Updates in Pediatric Dermatology

Joan Tamburro, DO
Cleveland Clinic
Department of Dermatology
Section Head for Pediatric Dermatology
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
Anxiety and depression are common among patients and caregivers.

Compounding these emotional disorders:
- the patients’ developmental needs
- Family dynamics
- Social acceptance

References:
- *Dermatol Clin.* 2013 Apr;31(2):211-21
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 Rheumomatol.* 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

Speak the Obvious

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

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
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
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

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

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
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

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
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”

Risk Stratification

• Moderate Risk
  – lateral face, scalp, hands and feet
  – Body folds
  – Segmental > 5 cm of trunk or extremities

• Low risk
  – Nonvisible areas

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 Hemangioma
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 without 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 $\beta$-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.
<table>
<thead>
<tr>
<th>Complications Recorded</th>
<th>No. of Patients/ Total No. of Patients in Papers Reporting Complication</th>
<th>Frequency (%) of Complication Among Papers Reporting Said Complication</th>
<th>Overall Frequency (%) of Total of 1175 Patients Reviewed in 85 Papers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic hypotension or hypotension (unspecified)</td>
<td>33/228</td>
<td>14.5</td>
<td>2.8</td>
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<tr>
<td>Symptomatic hypotension</td>
<td>3/46</td>
<td>6.5</td>
<td>0.3</td>
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<tr>
<td>Pulmonary symptoms (bronchoconstriction, bronchiolitis, wheezing, pulmonary obstruction, apneic episode)</td>
<td>16/201</td>
<td>8.0</td>
<td>1.4</td>
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<tr>
<td>Hypoglycemia</td>
<td>10/88</td>
<td>11.4</td>
<td>0.9</td>
</tr>
<tr>
<td>Asymptomatic bradycardia or bradycardia (unknown)</td>
<td>11/126</td>
<td>8.7</td>
<td>0.9</td>
</tr>
<tr>
<td>Symptomatic bradycardia</td>
<td>1/2</td>
<td>50</td>
<td>0.1</td>
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<tr>
<td>Sleep disturbance (including nightmares)</td>
<td>44/326</td>
<td>13.5</td>
<td>3.7</td>
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<tr>
<td>Somnolence</td>
<td>26/220</td>
<td>11.8</td>
<td>2.2</td>
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<tr>
<td>Cool or mottled extremities</td>
<td>20/225</td>
<td>8.9</td>
<td>1.7</td>
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<tr>
<td>Diarrhea</td>
<td>9/53</td>
<td>17.0</td>
<td>0.8</td>
</tr>
<tr>
<td>Gastroesophageal reflux disease or gastrointestinal upset</td>
<td>8/133</td>
<td>6.0</td>
<td>0.7</td>
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</table>
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 is 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 absorption
- 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 ($p = 0.04$).

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.

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

Criteria for the diagnosis of atopic dermatitis in children *(Hanifin & Rajka)*

**Major features (must have three)**

1. Pruritus
2. Typical morphology and distribution
   - Facial and extensor involvement during infancy and early childhood
   - Flexural lichenification in childhood or adolescence
3. Chronic or chronically relapsing dermatitis
4. Personal or family history of atopy

**Minor or less specific features**

- Xerosis
- Periauricular fissures
- Ichthyosis/ Hyperlinear palms/ Keratosis pilaris
- IgE reactivity (increased serum IgE, RAST, or prick test positivity)
- Hand or foot dermatitis
- Scalp dermatitis
- Susceptibility to cutaneous infections (especially *Staphylococcus aureus* and *herpes simplex*)
- Perifollicular accentuation (especially in darkly pigmented races)
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

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.)

Atopic Dermatitis Treatment

- First line Topical Therapy
  - Moisturization
  - Topical steroids
  - Calcineurin 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

<table>
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<tr>
<th>BODY PART</th>
<th>3-6 mos</th>
<th>1-2 yrs</th>
<th>3-5 yrs</th>
<th>6-10 yrs</th>
<th>Adults</th>
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<tbody>
<tr>
<td>FACE AND NECK</td>
<td>1</td>
<td>1.5</td>
<td>1.5</td>
<td>2</td>
<td>2.5</td>
</tr>
<tr>
<td>ARM AND HAND</td>
<td>1</td>
<td>1.5</td>
<td>2</td>
<td>2.5</td>
<td>4</td>
</tr>
<tr>
<td>LEG AND FOOT</td>
<td>1.5</td>
<td>2</td>
<td>3</td>
<td>4.5</td>
<td>8</td>
</tr>
<tr>
<td>TRUNK (FRONT)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>3.5</td>
<td>7</td>
</tr>
<tr>
<td>TRUNK (BACK INCLUDING BUTTOCKS)</td>
<td>1.5</td>
<td>3</td>
<td>3.5</td>
<td>5</td>
<td>7</td>
</tr>
</tbody>
</table>
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