

# Pediatric psoriasis: an update

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**Abstract:** Pediatric psoriasis consists broadly of 3 age groups of psoriatic patients: infantile psoriasis, a self-limited disease of infancy, psoriasis with early onset, and pediatric psoriasis with psoriatic arthritis. About one-quarter of psoriasis cases begin before the age of 18 years. A variety of clinical psoriasis types are seen in childhood, including plaque-type, guttate, erythrodermic, napkin, and nail-based disease. Like all forms of auto-immunity, susceptibility is likely genetic, but environmental triggers are required to initiate disease activity. The most common trigger of childhood is an upper respiratory tract infection. Once disease has occurred, treatment is determined based on severity and presence of joint involvement. Topical therapies, including corticosteroids and calcipotriene, are the therapies of choice in the initial care of pediatric patients. Ultraviolet light, acitretin and cyclosporine can clear skin symptoms, while methotrexate and etanercept can clear both cutaneous and joint disease. Concern for psychological development is required when choosing psoriatic therapies. This article reviews current concepts in pediatric psoriasis and a rational approach to therapeutics.

**Keywords:** psoriasis, autoimmunity, *Streptococcus*, etanercept, calcipotriene, topical corticosteroids

## Introduction

Psoriasis vulgaris is a common dermatologic disorder seen in about 3.5% of the population.<sup>1</sup> One-third of psoriasis cases in a dermatology center are pediatric.<sup>2</sup> Psoriasis is a T-cell mediated chronic inflammatory disorder of the skin characterized by hyper-proliferation of keratinocytes and consequent red scaly skin plaques. Pediatric onset psoriasis is somewhat different than adult disease, as pharyngitis, stress, and trauma are more common triggers of disease activity than in adulthood.<sup>3,4</sup> Despite the differences in pediatric psoriasis, the therapies used for pediatric psoriasis are essentially the same as those used in adulthood, with dosage and strength reductions calculated based on age, weight, and available formulations. This article looks at a rational approach to the diagnosis and management of pediatric psoriasis, with a careful focus on those aspects of disease unique to the pediatric patient.

## Demographics

About one-third of psoriasis vulgaris cases are seen in the pediatric age group.<sup>2</sup> Most children manifest with plaque-type psoriasis vulgaris (68.6%) in similar patterns to adult patients, with lesions localized to the scalp, post auricular region, elbows, and knees. Guttate disease is more common in pediatric than adult patients, seen in 28.9% of 277 children in a Chinese survey. Other patterns can be observed in

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childhood, including erythroderma (1.4%), pustular disease including palmoplantar pustular psoriasis (1.1%), and mucosal/glossitis can be observed as pediatric patterns of cutaneous psoriasis.<sup>5</sup> Diaper involvement is very common in infancy, but involvement of the groin is uncommon in older children. Inverse psoriasis with involvement of the folds of the skin (axillae, inner thighs) represents a small minority of children. Additionally, nail psoriasis can be noted in the setting of plaque-type psoriasis vulgaris, psoriatic arthritis, or with isolated nail disease, the last sometimes being called trachyonychia, although this is controversial. Involvement of joints with psoriatic arthritis is less prevalent in younger patients; however, it does occur in childhood disease and should be considered in the differential of pediatric arthritis.<sup>4</sup> The annual incidence of psoriasis has been noted to have doubled from 1970 to 2000, but pediatric incidence has not been noted to be increasing.<sup>6</sup> Psoriasis was not noted in a pediatric population survey of children aged 6 to 11 years in Taiwan, but in China the average age of pediatric psoriasis patients in China was noted to be 11 years, and median age of onset 10 years.<sup>5,7</sup>

Differences of onset between females and males have varied from study to study, with a male to female ratio of 1:1<sup>8</sup> in the largest survey of 1262 children seen from 1981 to 1995 in a children's hospital in Australia. In adulthood, female psoriatic arthritis patients suffer greater disability than males, but gender differences in childhood have not been reported.<sup>9</sup> The only ethnic variance in psoriasis vulgaris that has been described is a reduction noted among Inuit people, suggesting that diets high in omega three fatty acids appears to have a preventive effect on psoriatic onset.<sup>10</sup>

## Pathogenesis

The exact pathogenesis of psoriasis has not been completely elucidated; however, it is known to have a genetic basis, as 23.4% to 71% of children will have a family history of psoriasis<sup>3,8</sup> and psoriasis is more common in identical than fraternal twins (65% to 72% vs 15% to 30%).<sup>11,12</sup> HLA-Cw6 has been known to be a susceptibility gene in psoriasis.<sup>12</sup>

It is understood that upper respiratory infections are a common cause of disease onset in childhood, with 14.8% having upper respiratory infections<sup>3,8</sup> and 21.3% being pharyngeal culture positive for group A beta hemolytic streptococcus (*Streptococcus pyogenes*). The guttate psoriasis subset may have been linked to inflammatory focus in about two-thirds of cases, and is not caused by a specific subtype of group A beta hemolytic streptococcus, but rather by a host-specific response.<sup>2,13,14</sup> Cross-reactivity of keratinocytes

antigens with streptococcal antigens is thought to initiate psoriatic disease in this setting.<sup>15</sup>

Other infections that have been noted in psoriatic disease are presence of staphylococcal superantigens<sup>16</sup> and HPV DNA.<sup>17</sup>

No single gene has been found to be responsible for psoriasis vulgaris. A series of genes have been isolated in which mutations have been associated with psoriatic disease, including IL12-B9 (1p31.3), IL-13 (5q31.1), IL-23R (1p31.3), HLABW6 PSORS6 STAT2/IL-23A (12q13.2), TNFAIP3 (6q23.3), and TNIP1 (5q33.1). These genes play a role in Th2 cell and Th17 cell activity as well as NF- $\kappa$ B signaling, demonstrating both a role for Th2 and Th17 lymphocytes in the pathogenesis of psoriatic disease. Th17 cells have been noted in psoriatic lesions, as have collections of Th2 and Th1 cells.<sup>12,18,19</sup> Susceptibility loci for psoriasis may be shared with Crohn's disease (IL-12B and IL-23R) and ulcerative colitis (IL-23R). As a result, patients with Crohn's disease are 5 times more likely to develop psoriasis than other members of the population.<sup>12</sup>

## Relationship to autoimmunity

Psoriasis is one of more than 80 autoimmune conditions that have been described. Autoimmunity encompasses a broad spectrum of medical diseases in which the body forms an immune reaction against a normal organ, the most common being thyroid disease. Physicians with an interest in learning about the broad spectrum of autoimmunity can access some information on the topic from the National Institutes of Health.<sup>20</sup>

Many patients with psoriasis will have other autoimmune conditions, often of the skin, including morphea<sup>21</sup> and vitiligo vulgaris (sometimes this association is familial).<sup>22</sup> Family history of psoriasis and other forms of autoimmunity can be noted in patients with psoriasis and in patients with a personal history of other autoimmune diseases such as multiple sclerosis.<sup>23</sup> The concurrent incidence of autoimmune thyroiditis in adults has been reported in the literature to be variable, but there is no literature on co-morbid thyroid disease in pediatric psoriasis patients. One Italian study looking at adult patients with psoriatic arthritis (n = 80) and age-matched controls, demonstrating a greater incidence of thyroid disease in psoriatic arthritis patients, especially when the psoriatic arthritis patients had concomitant rheumatoid arthritis and in males with psoriatic arthritis.<sup>24</sup> Other studies have not demonstrated significant increases of thyroiditis markers in adult patients with psoriasis vulgaris compared to age-matched controls.<sup>25</sup>

Based on the conflicting data, annual thyroid screening has not been shown to be warranted in children; thyroid screening and screening for autoimmune thyroid disease should be performed in the setting of psoriatic arthritis, as there are some data to support an association of thyroiditis and psoriatic arthritis, and when psoriasis occurs in the presence of other autoimmune diseases such as vitiligo which have been associated which have a stronger association with thyroid disease.<sup>26</sup>

## Clinical characteristics and diagnosis (Table 1)

Psoriasis vulgaris occurs in a variety of clinical types, each of which is listed in Table 1. A few clinical features of psoriasis that are pertinent during physical examination include 1) the isomorphic response or Koebner phenomenon, which is occurrence of lesions in areas of trauma, 2) altered pigmentation with lesional clearance, 3) the Auspitz sign – pinpoint bleeding at the base of scale that has been removed, and 4) presence of nail pitting, which can aid in diagnosis of the disease.<sup>27</sup>

Severity grading for psoriasis is usually based on surface area and presence and co-morbid psoriatic arthritis. The Psoriasis Area and Severity Index (PASI) can be used to assess severity (Table 2). Others will divide disease into mild if less than 3% body surface area, moderate 3% to 10% body surface area, and severe >10% body surface area.<sup>28</sup>

## Differential diagnosis

The differential diagnosis of psoriasis includes other papulosquamous disorders of childhood including lichen planopilaris, psoriasiform ID reactions, nummular dermatitis, pityriasis rosea, and pityriasis rubra pilaris. Biopsy can be helpful in differentiating psoriasis from these other illnesses.

## Treatments

The treatments of psoriasis have expanded over the past decade; however the use of topical therapy in childhood is the first line of treatment for skin-limited disease, in combination with a trial of oral antibiotics where indicated. With chronicity of illness and in more severe cases, systemic therapy and phototherapy are added to help induce remission. Significant psychological disturbances are seen in children with psoriasis, no matter what the surface area.<sup>29</sup> Disease, although cutaneous, should be treated more aggressively when it is causing psychological disturbance, to improve quality of life.

## Topical therapy

Topical therapies for pediatric psoriasis include over-the-counter agents such as tar and salicylic acid, the latter of which aids in removal of hyperkeratosis. Tar has been a controversial medication in pediatric psoriasis, especially when combined with ultraviolet light in the Goeckermann regimen, because of demonstrable genotoxic risk, including chromosomal aberrations in peripheral lymphocytes and release of heat shock protein.<sup>30</sup> Prescription agents for psoriasis vulgaris in childhood include anthralin,<sup>31</sup> topical corticosteroids, topical calcipotriene with or without topical corticosteroids, and topical calcineurin inhibitors. Below the age of 12 years there have been no topical agents approved specifically by the FDA for treatment of psoriasis vulgaris in childhood. Off-label usage has been well described in the literature for childhood psoriatic disease, and all of the topical agents mentioned appear effective at times for pediatric psoriasis. Formulations chosen and strengths should be determined based on patient age, PASI score, quality of life, and patient age.

Anthralin 1% or dithranol are rarely used for localized areas and can cause localized irritation.<sup>31</sup> Topical clobetasol has been approved for use in children ages 12 and over in some formulations and can be quite effective for use in psoriatic lesions in adolescents, but runs a risk of atrophy because of class I status.<sup>32</sup> In pediatric psoriasis topical corticosteroids are usually prescribed similarly to prescriptions in atopic dermatitis of childhood. Low- to mid-potency corticosteroids, class 5–7, are chosen for facial and intertriginous lesions, while mid-potency class 2–4, are chosen for extremities and the scalp.<sup>33</sup> Topical corticosteroids run a risk of local atrophy and systemic absorption, the latter becoming more likely if used for larger surface areas. Topical calcipotriene<sup>34</sup> or calcitriol can be used for pediatric psoriasis, the latter being well tolerated for sensitive skin.<sup>35</sup> Side effects are generally limited to local intolerance or irritation. Systemic absorption and alteration of calcium levels are a theoretical risk; however, they are unlikely if used on limited body surface area. Topical calcineurin inhibitors, tacrolimus 0.3% ointment,<sup>36</sup> and pimecrolimus 1% can be beneficial for pediatric psoriasis, particularly in sites where atrophy is of risk, such as the face, intertriginous areas, and groin. Use in children under the age of 2 years is not recommended by the FDA.

## Phototherapy

Phototherapy is a safe and effective treatment for children old enough to stand still in a phototherapy booth, particularly

Table 1 Clinical variants of psoriasis vulgaris in childhood

Type of psoriasis	Typical clinical appearance	Diagnostic features and tests	Co-morbidities	Differential diagnosis	Treatment considerations
Plaque-type psoriasis	Erythematous plaques with micaceous scale in typical areas: Scalp extending to forehead, postauricular, elbows, knees, umbilical and buttocks	Clinical diagnosis can generally be made. Nail pitting can be noted as a clue to the diagnosis of psoriasis in children. Biopsy when need will demonstrate thickened epidermis with neutrophils in the horny layer the spongiform pustules of Kogoj and the subcorneal microabscess of Munro (collections of neutrophils in the epidermis)	Recent pharyngitis, specifically with <i>Streptococcus</i> , may precipitate disease. Pharyngeal bacterial culture or ASO testing can be helpful. Secondary infection with <i>S. aureus</i> can be noted. Other forms of autoimmunity can be seen. In the setting of obesity, disease severity can be a marker of cardiovascular risk	Nummular dermatitis Tinea capitis ID reaction Pityriasis rubra pilaris Lichen planopilaris Atopic dermatitis (overlap can rarely be seen)	Treatments must be tailored to the age of the patient, quality of life issues, and surface area affected. Systemic agents and phototherapy may be needed in moderate to severe disease
Guttate psoriasis	Annular localized erythematous to salmon colored plaques with hyperkeratosis, sometimes micaceous. Commonly noted on the trunk, abdomen and back	Clinical diagnosis is often possible. Biopsy is similar to that of plaque-type psoriasis	Recent pharyngitis, specifically with <i>Streptococcus</i> may precipitate disease. Pharyngeal bacterial culture or ASO testing can be helpful	Nummular dermatitis Pityriasis rosea ID reaction Tinea corporis Pityriasis rubra pilaris	Oral antibiotics are often used initially due to presumptive infectious precipitating factors and for anti-inflammatory capabilities (erythromycin, cephalosporins). Systemic agents and phototherapy may be needed in moderate to severe disease.
Inverse psoriasis	Localization of erythematous, sometimes macerated thick plaques to the folds of the skin, including axillae and groin. Can be associated with plaque type psoriasis in other sites	Although clinical diagnosis is often possible, similarity to other diseases may require biopsy for differentiation	Secondary infection with <i>Candida</i> and/or <i>Streptococcus</i> may require cutaneous culture and usage of topical anti-infectives	Intertrigo Erythrasma Tinea corporis	Topical medications should be non-steroidal or low-potency topical corticosteroids to avoid atrophy of the occluded skin. Oral or topical anti-infectives should be added where appropriate
Nail psoriasis	Classic: Pitting, oil spots, subungual hyperkeratosis Trachyonychia: Extensive pitting and subungual hyperkeratosis	Ruling out tinea infection or secondary candidal infection of the nail bed is needed when subungual hyperkeratosis is present. Fungal culture and nail plate biopsy	Secondary infections should be ruled out including pseudomonas, onychomycosis or candidal infections	Onychomycosis Lichen planus Pityriasis rubra pilaris	After treatment of any fungal super-infection, topical corticosteroids with tazarotene or calcipotriene can be applied to the paronychia skin. Intralesional kenalog can also be used in the same region to reduce the subungual inflammation
Napkin or diaper psoriasis	Macerated shiny erythema of the groin region including the folds and the genital skin	Biopsy may need to be performed	Bacterial and fungal cultures may be needed for suspected secondary infections or perianal strep	Diaper dermatitis Candidal diaper dermatitis Allergic contact dermatitis	Mild topical corticosteroids with or without topical anti-candidal agents can be helpful Barrier therapy with zinc oxide pastes reduces secondary irritant reactions

Erythroderma	Generalized erythema and thickening of the skin, sometimes with hyperkeratosis	Two biopsies are generally required from separate sites to differentiate psoriatic erythroderma from other causes of erythroderma in childhood	Fever, chills and malaise can accompany erythroderma, making bacteremia a possible co-morbidity which should be ruled out conclusively	Causes of erythroderma in childhood include: Atopic dermatitis Pityriasis rubra pilaris Mycosis fungoides Staph scalded skin syndrome	Topical anti-inflammatory agents can be used, however, systemic anti-inflammatory agents (never steroids orally) are often required to control the severe and extensive disease
Pustular psoriasis	Erythroderma accompanied by sterile pustule formation, sometimes localized to the distal extremities, sometimes generalized. Prior history of oral steroid usage may be noted	Biopsy is often needed and bacterial culture of the pustules. ASO titers can be drawn to rule out streptococcal precipitant	Secondary bacterial infection or tinea should be ruled out	Blistering distal dactylitis Tinea infection with <i>Tinea mentagrophytes</i> Herpetic whitlow	Topical corticosteroids are often ineffective and systemic agents or topical PUVA may be needed
Mucosal/oral psoriasis	Annular plaques on the tongue may be noted in patients with psoriasis	Generally a clinical diagnosis	Rarely has any morbidity	Geographic tongue Aphthosis Lichen planus White sponge nevus	No therapy is usually needed, however topical medicaments in an oral base can be used when needed

**Abbreviation:** ASO, antistreptolysin O.

teenagers with extensive disease. Generalized or hand foot therapy, either narrowband UVB (NBUVB) or psoralens and UVA (PUVA), can be used. Topical psoralens are preferable to oral psoralens because of the difficulty of wearing protective eyewear for a 24-hour time period after oral psoralens. As PUVA has been associated with long-term carcinogenicity in psoriatics, NBUVB is likely safer in childhood cases.<sup>36-38</sup>

## Systemic agents

Systemic agents should be saved for severe psoriasis, disabling psychological ramifications, and psoriatic arthritis. Usage of systemic agents is generally limited to a 6-month time period for immunosuppressants such as cyclosporine, acitretin or methotrexate. Longer usage periods have been observed to be safe in rheumatoid arthritis patients on etanercept, however usage beyond a one year time period has not been well assessed in pediatric psoriatics. Methotrexate has been used for pediatric patients for decades longer than etanercept. Oral antibiotics are the systemic therapy of choice in early disease, due to their superior side effect profile.

## Oral antibiotics

Oral antibiotics can be useful in treating psoriasis vulgaris, particularly in the setting of positive oral pharyngeal cultures, presence of perianal bacterial dermatitis, pustular psoriasis,<sup>39</sup> or in guttate psoriasis of childhood (but not adult guttate disease), as these settings are linked to a bacterial precipitant of psoriasis.<sup>40</sup> Use of oral antibiotics has demonstrated mixed results, many authors finding mixed results with use.<sup>41</sup> Oral antibiotics are often used at first sign of psoriasis in children, but no placebo-controlled trials have compared antibiotics with placebo. Furthermore, the ideal regimen of antibiotic use is unknown.

## Methotrexate

When pediatric psoriasis becomes chronic and severe (PASI > 10), systemic therapy provides the major source of improvements in pediatric quality of life. The original psoriatic systemic therapy used for extensive psoriasis is methotrexate, which has been used for over 3 decades for pediatric psoriasis and pediatric psoriatic arthritis. Two recent publications have evaluated cohorts of pediatric psoriatic patients treated with methotrexate. Methotrexate (dosed at 0.2 to 0.7 mg/kg/week) provides excellent clearance or PASI 75 (>75% PASI reduction) in most children.<sup>42</sup> While monitoring blood counts and liver function tests are required, liver function alteration is rarely observed and

**Table 2** Psoriasis Area and Severity Index (PASI) score

To determine PASI score, establish grade and severity and then use site-based weighting

Grade: surface area as below (0–6)

0% of involved area, grade: 0

- <10% of involved area, grade: 1
- 10%–29% of involved area, grade: 2
- 30%–49% of involved area, grade: 3
- 50%–69% of involved area, grade: 4
- 70%–89% of involved area, grade: 5
- 90%–100% of involved area, grade: 6

Severity: 0–4 none to severe

Erythema (redness)

Induration (thickness)

Desquamation (scaling)

**Notes:** The sum of all three severity parameters is then calculated for each section of skin, multiplied by the area score for that area and multiplied by weight of respective section (0.1 for head, 0.2 for arms, 0.3 for body and 0.4 for legs).

seems to be most associated with obesity and consequent fatty liver changes.<sup>43,44</sup> Methotrexate also has the advantage over cyclosporine in clearing or improving psoriatic arthritis. Therapy is started with a small dosage (7.5 mg) followed by escalating dosages while sequentially monitoring labs.<sup>42</sup> Addition of folic acid supplementation helps protect against pancytopenia and macrocytic anemia.<sup>45</sup>

## Cyclosporine A

Cyclosporine A, a systemic immunosuppressant used originally for prevention of transplant rejection, can be dosed for oral use at 3 to 5 mg/kg can improve cutaneous symptomatology in pediatric psoriatic patients. Alterations in renal function with altered serum urea nitrogen and creatinine and high blood pressure can be observed. Therefore, close monitoring is warranted. Risks of malignancy and lymphoproliferative disorders seem to be minimal in children treated for skin diseases due to limited courses of therapy and dosages that are below 5 mg/kg/day.<sup>42,46</sup>

## Retinoids

Acitretin orally 0.5 to 1 mg/kg per day has been used for disorders of cornification and psoriasis with good results. Because of teratogenicity, oral contraceptives in girls of childbearing age should be used concurrently, and for 3 years after drug discontinuation. Short-term side effects, such as elevations in lipids or alterations in blood counts, require monitoring. Long-term changes such as bony abnormalities can occur and treatment periods should be limited, using a cyclic approach. Bony evaluation may be required.<sup>42</sup>

## Biologics

Etanercept and infliximab, injectable and intravenous, respectively, tumor necrosis factor alpha (TNF- $\alpha$ ) inhibitor therapies have been used for a decade in pediatric autoimmune diseases including rheumatoid arthritis,<sup>47</sup> TNF- $\alpha$  receptor 1-associated periodic syndrome without fever (TRAPS),<sup>48</sup> juvenile idiopathic arthritis,<sup>49</sup> and Crohn's disease. Safety and efficacy data are available for up to 8 years' use in juvenile rheumatoid arthritis. Long-term use did not increase serious side effects. An ACR 70 was achieved by most children treated, with no cases of tuberculosis, opportunistic infections, malignancies, lymphomas, lupus, demyelinating disorders, or death. Long-term improvements on bony disease in arthritis of childhood have been demonstrated with etanercept.<sup>50</sup>

A recent clinical trial described the results of a phase II clinical trial of etanercept in 211 pediatric psoriatics aged 4 to 17 years using a 12-week, double-blind treatment phase, with a 24-week open-label phase. At week 12, 57% of patients achieved a PASI 75 compared with 11% of placebo-treated patients ( $P < 0.001$ ) and a PASI 90 was achieved in 27% of patients compared with 7% of placebo. Clearance was lost in 29 of 69 patients who withdrew in weeks 36 to 48 weeks. Four serious adverse events including 3 serious infections in children treated with open-label phase, all of which resolved.<sup>51</sup> These data significantly expand upon prior anecdotal data describing efficacy of etanercept for pediatric psoriasis.<sup>52</sup> Anecdotal report of a single case that failed etanercept responding to infliximab, suggests this may be an alternative therapy in etanercept-resistant cases.<sup>53</sup>

## Natural supplements

A common question asked by parents of children with psoriasis is "What dietary changes or natural supplements can I give my child to improve their skin disease?" While natural supplements or dietary alterations cannot cure psoriasis, they can improve disease severity. The best-known supplement is fish oil, rich in omega-3 fatty acids. The ingestion of this agent for psoriasis is based upon its preventive effects in the Inuit population. Oral and intravenous supplementation of omega-3 and, less effectively, omega-6 fatty acids<sup>54</sup> have been found effective in psoriatic adults, possibly through alterations in production and alterations in arachidonic acid (20:4 omega 6) and docosapentaenoic acid.<sup>55</sup> Fish meals 4 to 6 times per week can mimic the effects of omega-3 supplementation.<sup>56</sup>

Indigo naturalis, a traditional Chinese medicine, can be formulated into topical ointment with anecdotal reports of good results in childhood psoriasis when used for 8 weeks.<sup>57</sup>

## Conclusions

Recent advances in genetics and the unraveling of the processes responsible for psoriatic disease are making possible considerable advancements in the treatment of pediatric psoriasis.

## Disclosures

The author reports no conflicts of interest in the development of this work.

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