Pediatric Perspective on Psoriasis and Psoriatic Arthritis

Amit Garg, MD, FAAD
Associate Professor and Founding Chair
Department of Dermatology
Hofstra NSLIJ School of Medicine
North Shore LIJ Health System
Manhasset, New York

Pamela F. Weiss, MD, MSCE
Assistant Professor
Perelman School of Medicine
Director of Rheumatology Clinical Research
Children’s Hospital of Philadelphia
Philadelphia, Pennsylvania

Content Developers

Amit Garg, MD, FAAD
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Psoriasis in Infants, Children, and Adolescents

Epidemiology: Psoriasis

- Overall prevalence in adults: 2%-4%
- Childhood prevalence: 0.5%-1.1%
  - Increasing prevalence with age
    - 0.12% at 1 year, 1.2% at 18 years
- Incidence 40.8 cases/100,000 person years
- 1/3 develop disease during childhood
  - Average age of onset 7-11 years
  - Up to ¼ of pediatric cases develop by age 2
- Incidence increasing over time
  - 2-fold increase in children since 1970

Psoriasis

- Strong genetic component
  - If both parents affected, risk is 41%
  - If one parent affected, risk is 14%
  - If one sibling affected, risk is 6%
  - Concordance rate MZ>DZ twins
- Precipitating factors
  - Infection (streptococcus)
  - Stress
  - Trauma
- PSORS1
  - HLA-Cw06 is the PSORS-1 risk allele


Pediatric Psoriasis

- **Distribution**
  - Facial and flexural involvement more common
  - Diaper or napkin psoriasis
    - Inguinal fold involvement (vs contact dermatitis)
- Scalp and face often first site of involvement
- Often pruritic
- Guttate disease more common among children and adolescents
- Nail psoriasis less common

Plaque Psoriasis

- **Most common form in children (same as with adults)**
  - Plaque psoriasis: 75% of cases
  - Lesions: Scalp, face, extensor surfaces, flexures
  - Often smaller, thinner, less scaly than in adults

Facial Plaque Psoriasis

- Photos courtesy of Leslie Castelo-Soccio, MD Philadelphia, PA

Guttate Psoriasis

- 2nd most common form
- 15%-30% of cases
- Lesions: trunk, limbs, face

Psoriasiform Napkin Dermatitis

- ¼ pediatric cases present by age 2 if diaper eruption is included
- Unclear how many with diaper dermatitis develop true psoriasis
  - One report: 17%
- Disseminated lesions or positive family history confer the highest risk

Photos courtesy of Leslie Castelo-Soccio, MD Philadelphia, PA.
**Quality of Life Outcomes**

- 208 pediatric patients with moderate-to-severe plaque psoriasis (ages 4–17 years)
- Based on pooled baseline clinical trial data
  - Comparison groups: 1) healthy children, and patients with 2) arthritis, 3) psychiatric disorders, 4) asthma, 5) diabetes
  - Significantly poorer HRQOL compared to healthy children
  - Physical, emotional, social, school functioning
  - Pooled baseline clinical trial data

<table>
<thead>
<tr>
<th>PedsQL™ Scales</th>
<th>Number of</th>
<th>Mean (SD)</th>
<th>95% CI</th>
<th>Mean (SD)</th>
<th>95% CI</th>
<th>Difference</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Physical Functioning</td>
<td>25</td>
<td>79.1 (7.4)</td>
<td>76.7-81.5</td>
<td>78.5 (7.2)</td>
<td>76.1-80.8</td>
<td>0.67</td>
<td>0.97</td>
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<td>Emotional Functioning</td>
<td>25</td>
<td>69.3 (7.9)</td>
<td>65.6-73.1</td>
<td>68.3 (7.6)</td>
<td>64.7-71.8</td>
<td>0.77</td>
<td>0.41</td>
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<td>Social Functioning</td>
<td>5</td>
<td>51.2 (14.2)</td>
<td>43.0-59.5</td>
<td>52.7 (13.4)</td>
<td>44.6-60.9</td>
<td>1.51</td>
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<tr>
<td>School Functioning</td>
<td>5</td>
<td>34.7 (10.8)</td>
<td>29.4-40.1</td>
<td>36.7 (8.8)</td>
<td>32.0-41.3</td>
<td>2.00</td>
<td>0.08</td>
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<tr>
<td>Total Scale Score</td>
<td>25</td>
<td>67.0 (13.7)</td>
<td>61.3-72.7</td>
<td>66.5 (12.4)</td>
<td>61.7-71.3</td>
<td>0.57</td>
<td>0.59</td>
</tr>
</tbody>
</table>

Higher values equal better health-related quality of life. Effect sizes designated as small (0.20), medium (0.50), and large (0.80) and comparisons with healthy children scores

**Comorbidities Outcomes: Increased Risk of Obesity**

- Multicenter, cross-sectional study of 409 children with psoriasis
  - Excess adiposity (BMI >95th%) in:
    - 36% psoriasis
    - (did not differ by severity)
  - 20% controls
  - Odds of obesity (BMI >95th%) in psoriasis vs controls: 4.29 (95% CI: 1.96-9.39)

**Therapies for Children**

- Topical therapies
  - Mainstay for most children
  - Corticosteroids, Vitamin D analog, Calcineurin inhibitors
- Antibacterial strategies
- Phototherapy
- Mild-to-moderate plaques or guttate disease
- Retinoids
- Immunosuppressives and biologics
  - Moderate-to-severe disease, pustular or erythrodermic psoriasis

**Therapies**

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**Nail Psoriasis**

- Less common than in adults
- But cohorts report up to 40% affected

**Demographic and Clinical Features of Pediatric Psoriasis**

- Characteristic
  - Age, mean ± median
  - Male, n (%)
  - Race, n (%)
  - History of guttate streptococcus
  - Other medications*
  - Systemic
  - Phototherapy*

**Therapies**

- Traditional systemics
  - Cyclosporin
  - Methotrexate
- Biologics
  - Ustekinumab
  - Infliximab

**Increased Efficacy**

- Topicals
  - Corticosteroids, Vitamin D analogues
  - Calcineurin inhibitors

**Nail Pitting**

- More common than in adults
- Especially in severe disease
- May be associated with psoriatic arthritis

**Onycholysis**

- Erosion of nail plate
- Often associated with psoriasis
- May be progressive

**Images and Figures**

- Images and figures are not displayed in the text format.
Corticosteroids

- **Potency**
  - Low for thin skinned areas: face, folds
  - Mid to high potency for indurated plaques on acral areas

- **Vehicle**
  - Ointments improve penetration and augment potency
  - Creams and lotions (more cosmetically acceptable)

- **Schedule**
  - Rotational: 1-2 weeks on, 1-2 weeks off
  - Minimizes AEs and mitigates tachyphylaxis

- **Steroid sparing topical agents:**
  - Calcipotriene ointment, tacrolimus ointment
  - More effective as ointments
  - More effective when used BID
  - More effective on thin skinned areas

Antibacterial Strategies

- Precipitation or exacerbation of Guttate psoriasis has been linked to pharyngeal and perianal streptococcal infections
  - Proliferation of skin-homing T-cell lines in response to specific streptococcal Ag functioning as Super Ags

- Empiric systemic antibiotics, and occasionally tonsillectomy, have been recommended

- Two reviews concluded that these practices are not supported by the evidence

Phototherapy

- NB-UVB as monotherapy for guttate and thin-plaque psoriasis
- 2-3 treatments per week
- Clearance or near clearance achieved in up to 50% to 88% after 15 to 20 treatments
- Barriers: copays, time lost from school and for parents

Acitretin

- Pustular, guttate, and thin-plaque psoriasis
- Vitamin A analog, binds nuclear receptors to affect epidermal differentiation & apoptosis
- Dose range: 0.5 to 1 mg/kg/day, Avoid concomitant vitamin A supplements
- TERAUTOGEN
  - Dose dependent hyperlipidemia (TGs) in up to 25%
  - Mild transaminitis in up to 15%, resolves with discontinuation
  - Back pain, myalgias, arthralgias in more physically active patients
  - Rare AEs: corneal opacities, cataracts, retinopathy
  - Long-term, high-dose (>1 mg/kg/d) retinoid associated toxicity:
    - Premature epiphyseal closure, hyperostosis resembling diffuse idiopathic skeletal hyperostosis, calcification of anterior spinal ligaments, formation of periosteal bone, decreased bone mineral density

Methotrexate

- Plaque, pustular and erythrodermic psoriasis
- Dose range 0.2 to 0.7 mg/kg per week
- Solution for injection can be given orally
- Bone marrow toxicity May occur early (first 4-6 weeks)
  - Risk increased in children with renal disease, concurrent major illness, and concomitant use of TMP-SMX and high dose NSAIDs
- Hepatotoxicity: rarer in children
- Pulmonary toxicity: also rare

Cyclosporine

- Plaque, pustular or erythrodermic psoriasis
  - For recalcitrant disease and as a bridge to other therapies
- Dose range 3-5 mg/kg/day
  - Higher BSA to weight ratios and age-dependent differences in pharmacokinetics in children often require high end dosing
- Trough levels not typically monitored.
  - No guidelines correlating trough levels to response.
- Lowered risks of malignancy and lymphoproliferative disorders
  - When using ≤5 mg/kg/d
  - Without concomitant immunosuppressives
Biologics

- No adequate long-term safety data in children with psoriasis
  - Experience drawn from other indications
- One DBRCT for psoriasis in the US (etanercept)
- Rest are case series, case reports, and anecdotes
- No guidelines for dosing or monitoring

Other Biologics

- Case reports for use of infliximab, adalimumab and ustekinumab in children and adolescents with psoriasis
- Longer-term experience related to other anti-TNFα comes from use in JRA, Crohn’s
- PII multicenter DBRCT evaluating efficacy and safety of ustekinumab in the treatment of adolescent subjects with moderate to severe plaque psoriasis (CADMUS trial)

Etanercept

- PII DBRCT Etanercept 0.8 mg/kg weekly vs placebo in 211 patients ages 4 to 15 years over 48 weeks
  - At week 12: PASI 75 was 57% (vs 11% placebo)
  - At week 36: PASI 75 was 68% in ETN grp and 65% in placebo crossover
  - No deaths, cancers, opportunistic infections, tuberculosis, or demyelination events
- 264-week open-label extension with occurrence of adverse events as primary endpoint
  - 145/181 patients (80.1%) reported AEs
  - 5 serious AEs in 3 patients, none of which were treatment related
- FDA approved in children ≥2 yrs for inflammatory arthritides
- Longer-term safety data in these indications to support recommendations for use in the pediatric psoriasis population
- European Commission approved use of etanercept in children ≥8 yrs with chronic severe plaque psoriasis, inadequately controlled by, or intolerant of, other systemic therapies or phototherapy

Psoriatic Arthritis

- JIA
  - Most common rheumatologic disease among children
  - Prevalence: 4-8 per 100,000 children
  - 7 categories of JIA (clinical features during the first 6 months determine)
  - PsA accounts for 2%-11% of JIA
    - Incidence: ~3 cases per million
- Arthritis develops in 10%-30% of children with psoriasis
Classification Criteria: Juvenile Psoriatic Arthritis


- Arthritis before age 16
- Psoriasis preceding onset of arthritis or occurring within 15 years

Definite: criterion 1 & 2
Probable: criterion 1 plus 3 or 4
Possible: criterion 1 plus any of criterion 5-7

Arthritis before age 16 and arthritis or arthritis plus 3 of the following:
1. Dactylitis
2. Nail dystrophy
3. Family history of psoriasis (1st degree relative)
4. Enthesitis

Vancouver criteria

Arthritis before age 16
Psoriasis
Genetic predisposition by HLA system
Family history of psoriasis
DIP arthritis
Dactylitis
Onychopathy

Definite JPsA: Arthritis before age 16 and psoriasis or 3 of the following:
• Dactylitis
• Nail dystrophy
• Psoriasis-like rash
• Family history of psoriasis

Probable JPsA: Arthritis before age 16 plus any 2 minor criteria

JP sA: Early vs Late Onset

Comparison of Early-onset and Late-onset Psoriatic Juvenile Idiopathic Arthritis

<table>
<thead>
<tr>
<th>Feature</th>
<th>Early-onset PsJA</th>
<th>Late-onset PsJA</th>
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</thead>
<tbody>
<tr>
<td>Seronegativity</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>HLA-DR5</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Enthesitis</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Dactylitis</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Peak age</td>
<td>1-2 years</td>
<td>6-12 years</td>
</tr>
<tr>
<td>Gender balance</td>
<td>Male&gt;Female</td>
<td>Female&gt;Male</td>
</tr>
<tr>
<td>ANA</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>RF</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Chronic uveitis</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Acute anterior uveitis</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

Exclusions: RF+

Clinical Characteristics: Nail Dystrophy

- Nail dystrophy
  - Nail pitting most common (40%)
  - Ridging (15%)
  - Hyperkeratosis (13%)

Clinical Characteristics: Uveitis

- Anterior uveitis
  - Often bilateral
  - Asymptomatic
  - Associated with ANA+

Clinical Characteristics:

- Most have oligoarticular onset
- Arthritis are most common
- 1/3 have symmetric arthritis of hands or toes
- Age at onset: 2 peaks
  - Peak #1 before 4 years of age: girls>boys
  - Peak #2 early adolescence: boys>girls
- Family history of psoriasis in 1st or 2nd degree relatives 40%-70%
- Sacroiliac joint involvement 10%-40%
- 50% have HLA-B27
  - Girls>boys
- Enthesitis
  - Plantar fasciitis and Achilles tendon insertions are most common
  - May be associated with HLA-B27

Clinical Characteristics:

- Nail dystrophy
- Dactylitis in 50%

Clinical Characteristics: Uveitis

- Anterior uveitis
  - Often bilateral
  - Asymptomatic
  - Associated with ANA+
Treatments for Disease Involving ≤ 4 Joints

- **Initial therapy**
  - Intra-articular injections
  - NSAIDs
  - Methotrexate
    - Typically reserved for MD assessment of "high activity"
    - OR
    - Poor prognostic features (arthritis of hip, cervical spine; ankle or wrist and elevated ESR/CRP; radiographic damage)

- **Escalation of therapy**
  - TNF-α inhibitor
    - After 3-6 months of MTX if disease activity remains moderate to high


Treatments for Disease Involving ≥ 5 Joints

- **Initial therapy**
  - NSAIDs
  - Methotrexate
    - Typically reserved for MD assessment of "high activity"
    - OR
    - Poor prognostic features (arthritis of hip, cervical spine; ankle or wrist and elevated ESR/CRP; radiographic damage)

- **Escalation of therapy**
  - TNF-α inhibitor
    - After 3-6 months of MTX if disease remains active


Medication Use during Disease Course

<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Any DMARD</strong></td>
<td>39 (34)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>35 (23)</td>
</tr>
<tr>
<td>Anti-TNF agent*</td>
<td>10 (8.7)</td>
</tr>
<tr>
<td>Etanercept</td>
<td>9 (6)</td>
</tr>
<tr>
<td>Infliximab</td>
<td>2 (2)</td>
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<tr>
<td>Prednisone</td>
<td>10 (9)</td>
</tr>
<tr>
<td><strong>Any DMARD</strong></td>
<td>142 (84)</td>
</tr>
<tr>
<td>Anti-TNF agent</td>
<td>99 (58)</td>
</tr>
<tr>
<td>Intrarticular injection</td>
<td>60 (35)</td>
</tr>
<tr>
<td>Prednisone</td>
<td>56 (33)</td>
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<tr>
<td>NSAIDs</td>
<td>72 (42)</td>
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</table>

* 1 patient was treated with etanercept and infliximab.


Outcomes vs Other JIA Categories

- Less likely to achieve an ACR Pedi70 at 6 months
- At 6 months
  - 45% AJC = 0
  - 35% MD global = 0
  - 55% function (CHAQ) is 0 (normal)


Questions & Answers