Pre-Activity Question 1

How confident are you in your ability to select appropriate therapies for children with psoriasis and PsA?
1. Very confident
2. Confident
3. Somewhat confident
4. Not confident

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

Epidemiology: Psoriasis

- 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

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

Facial 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

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

Pediatrics = MORE

Flexural Surface Involvement

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

## Nail Psoriasis

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

## Demographic and Clinical Features of Pediatric Psoriasis - 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All children with psoriasis, n (%)</th>
<th>MP, n (%)</th>
<th>SP, n (%)</th>
<th>P for MP versus SP</th>
<th>Boys, n (%)</th>
<th>Girls, n (%)</th>
<th>P for male versus female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>33 (18.2)</td>
<td>14 (18.0)</td>
<td>19 (18.5)</td>
<td>.90</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>22 (12.2)</td>
<td>9 (11.5)</td>
<td>13 (12.6)</td>
<td>.77</td>
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<td></td>
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<tr>
<td>White (non-Hispanic)</td>
<td>110 (60.8)</td>
<td>49 (62.8)</td>
<td>61 (59.2)</td>
<td>&gt;.99</td>
<td>48 (65.8)</td>
<td>62 (57.4)</td>
<td>.42</td>
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<tr>
<td>Other</td>
<td>7 (3.9)</td>
<td>3 (3.9)</td>
<td>4 (3.9)</td>
<td>.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration, years, median (interquartile range)</td>
<td>73 (40.3)</td>
<td>27 (34.6)</td>
<td>46 (44.7)</td>
<td>.15</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>History of guttate streptococcus, n (%)</td>
<td>93 (51.4)</td>
<td>35 (44.9)</td>
<td>58 (56.3)</td>
<td>.13</td>
<td>41 (56.2)</td>
<td>52 (48.2)</td>
<td>.29</td>
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<tr>
<td>Nail involvement</td>
<td>71 (39.2)</td>
<td>26 (33.3)</td>
<td>45 (43.7)</td>
<td>.01</td>
<td>40 (54.8)</td>
<td>31 (28.7)</td>
<td>.001</td>
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<td>Family history of psoriasis, n (%)</td>
<td>85 (46.4)</td>
<td>30 (40.0)</td>
<td>55 (52.6)</td>
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<td>41 (56.2)</td>
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## Demographic and Clinical Features of Pediatric Psoriasis - 2

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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

Quality of Life Outcomes - 1


Quality of Life Outcomes - 2

PedsQL™ 4.0 Generic Core Scales scores for pediatric plaque psoriasis patient sample and comparisons with healthy children scores

<table>
<thead>
<tr>
<th>PedsQL™ Scales</th>
<th>Number of Items</th>
<th>Pediatric Plaque Psoriasis (n=208)</th>
<th>Healthy (n=5079)</th>
<th>Difference</th>
<th>Effect Size</th>
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</thead>
<tbody>
<tr>
<td>Total Score</td>
<td>23</td>
<td>76.5 (17.4)</td>
<td>83.6 (12.5)</td>
<td>8.4***</td>
<td>0.67</td>
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<tr>
<td>Physical</td>
<td>8</td>
<td>82.5 (18.0)</td>
<td>87.8 (13.2)</td>
<td>5.3***</td>
<td>0.41</td>
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<tr>
<td>Emotional</td>
<td>5</td>
<td>67.1 (24.3)</td>
<td>78.7 (18.5)</td>
<td>12.1***</td>
<td>0.67</td>
</tr>
<tr>
<td>Social</td>
<td>5</td>
<td>80.7 (18.6)</td>
<td>84.5 (16.7)</td>
<td>4.3***</td>
<td>0.26</td>
</tr>
<tr>
<td>School Functioning</td>
<td>5</td>
<td>70.2 (19.7)</td>
<td>81.3 (16.1)</td>
<td>11.1***</td>
<td>0.89</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)


Quality of Life Outcomes - 3

Poorer HRQOL than children with diabetes

Comparable HRQOL to children with arthritis and asthma


Comorbidity Outcomes: Increased Risk of Obesity

- Multicenter, cross-sectional study of 409 children with psoriasis
- Excess adiposity (BMI > 95th %) in:
  - 38% psoriasis
  - 20% controls
- Odds of obesity (BMI > 95th %) in psoriatic vs controls: 4.29 (95% CI: 1.96-9.39)
  - Severe psoriasis: 4.92 (2.20-10.99)
  - Mild psoriasis: 3.60 (1.56-8.30)


Therapies for Children

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

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

Other topical agents

- 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

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
- TERATOGEN
- 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 epiphysial 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 erythrodermis 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

Etanercept - 2

- 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

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
- Pilli multicenter DBRCT evaluating efficacy and safety of ustekinumab in the treatment of adolescent subjects with moderate to severe plaque psoriasis (CADMUS trial)

Etanercept - 1

- Pilli DBRCT Etanercept 0.8 mg/kg weekly vs placebo in 211 patients ages 4 to 16 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

Biologics

- At present, TNF-α inhibitors carry black-box warning for increased risk of malignancy in the pediatric population
- 48 reports of cancer, half of which were lymphomas, in patients ≤18 years starting TNF-α inhibitors
- Reports in adolescents and young adults who develop hepatosplenic T-cell lymphoma while taking TNF-α inhibitor in combination with azathioprine or 6-mercaptopurine
Psoriatic Arthritis

Psoriatic Arthritis: Epidemiology

- Juvenile idiopathic 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

JIA = juvenile idiopathic arthritis.

Classification Criteria: Juvenile Psoriatic Arthritis

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

Vancouver criteria: Southwood et al. (1990)
- Arthritis before age 16 and arthralgia or arthritis plus any of the following:
  - Dactylitis
  - Nail pitting
  - Family history of psoriasis
- Probable (PsA): Arthritis before age 16 plus any of criterion 5-7
- Possible (PsA): Arthritis before age 16 plus any of criterion 5-7

International League of Associations for Rheumatology criteria (ILAR) (2004)
- Arthritis before age 16
- Arthritis or arthralgia plus 2 of the following:
  - Dactylitis
  - Nail pitting
  - Family history of psoriasis
  - Probable (PsA): Arthritis before age 16 plus any of criterion 5-7
  - Exclusions: RF+

JPas: Early vs Late Onset

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

<table>
<thead>
<tr>
<th>Feature</th>
<th>Early-onset PsA</th>
<th>Late-onset PsA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sacroilitis</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>8-12 years</td>
</tr>
<tr>
<td>Gender balance</td>
<td>Female:male</td>
<td>Female: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>+</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

AN = antinuclear antibody; HLA = human leukocyte antigen; PsA = psoriatic juvenile idiopathic arthritis; RF = rheumatoid factor. Adapted from [10,23].
Clinical Characteristics: Nail Dystrophy

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

Clinical Characteristics: Dactylitis

- 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”
    - 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”
    - 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>
<th></th>
<th>Total Cohort = 115 (%)</th>
<th>Total Cohort = 170 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any DMARD</td>
<td>39 (34)</td>
<td>142 (84)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>35 (23)</td>
<td>99 (58)</td>
</tr>
<tr>
<td>Anti-TNF agent*</td>
<td>10 (8.7)</td>
<td>60 (35)</td>
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<tr>
<td>Etanercept</td>
<td>9 (8)</td>
<td>56 (33)</td>
</tr>
<tr>
<td>Infliximab</td>
<td>2 (2)</td>
<td></td>
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<tr>
<td>Prednisone</td>
<td>10 (9)</td>
<td></td>
</tr>
</tbody>
</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% AUC = 0
  - 35% MD global = 0
  - 55% function (CHAQ) is 0 (normal)


Post-Activity Question 1

How confident are you in your ability to select appropriate therapies for children with psoriasis and PsA?

1. Very confident
2. Confident
3. Somewhat confident
4. Not confident

Questions & Answers