A biological precursor of mycophenolic acid, mycophenolate
- mofetil inhibits *de novo* purine synthesis, in particular
- the proliferative responses of T and B lymphocytes. Mycophenolic
- acid, the active metabolite of mycophenolate
- mofetil, has been shown to act directly on B lymphocytes by inhibiting Ig formation, particularly IgE

Clinical Pearls for Atopic Dermatitis

Must be itchy

Must walk parents through this process have the patient back 2- 4 weeks initially

Strengthening the differential diagnosis

Let’s go over what isn’t eczema

The End

- My email – tamburj@ccf.org
- We welcome two new Pediatric Dermatologists to our Cleveland Clinic Section of Pediatric Dermatology
- Dr. Mahwish Irfan
- Dr. Cheryl Bayart
- For consults please fax to 216-636-5151