Practical Approach to Treating Children with Psoriasis

a report by

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Treating psoriasis in childhood is a challenge. Whereas psoriasis in the adult is one of the most prevalent inflammatory dermatoses, psoriasis is less frequent in pre-pubertal children, and in paediatric dermatology clinics these patients are vastly outnumbered by patients diagnosed with other skin diseases such as atopic dermatitis. Novel treatments are usually first introduced into the adult psoriatic population and implementation in paediatric patients is slower, if it happens at all. Also, children are by no means small adults and special consideration and caution must be exercised when treating an individual who is not yet fully developed and who will likely require long-term therapy. However, the up-side is that there may be a theoretical potential to interfere with the natural course of the disease by intervening at an early stage of the disease process. We are not yet there, but the rapid progress in our understanding of psoriasis pathophysiology means there is reason for optimism.

There is substantial variation across – and even within – countries in terms of who manages children with psoriasis: paediatricians, general practitioners and dermatologists may all be involved and, if joint problems are present, these children will generally be managed within paediatric rheumatology. Obviously, therapy traditions and treatment choices may differ depending on where the patient is being monitored.

Clinical Presentation

The onset of psoriasis can occur at all ages, but there is a peak in adolescence, with onset before 25 years of age in roughly 50% of patients. Manifestations of psoriasis prior to puberty are less common and the diagnosis can be uncertain at an early age. Lesions are typically less infiltrated and less scaly and can easily be mistaken for eczema. The phenotypic presentation of psoriasis varies widely, but some phenotypes are more common in childhood. The diagnosis relies on clinical examination and there is still no laboratory test to confirm diagnosis. Tissue histopathology can support the diagnosis, but usually reflects the clinical presentation and, if a trained dermatologist remains uncertain, the micromorphology may be equally uncertain. There seems to be no apparent gender difference; psoriasis appears to be roughly equally common in both sexes. Females typically have their onset one to two years before males, reflecting earlier onset of puberty.[1]

In infants, the first manifestation of psoriasis is commonly nappy rash, sometimes with disseminated lesions. The diagnosis at this stage can be uncertain and sometimes the psoriasis diagnosis is established in retrospect. In addition to nappy rash, the two most common phenotypes in pre-pubertal children appear to be plaque psoriasis and psoriasis in the scalp (see *Figure 1*). A positive family history of psoriasis can be very helpful in children since the genetic background is much stronger in early-onset psoriasis compared with late-onset psoriasis. Guttate psoriasis is a distinctive phenotypic presentation of acute widespread droplet psoriasis lesions usually occurring in young adolescent patients. The guttate phenotype is strongly associated with concurrent throat infections where streptococci is commonly isolated from swabs. In some patients, recurrent throat infections are associated with exacerbations of the disease.[2–4] These patients should receive antibiotics to eradicate their throat infection, which may have a beneficial effect on their skin lesions.[5,6] Tonsillectomy is claimed to help some patients with frequent flares;[6–8] the hypothesis is that there is molecular mimicry, with T cells in the tonsils and in the skin sharing receptor re-arrangement and reacting to an hitherto unknown antigen.[9] The prognosis of guttate psoriasis may be more favourable, but a proportion of patients will develop chronic plaque lesions.[10] However, reliable structured long-term follow-up of these patients is lacking.

General Therapeutic Considerations

The paediatric patients are quite a heterogenous population, comprising the diverse biological ages from infancy up to adolescence, which likely encompass different attitudes to the disease and require distinct treatment modalities. Also, within the same age group, disease severity varies considerably. In the subpopulation of children with severe psoriasis, there is increased awareness of the need to control disease activity to hopefully limit subsequent complications and co-morbidities. In these patients, systemic treatments should be considered. Established treatment guidelines are missing for childhood psoriasis.

Topical Treatments

Topical treatments are central in paediatric psoriasis care. Most patients can be managed with topicals, although compliance may be a limiting factor. Emollients and moisturisers by themselves have a marginal yet beneficial effect in reducing redness and scaling of the skin lesions in most patients. In cases of thick severe scaling, salicylic acid preparations are helpful; however, they should be avoided in infants and small children since percutaneous

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Figure 1: 13-year-old Boy with Severe Plaque Psoriasis with Scalp Involvement

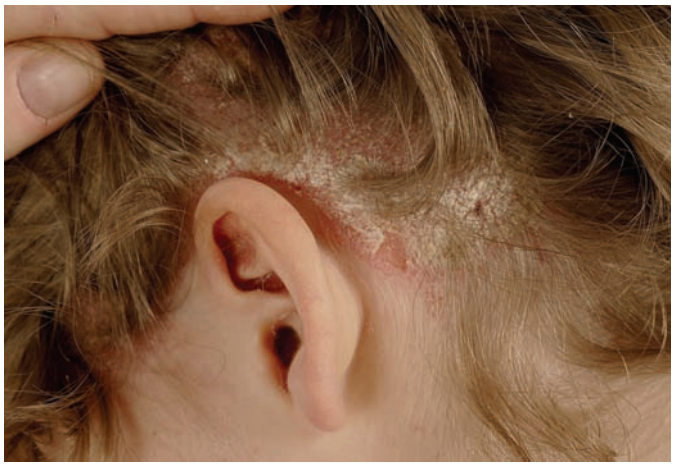
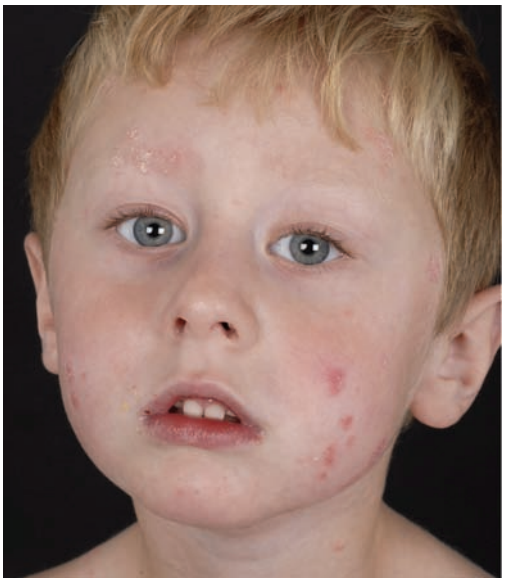


Figure 2: Five-year-old Boy with Facial Involvement of Psoriasis



salicylate intoxication with serious complications can occur.[11] Thus, general skin care is important, but as with all topicals, compliance in children may be a problem in chronic disease. Parent education and 'psoriasis schools' have an important role in establishing and maintaining disease control.

For decades, tar compounds were the standard treatment for psoriasis as well as for eczema. With the advent of topical corticosteroids, treatment with tar compounds became the exception, but they are still used occasionally. The effect seems moderate, but tar-containing shampoos in particular are popular with some patients. The characteristic odour may be a limiting factor in some patients.

Anthralin (dithranol) is an established and effective antipsoriatic treatment for stable plaque psoriasis.[12] In outpatients it is used as short-contact therapy for 10–60 minutes to control side effects such as irritation and staining of clothes and surrounding skin. Anthralin is available in different concentrations, and to obtain optimal effect the concentration should be increased every few days. As athralin treatment requires detailed hands-on instruction for compliance and is rather cumbersome and time-consuming, it is less commonly used today.

Topical steroids have changed the lives of psoriasis and eczema patients. Onset of the anti-inflammatory effect is rapid and itching, if present, is relieved. However, continuous treatment is usually needed, and when treating psoriasis high-potency steroids are required, which carries a risk of skin atrophy and also the potential for systemic effects with suppression of the hypothalamic–pituitary–adrenal axis if an extensive body area is involved. Upon abrupt discontinuation of topical steroids there is usually rather quick recurrence of lesions, which may require slow tapering of the application frequency. Still, topical corticosteroids are valuable, and for some body locations where medium-potency rather than high-potency corticosteroids should be used – such as intertriginous areas, the genitals and the face – there are few if any effective alternatives. Fixed combinations of corticosteroids with topical vitamin D_3 analogues are more efficacious and have become a popular and convenient therapy in adult psoriasis. The advantage is that only one application per day is required, which likely improves compliance and reduces the need for several different ointments/creams. However, in children the combination is only starting to be used, and long-term safety using the high-potency corticosteroid in combination needs monitoring and close surveillance.

Today, the vitamin D_3 analogues calcipotriol, tacalcitol and calcitriol are first-line topical treatments, particularly in plaque psoriasis. In contrast to older treatments, calcipotriol in particular has been thoroughly evaluated in children with psoriasis. In a controlled trial using the ointment base as comparator, a 52% reduction of Psoriasis Area and Severity Index (PASI) was established using calcipotriol versus 37% PASI reduction in the control group.[13] Calcipotriol should be applied twice daily and is available as a cream as well as an ointment. The cream is cosmetically more attractive for use during the day, while the ointment could preferably be applied at night. The ointment is rather effective in removing scales, which reduces the need for exfoliative pre-treatment. A major concern with using calcipotriol, especially in children, has been a potential impact on serum calcium. However, trials have shown that when applying twice daily, a dose of 45g/week/m^2 is established as safe in children two to 14 years of age.[14] Calcipotriol can be combined with ultraviolet (UV) treatment, which enhances the efficacy. Side effects include burning and irritation, especially in sensitive skin areas such as intertriginous regions and the face.

Topical retinoids are not widely used in childhood psoriasis. Tazarotene is approved for adult psoriasis, but seems not to have gained popularity in the paediatric population, possibly due to only moderate efficacy and a tendency for local irritation.

Phototherapy

Phototherapy has been and still is a core treatment for psoriasis in the adult population. Over the years, substantial efforts have been undertaken to optimise the antipsoriatic effect from UV light, culminating (so far) in psoralen UVA (PUVA), which was used extensively during the 1980s. PUVA combines UVA with the photosensitising chemical psoralen; this treatment is highly efficacious in controlling psoriasis in the majority of patients. However, the effect comes at the cost of a high risk of skin cancer after a certain accumulated dose. PUVA was hardly ever used in children due to the cancer risk, which was perceived to be even higher in the young. Today, the standard phototherapy in psoriasis is narrow-band UVB, making optimal use of the UV wavelengths that have a maximal effect on psoriasis lesions. When starting a course of UV therapy, treatments should be given two to three times a week to obtain maximal effect, and the result should be evaluated after 20–30

Generally, UV is used with caution in children. In the very young it is simply not practically possible to administer UV treatment. Even in older children there is a restrictive attitude that extensive UV exposure may prime the skin to photoageing and subsequent cancer development. This is particularly valid in severe disease, where there may be a need for systemic immunosuppressive therapy. However, in children who do not have an apparent risk phenotype for skin cancer (freckles, red hair and fair skin), UV treatment may be used by itself and in combination with topical treatments such as calcipotriol.[15]

Psoriasis on the Face

The face is not considered a predilection site for psoriasis, but appears to be more commonly affected in children than in adults and can present as rather infiltrated plaques around the eyes (see *Figure 2*). Also, in association with guttate psoriasis, involvement of the face is commonly seen with less demarcated and thinner lesions. Treatment of facial lesions represents particular problems: the incentive to treat is usually high because of the visible location, but first-line topical treatment with calcipotriol is not suitable due to irritation and risk of eczematous flare. Here, corticosteroids of medium potency remain the most commonly used topical agents. During recent years, a new class of immunomodulatory agent, calcineurin inhibitors, has been launched for topical treatment of atopic eczema, and facial involvement is a primary indication. These compounds – tacrolimus and pimecrolimus – are now also being used in the treatment of psoriasis, particularly in facial lesions.[16,17] However, even though these drugs do not cause skin atrophy and constitute a valuable addition to our treatment options, a word of warning may be appropriate. According to the label, these drugs should not be combined with phototherapy and sun exposure since long-term effects on immune surveillance in the skin are unknown.

Systemic Treatments

In severe disease that cannot be sufficiently controlled with topical treatment, systemic therapy must be considered. Admittedly, assessment of disease severity does not rely on absolute measurements, but entails an integration of the extent and management of skin lesions, associated joint disease and also an assessment of the impact of the disease on the child's quality of life and development. Systemic antipsoriatic drugs established for psoriasis in adults are also used in children, even though controlled clinical trials are scarce.

Retinoids

The retinoid compounds acitretin and etretinate were introduced more than two decades ago and were initially widely prescribed in severe psoriasis. Subsequently, retinoids have been found to be most effective in pustular psoriasis (see *Figures 3* and *4*).[18] Side effects include cheilitis, xerosis and hair loss. In children, retinoids can influence bone development and lead to premature epiphyseal closure, which must be monitored during long-term treatment.[19] Also, retinoids are highly teratogenic, which limits their use in fertile females. However, retinoid treatment does not entail general immunosuppression and they are in fact protective against skin cancer development in at-risk individuals, which is an advantage for the proportion of psoriasis patients heavily exposed to UV therapy. Retinoids can be combined with UV therapy, thereby reducing the dose of retinoids as well as of UV light.[20]

Ciclosporin

Ciclosporin inhibits activation of T cells via inhibition of calcineurin. It has proven efficacy and it is preferentially used to control severe pustular and/or erythrodermic psoriasis. There are no controlled trials in children with psoriasis, but there are reports showing its efficacy.[21] The initial dose of ciclosporin is 3–5mg/kg/day, which should be gradually tapered to the lowest possible dose. With long-term use there are substantial side effects such as renal dysfunction and hypertension, and in patients exposed to UV treatment there is a significant risk of skin cancer development.[22] Given the increasing options for systemic treatments, it is our view that ciclosporin should be reserved for use during limited periods as a rescue drug to suppress severe flares of psoriasis.

Figure 3: Nine-year-old Boy with Pustular Psoriasis

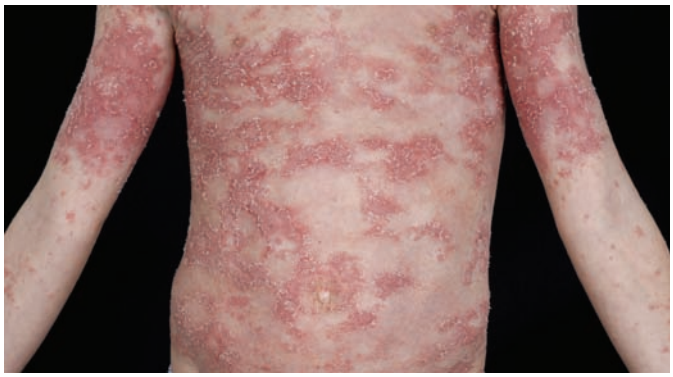
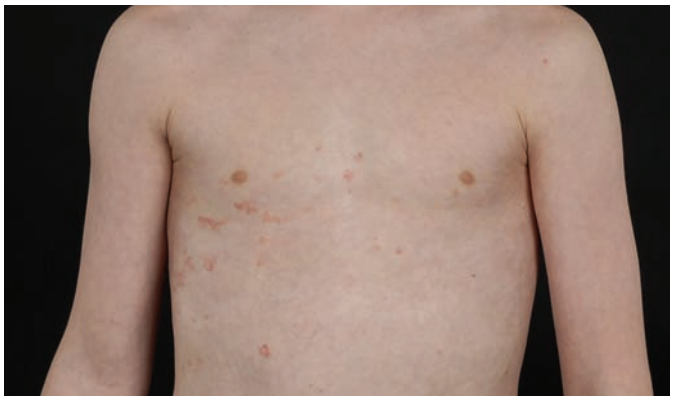


Figure 4: Same Patient as in *Figure 3* After Three Months of Acitretin Treatment (0.5mg/kg/day)



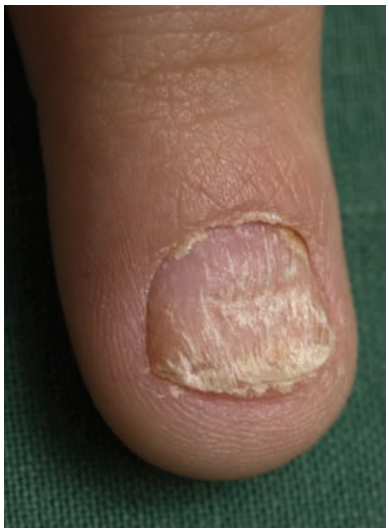
Methotrexate

In many countries, methotrexate is the first-line systemic treatment for moderate to severe psoriasis in the adult. Side effects and major concerns include hepatotoxicity and bone marrow depression, as well as teratogenicity. Thus, regular monitoring is needed to identify signs of organ toxicity. Obviously, as with other systemic drugs, controlled trials in children are lacking, even though the drug is used and reports describing efficacy are available.[23,24] Recommended doses in children are 0.2–0.4mg/kg once weekly. Nausea can be a limiting factor, and for these patients injectable methotraxate is now available. Folate supplementation to reduce potential side effects is recommended according to guidelines in adults.[25,26] The regimen for folic acid varies, but 5mg per day every day except the day on which methotrexate is given is widely used in dermatological practice.

Biologics

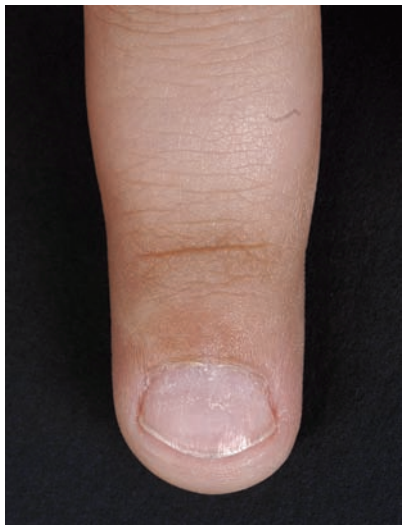
Etanercept is a soluble tumour necrosis factor (TNF) receptor, and is the first biologic drug approved for use in paediatric psoriasis;[27] it had already been approved for treating children with juvenile rheumatoid

Figure 5: 10-year-old Boy with Plaque Psoriasis and Involvement of All Fingernails



The patient had an extremely strong family history of psoriasis and psoriatic arthritis in first-degree relatives.

Figure 6: Same Patient as in *Figure 5* After Five Months of Subcutaneous Etanercept Treatment



Excellent clinical response – complete remission of skin lesions (not shown) and nail dystrophy.

arthritis. *Figures 5* and *6* show a 10-year-old boy with plaque psoriasis and involvement of all fingernails. The subject had an extremely strong family history of psoriasis and psoriatic arthritis in first-degree relatives. He was treated with etanercept subcutaneously for five months, with excellent clinical response that resulted in complete remission of skin lesions and nail dystrophy. Side effects of etanercept include injection reactions that are usually transient. Adverse events noted during the study were three cases of infections in roughly 200 patients who received etanercept during the study. After withdrawing the drug at week 36, 42% of patients had lost the response by week 48. Undoubtedly, the approval of etanercept for childhood psoriasis will be followed by other biologic drugs, and there are already case reports documenting efficacy using the monoclonal anti-TNF antibodies infliximab and adalimumab.[28] The deepening understanding of psoriasis pathogenesis will lead to the development of new drugs, such as the anti-p40 antibody targeting the subunit shared between the interleukin (IL)-23 and IL-12 receptor, which is already showing impressive efficacy in adult psoriasis.

Concluding Remarks

The increasing awareness of psoriasis as a systemic disease with the risk of significant co-morbidities associated with high disease activity will likely lead to more active treatment in children with severe disease. Also, widespread psoriasis may have a major psychosocial impact, leading to stigmatisation and a profound impairment of quality of life. Safety issues obviously remain vital in the paediatric population, and post-marketing surveillance of both long-term efficacy and side effects of novel drugs will be critical. Even though there is as yet no cure for psoriasis, the rapid development of new and effective treatments for psoriasis is highly encouraging. ■

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