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REVIEW

Childhood guttate psoriasis: an updated review

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Abstract

Background: Guttate psoriasis is common and affects 0.5–2% of individuals in the paediatric age group. This review aims to familiarize physicians with the clinical manifestations, evaluation, diagnosis and proper management of guttate psoriasis.

Methods: A search was conducted in July 2023 in PubMed Clinical Queries using the key term "guttate psoriasis". The search strategy included all observational studies, clinical trials and reviews published within the past 10 years. The information retrieved from the search was used in the compilation of the present article.

Results: Guttate psoriasis typically presents with an abrupt onset of numerous, small, scattered, tear-drop-shaped, scaly, erythematous, pruritic papules and plaques. Sites of predilection include the trunk and proximal extremities. There may be a history of preceding streptococcal infection. Koebner phenomenon is characteristic. Guttate psoriasis may spontaneously remit within 3–4 months with no residual scarring, may intermittently recur and, in 40–50% of cases, may persist and progress to chronic plaque psoriasis. Given the possibility for spontaneous remission within several months, active treatment may not be necessary except for cosmetic purposes or because of pruritus. On the other hand, given the high rates of persistence of guttate psoriasis and progression to chronic plaque psoriasis, some authors suggest active treatment of this condition.

Conclusion: Various treatment options are available for guttate psoriasis. Triggering and exacerbating factors should be avoided if possible. Topical corticosteroids alone or in combination with other topical agents (e.g. tazarotene and vitamin D analogues) are the most rapid and efficient treatment for guttate psoriasis and are therefore the first-line treatment for mild cases. Other topical therapies include vitamin D analogues, calcineurin inhibitors, anthralin, coal tar and tazarotene. Ultraviolet phototherapy is the first-line therapy for moderate-to-severe guttate psoriasis, as it is more practical than topical therapy when treating widespread or numerous small lesions. Systemic immunosuppressive and immunomodulatory therapies (e.g. methotrexate, cyclosporine, retinoids, fumaric acid esters and biologics) may be considered for patients with moderate-to-severe guttate psoriasis who fail to respond to phototherapy and topical therapies.

Keywords: biologics, Koebner phenomenon, methotrexate, pruritus, tear-drop-shaped papules/plaques, topical corticosteroids, ultraviolet phototherapy.

Citation

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Introduction

Psoriasis is a chronic, inflammatory, immune-mediated, cutaneous disorder. Guttate psoriasis is a distinct variant of psoriasis that typically presents with an abrupt onset of numerous, erythematous, 'drop-like' scaly papules and plaques on the extremities and trunk, classically triggered by streptococcal infection.[1,2] This narrative review aims to familiarize physicians with the clinical manifestations, evaluation, diagnosis and proper management of guttate psoriasis.

Methods

A search was conducted in July 2023 in PubMed Clinical Queries using the key term "guttate psoriasis". The

search strategy included all observational studies (including case reports and case series), clinical trials (including open trials, non-randomized controlled trials and randomized controlled trials) and reviews (including narrative reviews, clinical guidelines and meta-analyses) published within the past 10 years. UpToDate, Google and Wikipedia were also searched to enrich the review. Additional articles were culled by going through the reference lists. Only papers published in the English literature were included in this review. The information retrieved from the search was used in the compilation of the present article.

Review

Epidemiology

Worldwide, psoriasis affects 0.5–2% of individuals in the paediatric age group.[3] Several variants of psoriasis are recognized: plaque psoriasis also known as psoriasis vulgaris is most common, followed by guttate psoriasis.[4–6] Other variants are uncommon and include erythrodermic psoriasis, pustular psoriasis and inverse psoriasis.[6,7] Guttate psoriasis is most frequently seen in children, adolescents and young adults, although individuals of other age groups may also be affected.[2] The sex ratio is approximately equal.[2,8] A family history of psoriasis is common,[6,9] and a family outbreak of guttate psoriasis and simultaneous occurrence in monozygotic twins have been reported.[10,11]

Aetiopathogenesis

The aetiopathogenesis is multifactorial and complex. Guttate psoriasis is a chronic T cell-mediated inflammatory disease due to an altered balance between T helper 1 (T_H1) and T_H2 cells, transcription factor genes and their products.[12] In guttate psoriasis, T_H1 cytokines, such as IL-2, IL-17, interferon-γ (IFNγ) and tumour necrosis factor (TNF), are upregulated whereas T_H2 cytokines, such as IL-10, are downregulated.[13,14] IL-2 stimulates growth of T cells, IFNγ inhibits apoptosis of keratinocytes, and TNF increases proliferation of proinflammatory cytokines and adhesion molecules.[15] Adhesion molecules further stimulate T cells to produce cytokines.[16] A complicated interplay between genetic and environmental factors may contribute to disease development.[3,8] A family history of psoriasis in a first-degree relative is present in approximately 30% of patients with childhood-onset psoriasis.[17] The concordance rate in monozygotic and dizygotic twins is approximately 70% and 20%, respectively.[18] The *PSORS1* gene has been mapped to chromosome 6p; individuals with the *PSORSI* gene are more prone to psoriasis.[8] Guttate psoriasis is strongly associated with certain human leukocyte antigens (HLA) such as HLA-Cw 6 (particularly, HLA-Cw*0602 allele), HLA-B13 and HLA-B17.[19–27]

Streptococcal infection, such as streptococcal tonsillopharyngitis (most common), streptococcal perianal dermatitis, streptococcal vulvovaginitis and streptococcal balanoposthitis, may be associated with guttate psoriasis.[28–45] In one study, a preceding streptococcal infection was found nine times more often in individuals with guttate psoriasis than in other variants of psoriasis.[37] Typically, guttate psoriasis develops 2–4 weeks after a streptococcal infection[46,47] and is more likely to develop in patients with pre-existing plaque psoriasis.[48] It is postulated that streptococcal infection precipitates guttate psoriasis through streptococcal superantigen-driven activation of cutaneous lymphocyte-associated antigen (CLA)-positive lymphocytes, inducing mediators such as IL-17.[49–56] In this regard, it has been shown that streptococcal pyrogenic exotoxins and streptococcal M proteins act as superantigens.[47,53]

Other bacterial infections (e.g. *Staphylococcus aureus*, *Helicobacter pylori* and *Borrelia burgdorferi*),[57,58] viral infections (e.g. COVID-19, HIV, human papillomavirus, hepatitis B virus, hepatitis C virus, varicella-zoster virus, Epstein–Barr virus, chikungunya virus and coxsackievirus),[58–71] fungal infections (e.g. *Malassezia* species and *Candida albicans*),[58,72] vaccinations (e.g. COVID-19, influenza and BCG),[73–80] Kawasaki disease,[81,82] trauma (e.g. physical or chemical injury to the skin),[83,84] medications (e.g. dupilumab, certolizumab, efalizumab, brentuximab vedotin, imatinib, IFNα2b, propranolol, digoxin, clonidine, quinidine, chloroquine, hydroxychloroquine, lithium, cimetidine, carbamazepine, fluoxetine, olanzapine and 3,4-methylenedioxy-methamphetamine also known as ecstasy),[85–100] family or personal history of psoriasis[101–103] and stressful life events[9,84] are suggested as triggering factors.[6] In a study of 1017 patients with psoriasis, 663 (65.2%) patients had onset of psoriasis before 40 years of age and 354 (34.8%) had onset on or after 40 years of age.[104] Patients with onset of psoriasis before 40 years of age had a significantly higher likelihood of both a family history of the disease and guttate psoriasis (p=0.005).[104]

Histopathology

Histopathological findings include epidermal spongiosis (in early lesions), epidermal acanthosis, hyperkeratosis, parakeratosis, elongation of the rete ridges, presence of neutrophils in the parakeratotic mound in the epidermis, dilated capillaries in the papillary dermis, perivascular lymphocytic infiltrate in the dermis and hypogranulosis.[2,8,105]

Clinical manifestations

Guttate psoriasis typically presents with an abrupt onset of numerous, small, scattered, tear-drop-shaped ('guttate'), scaly, erythematous papules and plaques (Figures 1 and 2).[1,2,8] Lesions are usually widespread and

Figure 1. Guttate psoriasis presenting as numerous erythematous, scaly papules on the back.

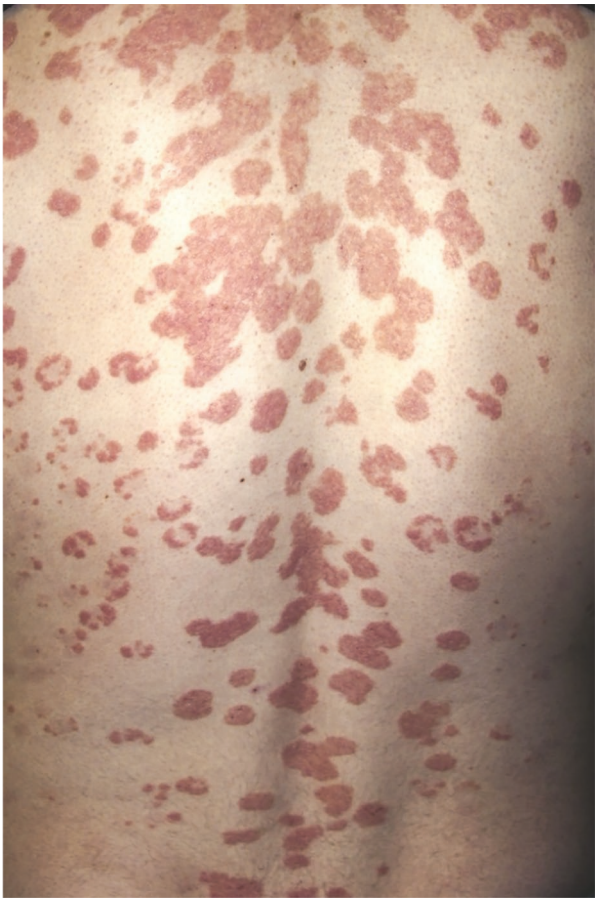
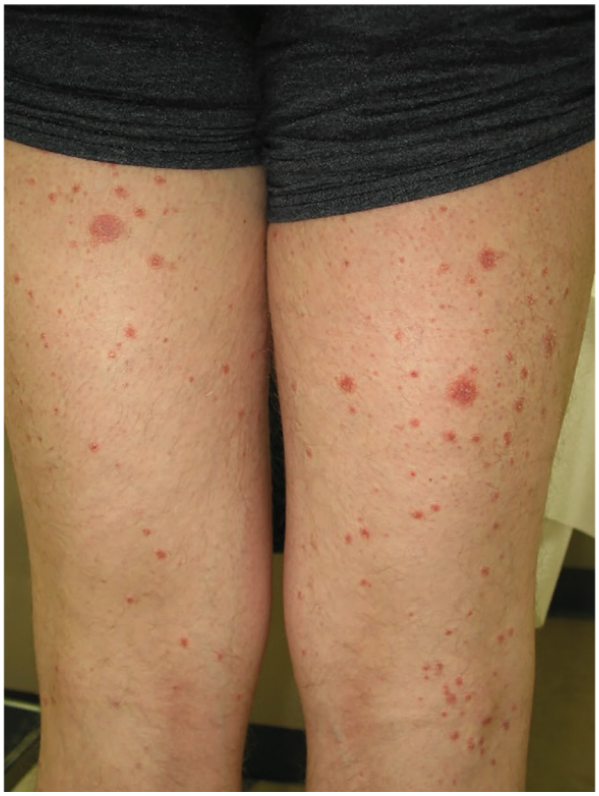


Figure 2. Guttate psoriasis presenting as numerous erythematous, scaly papules on posterior thighs.



an individual lesion typically measures 2–6 mm in diameter.[8] Sites of predilection include the trunk and proximal extremities (Figures 1 and 2).[106] The scalp, face, ears, hands and feet may also be affected but the palms and soles are usually spared.[106,107] Lesions are usually pruritic.[107,108]

Unlike other variants of psoriasis, guttate psoriasis is most frequently seen in children (particularly in adolescents) than in adults.[109,110] In guttate psoriasis, there may be a history of preceding streptococcal infection such as streptococcal pharyngitis (Figure 3) and streptococcal perianal dermatitis (Figure 4).[106] The eruption may arise de novo in patients without a history of psoriasis or as a new variant of psoriasis in patients with pre-existing plaque psoriasis.[48] As with all variants of psoriasis, Koebner phenomenon is characteristic.[8]

Diagnosis

The diagnosis is mainly clinical based on the characteristic physical findings (widespread, numerous, small, scattered, scaly, erythematous, oval papules and plaques on the trunk and extremities), especially if there is a preceding history of streptococcal infection. The diagnosis can be aided by dermoscopy, which typically shows a dull-red or bright-red background, with dotted vessels distributed in a diffuse pattern, and diffuse white scales.[111–113] Laboratory tests are usually not necessary in patients without symptoms and signs of streptococcal infection. In patients with features of streptococcal infection, culture from an appropriate site (e.g. throat and perianal area) and measurement of serum antistreptococcal antibody titres (such as anti-DNase, anti-hyaluronidase and antistreptolysin-O) can be helpful.[36] The antibody titres usually peak at 3–6 weeks and remain elevated for months.[36] A skin biopsy is usually not necessary but may be considered if the diagnosis is in doubt.

Differential diagnosis

Guttate psoriasis should be differentiated from other variants of psoriasis such as plaque psoriasis (sharply demarcated, erythematous plaques with adherent silvery micaceous scales; lesions usually symmetrically distributed and pruritic; Auspitz sign; sites of predilection include the knees, elbows and lower back), erythrodermic psoriasis (generalized erythema with overlying silvery scaly plaques involving all or most of the body

Figure 3. Enlarged left tonsil with tonsillar exudate in a 10-year-old boy with streptococcal pharyngitis. This was followed by the development of guttate psoriasis 2 weeks later.

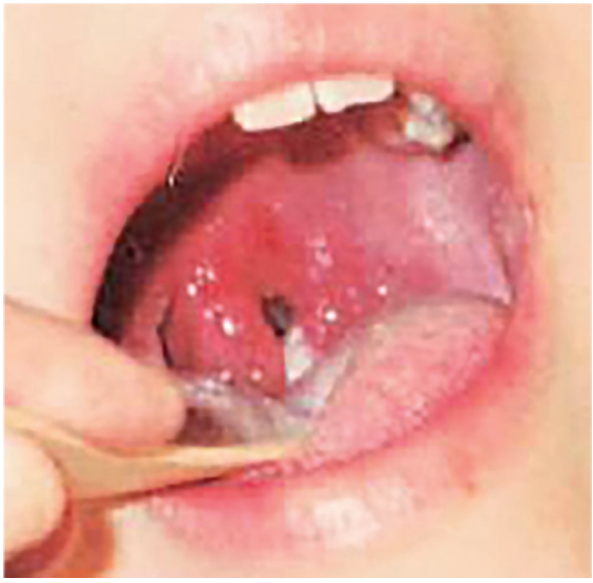
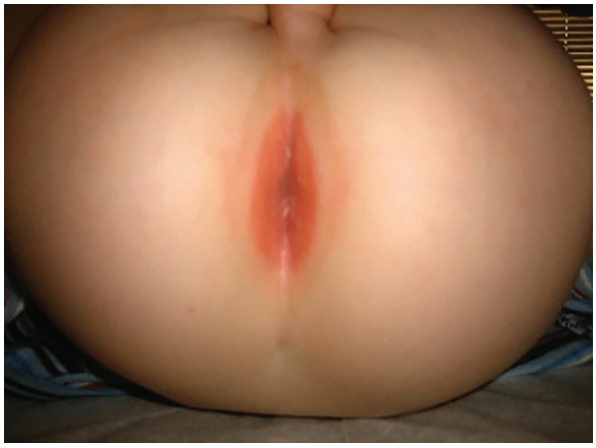


Figure 4. A 4-year-old boy with streptococcal perianal dermatitis. The child developed guttate psoriasis 3 weeks later.



surface area; pruritus; massive desquamation), pustular psoriasis (widespread erythema and scaling with macroscopic sterile pustules) and inverse psoriasis (smooth, well-demarcated, shiny, erythematous plaques involving intertriginous or flexural areas).[114–117]

Other differential diagnoses include pityriasis rosea (asymptomatic 'herald' or 'mother' patch, followed by a generalized, symmetrical eruption 4–14 days later; inward-facing scale (collarette); characteristic 'fir tree' or 'Christmas tree' appearance on the back), tinea corporis (sharply circumscribed, well-demarcated, erythematous annular plaques; scaly raised border with central clearing), tinea versicolor (hyperpigmented and hypopigmented macules/patches in fair-skinned and dark-skinned individuals, respectively), nummular eczema (well-demarcated, markedly pruritic, coin-shaped, symmetrical, eczematous, scaly lesions) and pityriasis lichenoides chronica (recurrent crops of polymorphic red-brown papules with overlying mica-like scales).[118–127] The distinctive features of these conditions usually allow a straightforward diagnosis to be made.

Complications

The condition is cosmetically unsightly and may have an adverse impact on quality of life for affected children and their families.[128] Post-inflammatory hypopigmentation or hyperpigmentation may occur.[106] Comorbidities include atopic dermatitis, allergic contact dermatitis, alopecia areata, vitiligo, obesity, diabetes mellitus, hypertension, hyperlipidaemia, dyslipidaemia, cerebrovascular disease, ischaemia heart disease, Crohn's disease, rheumatoid arthritis and depression.[129–131]

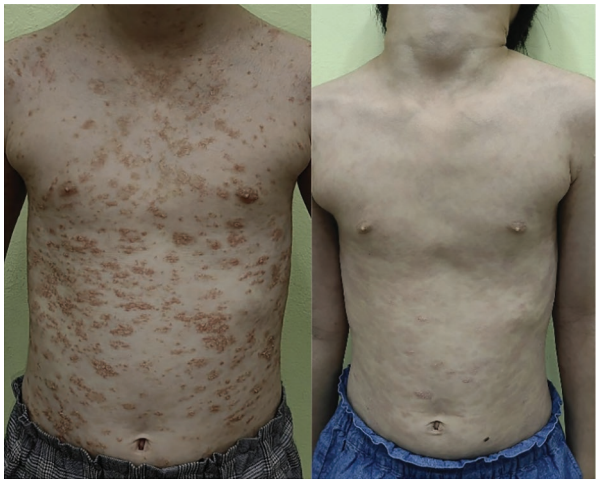
Prognosis

In general, guttate psoriasis has a better prognosis than other variants of psoriasis.[132] Guttate psoriasis may spontaneously remit within 3–4 months with no residual scarring (Figure 5), may intermittently recur and, in 40–50% of cases, may persist and progress to chronic plaque psoriasis.[133] In one study of 181 children with plaque psoriasis, children with severe psoriasis (35.9%) were more likely to have a past history of guttate psoriasis than did those with mild psoriasis (21.8%) (p=0.02).[133] In another study of 120 patients with new-onset guttate psoriasis, 50 (49.1%) patients had persistent psoriasis[110] and 21 (17.5%) patients progressed to chronic plaque psoriasis.[110]

Management

Given the possibility for spontaneous remission within several months, active treatment may not be necessary except for cosmetic purposes or for the management of pruritus. On the other hand, because in 40–50% of cases, guttate psoriasis may persist and progress to chronic plaque psoriasis, some authors suggest active treatment of this condition.[2] In this regard, patient age, severity of the disease, impact of the disease on quality of life, presence of comorbidities, response to previous treatment and patient preferences should be considered. Although there is currently no cure for guttate psoriasis, various treatment options are available (Box 1), which can help to relieve the symptoms and signs and to clear skin lesions of guttate psoriasis. Although many treatment modalities have been extensively studied

Figure 5. A 14-year-old boy with guttate psoriasis (a) and following spontaneous remission of guttate psoriasis 4 months later (b).



Box 1. Treatment options for guttate psoriasis.

A. General measures
   1. Avoidance of triggering and exacerbating factors
   2. Optimal skin care
B. Topical therapies
   1. Corticosteroids
   2. Vitamin D analogues
   3. Calcineurin inhibitors
   4. Anthralin
   5. Coal tar
   6. Tazarotene
C. Phototherapy
D. Systemic therapies
   1. Methotrexate
   2. Cyclosporine
   3. Retinoids
   4. Fumaric acid esters
   5. Biologics
E. Antistreptococcal interventions
   1. Systemic antibiotic therapy
   2. Tonsillectomy

for the treatment of plaque psoriasis, these treatment modalities have not been formally evaluated for the treatment of guttate psoriasis. As such, the current recommendations are based mainly on the results of clinical trials targeted to the treatment of plaque psoriasis.

General measures

Triggering and exacerbating factors should be avoided if possible. Scratching should be discouraged, which may lead to the development of new psoriatic psoriasis (Koebner phenomenon). Optimal skin care requires constant attention to hydration and lubrication. Emollients, moisturizers and keratolytics (e.g. urea, lactic acid, dimethicone and salicylic acid) can help to soften the scaly, hyperkeratotic surface of the affected area and are useful adjuncts to successful treatment.[134]

Topical therapies

Corticosteroids

Topical corticosteroids are the most rapid and efficient treatment for guttate psoriasis and are therefore the first-line treatment for mild guttate psoriasis.[135,136] Various delivery vehicles for corticosteroids can be employed, including lotions, sprays, creams, gels, foams and shampoos.[137] Local side-effects associated with the use of topical corticosteroids include cutaneous atrophy, depigmentation, striae, telangiectasia, steroid rosacea, acneiform eruption, perioral dermatitis, folliculitis and decreased subcutaneous adipose tissue.[138,139] Systemic side-effects associated with the prolonged use of potent topical corticosteroids include adrenal suppression, Cushing syndrome, growth retardation, osteopenia/osteoporosis, glaucoma and cataract.[139] Because of the risks of side-effects, the least potent topical corticosteroid that can control the disease should be used and the medication should be applied no more than twice a day.[139] Topical corticosteroids should be tapered, stopped or used intermittently once sufficient improvement has been obtained. Prolonged use of topical corticosteroids should be discouraged.[139] Topical corticosteroids can be used alone or in combination with other topical agents such as vitamin D analogues, tazarotene and keratolytics (e.g. lactic acid and salicylic acid).[129,140]

Vitamin D analogues

Topical vitamin D analogues (e.g. calcitriol and calcipotriene) act by promoting keratinocyte differentiation and inhibiting the proliferation of keratinocytes.[129,134] Both calcitriol and calcipotriene have been shown to be safe, effective and well tolerated for the treatment of plaque psoriasis.[141–146] The main side-effect is cutaneous irritation.[147] As transcutaneous absorption of calcitriol and calcipotriene may lead to hypercalcaemia, they should only be used once a day on less than 30% of the total body surface area.[148] Topical calcitriol and calcipotriene may be used alone or in conjunction with topical corticosteroids for the treatment of guttate psoriasis.[2] A combination of topical vitamin D analogues and topical corticosteroids has been suggested because these medications work synergistically.[149,150]

Calcineurin inhibitors

Topical calcineurin inhibitors (e.g. tacrolimus and pimecrolimus) inhibit the activity of calcineurin to dephosphorylate the nuclear factor of activated T cells, and thus interfere with the inflammatory processes of the skin.[134]

Unlike topical corticosteroids, topical calcineurin inhibitors do not decrease collagen synthesis or cause skin atrophy, depigmentation, or other skin abnormalities.[134] The most common side-effects are transient stinging or burning sensation, pruritus and erythema at the site of application during the first few days of application.[134] Although preliminary non-randomized trials showed that topical calcineurin inhibitors were effective in the treatment of childhood psoriasis, these agents have not been approved for the treatment of psoriasis, and their use for the treatment of psoriasis is off label.[134]

Anthralin

Anthralin (dithranol) has both antiproliferative and antipsoriasis-mediated inflammatory properties and has been shown to be effective in the treatment of childhood psoriasis.[151,152] Topical application of anthralin leads to improvement of psoriatic plaques and is relatively safe, with no systemic absorption.[129] The main side-effects include skin irritation and staining of the skin and clothing.[129] Anthralin should be applied strictly to the affected skin and should not come into contact with the intertriginous areas or the eyes.[134]

Coal tar

Coal tar contains substances such as phenols, polycyclic aromatic hydrocarbons and heterocyclic compounds.[134] Studies have shown that coal tar has antiproliferative, anti-inflammatory and antipruritic properties and may thus be of help in the treatment of psoriasis.[134] The strong odour, skin irritation, tendency to stain skin and clothing, and the risk of folliculitis limit the use of coal tar in the treatment of psoriasis, especially in the paediatric age group.[137] Coal tar is rarely used nowadays.

Tazarotene

Tazarotene, a vitamin A derivative, has antiproliferative and anti-inflammatory properties and has been shown to be effective for the treatment of plaque psoriasis in adults.[153] The medication is not licenced for use in children. Common side-effects include pruritus, irritation and burning sensation at the site of application.[134]

Phototherapy

Ultraviolet (UV) phototherapy is the first-line therapy for moderate-to-severe guttate psoriasis (guttate psoriasis that is refractory to topical therapy and guttate psoriasis involving more than 10% of the body surface area) due to its documented efficacy, being relatively free of serious side-effects and its ability to treat a large body surface area.[2,137] The clinical efficacy of narrow-band UVB (wavelength 311–313 nm) for the treatment of paediatric psoriasis has been demonstrated by several studies.[154–156] Studies have also shown that narrow-band UVB is more effective than broad-band UVB (wavelength 290–320 nm).[157–161] As such, narrow-band UVB is the preferred phototherapy for guttate psoriasis in children over 6 years of age.[157–161] Psoralen plus UVA (wavelength 320–400 nm) (PUVA) phototherapy has also been used for the treatment of guttate psoriasis.[162] In one randomized double-blind trial involving 88 patients with plaque psoriasis, 43 patients were treated with PUVA and 45 with narrow-band UVB.[163] PUVA was more effective than narrow-band UVB at achieving clearance of psoriatic lesions (84% *versus* 65%; p=0.02).[163] Short-term side-effects associated with the use of phototherapy include cutaneous erythema, xerosis, pruritus, blistering and pigmentation, whilst potential long-term side-effects include premature photoaging and cutaneous malignancy such as squamous cell carcinoma and possibly melanoma (particularly for PUVA).[129] Because of the greater risk for side-effects and the long-term carcinogenicity, PUVA therapy is not recommended for the treatment of psoriasis in children and adolescents.[164] Narrow-band UVB therapy appears to be safer in this regard.[164] Additionally, narrow-band UVB therapy is more convenient to use than PUVA therapy because it does not require the use of an exogenous photosensitizer.[165] Phototherapy can be used alone or, more often, in combination with topical therapies to decrease the carcinogenic risk and enhance its efficacy.[129]

Systemic therapies

Systemic immunosuppressive and immunomodulatory therapies may be considered for patients with moderate-to-severe guttate psoriasis who fail to respond to phototherapy and topical therapies.

Methotrexate

Methotrexate, a folic acid analogue, is a first-line systemic therapy for moderate-to-severe psoriasis in the paediatric age group given the medication is effective, low cost, reasonably safe and available in an oral formulation.[129,137] Studies have demonstrated the efficacy of methotrexate for the treatment of psoriasis in children.[166–168] Methotrexate can be given either orally or subcutaneously once per week.[164] The recommended dose is 10–15 mg/m^2 per week with a maximum weekly dose of no more than 25 mg per week.[164] Folic acid supplementation should be given during methotrexate therapy to reduce the risk of folic acid deficiency.[169,170] Methotrexate is much more commonly used for plaque-type psoriasis as opposed to guttate psoriasis. Side-effects associated with the use of methotrexate include nausea, loss of appetite, vomiting, abdominal pain, diarrhoea, fatigue, asthenia, alopecia, headaches, upper respiratory tract infections, bone marrow suppression, hepatotoxicity, teratogenicity and pulmonary toxicity.[2,129]

Cyclosporine

Cyclosporine, an immunosuppressant agent, inhibits the function of T cells and reduces levels of pro-inflamma-

tory cytokines.[3,129] Studies have shown that cyclosporine is effective in the treatment of recalcitrant plaque psoriasis and generalized pustular psoriasis.[171–175] Cyclosporine has a rapid onset of action with clinical improvement noted within 4 weeks.[174] The recommended oral dose is 2.5–5 mg/kg/day in two divided doses.[3] The use of cyclosporine should be considered for induction therapy of moderate-to-severe psoriasis in children who cannot tolerate or fail to respond to other systemic therapies such as methotrexate.[164] Side-effects associated with the use of cyclosporine include headache, nausea, myalgias, diarrhoea, gingival hyperplasia, hypertrichosis, arterial hypertension, hepatotoxicity and nephrotoxicity.[3,129] Cyclosporine can be used alone or, more commonly, in combination with other topical or systemic agents to reduce the duration and total dose of the two combined agents.[129] Because of the potential long-term risk of developing lymphoma and non-melanoma skin cancer, the combination of cyclosporine and phototherapy should be avoided.[129,150]

Retinoids

Retinoids are helpful for the treatment of guttate psoriasis.[176] Advantages of retinoid therapy include lack of immunosuppression and ease of administration (can be given orally).[137] The recommended oral dose is 0.25–1 mg/kg/day.[3] Side-effects include xerosis, dryness of mucosal membranes, cheilitis, skin fragility, epistaxis, headache, photosensitivity, hair thinning/loss, myalgia, hepatotoxicity, premature epiphyseal closure, bone hyperostosis and teratogenicity.[3,129] Oral retinoids should be avoided in females with childbearing potential and if they have to be given, contraception is mandatory during the course of treatment and for 3 months after cessation of treatment.[3,164] Due to the shorter half-life of isotretinoin, sometimes it is the preferred agent in females of childbearing age.

Fumaric acid esters

Several clinical trials showed that fumaric acid esters given orally are effective for the treatment of moderate-to-severe psoriasis in both adults and children.[177–182] Fumaric acid esters work by exerting immunomodulatory effects on the interaction of glutathione with dimethyl fumarate.[183,184] The medication is given orally and is well tolerated.[180] Side-effects include nausea, abdominal pain, diarrhoea, headache, flushes, pruritus, proteinuria and lymphopenia.[168,179]

Biologics

Biologic agents target and interfere with specific portions of the immune system, which may help to treat and/or prevent immune-mediated inflammatory disorders. Many randomized clinical trials have shown that biologic agents are more effective and safer than non-specific immunosuppressants for the treatment of psoriasis in both adults and children.[137] However, the high cost limits the use of these biologic agents. Biologic agents should be considered for the treatment of moderate-to-severe psoriasis in patients who cannot tolerate or do not respond to phototherapy or other systemic therapies. If there is concomitant psoriatic arthritis, there is good reason to consider biologic therapies. Biologic agents that have been used for the treatment of paediatric psoriasis include TNF inhibitors, IL-12/IL-23 inhibitors and IL-17 inhibitors.[185]

Etanercept, a TNF inhibitor, works by competitively inhibiting the binding of endogenous TNF to its receptor. The medication has the longest history of use for the treatment of childhood psoriasis and is the only biologic agent approved by the FDA for use in children as young as 4 years of age for the treatment of moderate-to-severe childhood psoriasis.[137] Although etanercept is more effective than placebo,[186] it is less effective than other biologic agents for the treatment of childhood psoriasis.[187–191] Etanercept is administered subcutaneously. The recommended dose is 0.8 mg/kg (maximum 50 mg) once weekly.[129,137]

Adalimumab, a TNF inhibitor, has been shown to be effective in the treatment of paediatric psoriasis.[192] In a double-blind study, 114 children aged 4–17 years of age with severe plaque psoriasis were randomized 1:1:1 to receive either 0.4 mg/kg/week of adalimumab every other week, 0.8 mg/kg/week of adalimumab every other week, or 0.1–0.4 mg/kg/week of methotrexate weekly.[192] After 16 weeks of treatment, more patients in the adalimumab 0.8 mg/kg/week group achieved ≥75% improvement from baseline in the Psoriasis Area and Severity Index (PASI) score than patients in the methotrexate group (58% *versus* 32%).[192] Adalimumab is administered subcutaneously. The recommended dose is 0.8 mg/kg (maximum 40 mg).[137] The first two doses are given once weekly with subsequent doses given every other week.[137,164]

Infliximab, another TNF inhibitor, has also been shown to be effective in the treatment of paediatric psoriasis.[193–196] Infliximab is administered via intravenous infusion.[194] The recommended dose is 5 mg/kg at weeks 0, 2, and 6 and every 8 weeks thereafter.[194] Compared with other TNF inhibitors, infliximab has a high rate of side-effects.[129]

Ustekinumab, an IL-12 and IL-23 inhibitor, has been shown to be effective in the treatment of plaque psoriasis, guttate psoriasis and psoriatic arthritis.[197,198] It is more effective when compared with etanercept.[199] Ustekinumab has been used with success for the treatment of moderate-to-severe psoriasis in children ≥6 years of age.[200,201] The medication is administered subcutaneously at weeks 0 and 4, and then every 12 weeks thereafter.[137,164] The recommended dose is 0.75 mg, 45 mg and

90 mg for patients weighing less than 60 kg, 60–100 kg and >100 kg, respectively.[137,164] Ustekinumab has a rapid onset of action and a convenient dosing schedule making it a promising treatment option.[129]

Ixekizumab, an IL-17A inhibitor, has been shown to be effective in the treatment of moderate-to-severe plaque psoriasis and guttate psoriasis.[202–205] In a double-blind study, 171 patients (aged 6–17 years) with moderate-to-severe plaque psoriasis were randomized 2:1 to receive ixekizumab (*n*=115) or placebo (*n*=56) every 4 weeks through week 12.[205] At week 12, 102 (89%) of 115 patients in the ixekizumab group achieved PASI 75 *versus* 14 (25%) of 56 patients in the placebo group. Studies have shown that ixekizumab has greater efficacy than other biologics such as etanercept, adalimumab and ustekinumab.[199] Ixekizumab is administered subcutaneously every 4 weeks.[137] The recommended loading dose is 40 mg, 80 mg and 160 mg for patients weighing less than 25 kg, 25–50 kg and >50 kg, respectively, with a maintenance dose of 20 mg, 40 mg and 80 mg every 4 weeks, respectively.[137]

Secukinumab, another IL-17A inhibitor, has also been shown to be effective in the treatment of moderate-to-severe plaque psoriasis and guttate psoriasis.[206–208] In a double-blind, multicentre study, 162 patients (aged 6–17 years) with severe chronic plaque psoriasis were randomized to receive weight-based low-dose secukinumab (*n*=40), weight-based high-dose secukinumab (*n*=40), etanercept (*n*=41) or placebo (*n*=41).[187] Both weight-based low-dose and high-dose secukinumab were superior to etanercept and placebo in achieving PASI 75. Studies have shown that secukinumab is more efficacious than etanercept, adalimumab and ustekinumab in the treatment of psoriasis.[199] Secukinumab is administered subcutaneously weekly for the first 5 weeks and then every 4 weeks.[137] The recommended dose is 75 mg and 150 mg for patients weighing less than 50 kg and >50 kg, respectively.[137]

Guselkumab, an IL-23 p19 subunit inhibitor, is effective in the treatment of moderate-to-severe plaque psoriasis and guttate psoriasis.[209–215] It has been shown that guselkumab is more efficacious than ustekinumab but less efficacious than secukinumab in the treatment of plaque psoriasis.[216,217] However, guselkumab is not more efficacious than ustekinumab at later time points (6–12 months). Guselkumab is administered subcutaneously. The recommended dose for the adult population is 100 mg on day 1, to be repeated 4 weeks later and then every 8 weeks thereafter. The safety and efficacy have not been established in the paediatric population.

Like guselkumab, other biologic agents, such as risankizumab, certolizumab pegol, brodalumab and tildrakizumab, have also been shown to be effective in the treatment of plaque psoriasis and guttate psoriasis in adults;[218–226] however, the safety and efficacy of these biologic agents have not been established in the paediatric group.

The most common side-effects associated with biologic therapies include reactions at the site of injection (e.g. pain, tenderness, erythema and swelling) and infections (particularly upper respiratory tract infections).[137] Some investigators are concerned that there may be an increased risk of opportunistic infections and malignancy associated with the use of biologic agents.[137] In a randomized, double-blind, multiperiod, phase III trial that compared adalimumab with methotrexate, the rates of infection were similar in the two treatment groups: 22 (56%) of 39 patients in the adalimumab group *versus* 21 (57%) of 37 patients in the methotrexate group.[227] As far as increased risk of malignancy is concerned, this has not been reported in the paediatric population.[137] Nevertheless, an increased risk of inflammatory bowel disease has been reported in patients treated with IL-17 inhibitors such as secukinumab and ixekizumab.[228,229] It is advisable that children with psoriasis who are going to receive biologic therapy should have pretreatment screening, including complete blood cell count, chest radiograph, tuberculosis screening, liver function tests, and tests for hepatitis B and C and HIV.[129]

Antistreptococcal interventions

Systemic antibiotic therapy

Systemic antibiotic therapy is indicated in patients with an acute streptococcal infection such as streptococcal tonsillopharyngitis (most common), streptococcal perianal dermatitis, streptococcal vulvovaginitis and streptococcal balanoposthitis.[36,230] Oral penicillin V is the first-line treatment. In the paediatric age group, amoxicillin is often preferred over penicillin V because of the better taste of the amoxicillin suspension and availability of amoxicillin as a once-daily extended-release and chewable tablet formulations. For patients who have a non-anaphylactic allergy to penicillin, an oral cephalosporin is an acceptable alternative.[34,231] For patients with a history of immediate, anaphylactic-type hypersensitivity to penicillin, oral clarithromycin, clindamycin and azithromycin are acceptable alternatives.[231,232]

Thus far, data from studies on whether systemic antibiotic therapy should be used in the management of established guttate psoriasis are controversial.[233] These studies were of very low quality with uncertain accuracy.[233–236] It is hoped that future large scale, well-designed, high-quality, randomized controlled studies will clarify whether systemic antibiotic therapy should be routinely used for the treatment of guttate psoriasis.

Tonsillectomy

Because tonsils are a major site of streptococcal infection, theoretically, tonsillectomy may limit the reservoir of group A β-haemolytic streptococcus (GABHS), the superantigen of which may trigger immune reactions leading to the development of guttate psoriasis. Many uncontrolled studies have shown that tonsillectomy is beneficial in the treatment of recurrent guttate psoriasis associated with recurrent GABHS tonsillitis and pharyngitis.[237–241] Thus, tonsillectomy may be a therapeutic option for selected patients with recurrent and recalcitrant psoriasis associated with recurrent GABHS tonsillitis and pharyngitis.[3] A systematic review of 20 articles published between August 1960 and September 2013 showed that 290 out of 410 patients with psoriasis experienced improvement of psoriasis after tonsillectomy.[242] These 20 articles were case reports and case series that lacked control groups. Additionally, publication bias favouring reporting of positive findings should also be considered. Further well-designed, controlled studies with long-term follow-up are necessary to evaluate the efficacy and benefits of tonsillectomy in patients with recurrent guttate psoriasis associated with recurrent GABHS tonsillitis and pharyngitis as well as to determine the type of patients who are most likely to benefit from tonsillectomy.

Conclusion

It is important for clinicians to recognize guttate psoriasis so that it can be treated appropriately. As guttate psoriasis may follow a streptococcal infection that might be treated with an antibiotic, it is important not to confuse guttate psoriasis with an eruption secondary to an allergy to the antibiotic used for the treatment of streptococcal infection. Additionally, guttate psoriasis has to be differentiated from other variants of psoriasis and conditions that mimic guttate psoriasis so that unnecessary investigations can be avoided, and appropriate treatment can be rendered. Given the possibility for spontaneous remission within several months, active treatment may not be necessary except for cosmetic purposes. For patients with mild guttate psoriasis who desire treatment, topical corticosteroids or combination products can be used as a first-line treatment. Most cases of guttate psoriasis are too extensive to treat with topical therapy. Phototherapy (particularly, narrow-band UVB) is the first-line therapy for moderate-to-severe guttate psoriasis (guttate psoriasis that is refractory to topical therapy and guttate psoriasis involving more than 10% of the body surface area). The disadvantage of phototherapy is that phototherapy requires three visits a week for months. Systemic immunosuppressive and immunomodulatory agents may be considered for patients with guttate psoriasis who fail to respond to topical therapies and phototherapy, or when phototherapy is inaccessible. Systemic immunosuppressive and immunomodulatory agents are quite expensive unless the treatment can be limited to 3–4 months. The use of systemic antibiotics and tonsillectomy is controversial for routine treatment of guttate psoriasis. Systemic antibiotic therapy is indicated for the treatment of active GABH infection.

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