Diagnosis and management of psoriasis

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Abstract

Objective To provide primary care clinicians with an up-to-date and practical overview of the diagnosis and management of psoriasis.

Quality of evidence PubMed, MEDLINE, EMBASE, and Cochrane databases were searched for relevant meta-analyses, randomized controlled trials, systematic reviews, and observational studies about the diagnosis and management of psoriasis.

Main message Psoriasis is a chronic, multisystem inflammatory disease with predominantly skin and joint involvement. Beyond the physical dimensions of disease, psoriasis has an extensive emotional and psychosocial effect on patients, affecting social functioning and interpersonal relationships. As a disease of systemic inflammation, psoriasis is associated with multiple comorbidities, including cardiovascular disease and malignancy. The diagnosis is primarily clinical and a skin biopsy is seldom required. Depending on the severity of disease, appropriate treatment can be initiated. For mild to moderate disease, first-line treatment involves topical therapies including corticosteroids, vitamin D3 analogues, and combination products. These topical treatments are efficacious and can be safely initiated and prescribed by primary care physicians. Patients with more severe and refractory symptoms might require further evaluation by a dermatologist for systemic therapy.

Conclusion Many patients with psoriasis seek initial evaluation and treatment from their primary care providers. Recognition of psoriasis, as well as its associated medical and psychiatric comorbidities, would facilitate timely diagnosis and appropriate management with effective and safe topical therapies and other medical and psychological interventions, as needed. More severe and refractory cases might warrant referral to a dermatologist for further evaluation and possible systemic therapy.

Psoriasis is a chronic disease that is estimated to affect approximately 1.7% of the Canadian population.[1] Psoriasis is a multisystem inflammatory disease with predominantly skin and joint involvement. It has a bimodal age of onset (16 to 22 and 57 to 60 years)[2] and affects both sexes equally.[3] Pathogenesis is multifactorial, involving dysregulated inflammation and genetic associations.[4] Beyond the physical dimensions of disease, psoriasis has an extensive emotional and psychosocial effect on patients; it can result in stigmatization, poor self-esteem, and increased stress, affecting social functioning and interpersonal relationships.[1]

Despite its considerable effect on quality of life, psoriasis is underdiagnosed and undertreated.[5,6] This calls for a better understanding of the disease and the available treatment options to provide optimal management of psoriasis. Because many patients seek initial evaluation and treatment at the primary care level, family physicians are well positioned to provide diagnosis and initiate treatment of psoriasis. In this review, we provide an update and the latest evidence for a practical and comprehensive overview of the diagnosis and treatment of psoriasis.

EDITOR'S KEY POINTS

- Psoriasis is a chronic, multisystem inflammatory disease that is underdiagnosed and undertreated despite its prevalence and considerable effect on quality of life.
- Beyond skin and joint involvement, psoriasis is also associated with an array of important medical and psychiatric comorbidities, including psoriatic arthritis, cardiovascular disease, diabetes, malignancy, depression, and anxiety, that require timely therapy to improve long-term outcomes.
- Severity of disease can be helpful in guiding management. A variety of topical treatments are safe and effective for mild to moderate disease. More severe disease might require systemic therapy, including phototherapy, acitretin, methotrexate, cyclosporine, or biologic therapy.

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Quality of evidence

Using the term *psoriasis,* we searched the PubMed, MEDLINE, EMBASE, and Cochrane databases for meta-analyses, randomized controlled trials (RCTs), systematic reviews, and observational studies. We included studies published in English between January 1991 and December 2015. We also manually searched the references of relevant articles retrieved.

Main message

Diagnosis. The diagnosis of psoriasis is primarily clinical. There are different clinical types of psoriasis (**Table 1**),[1] the most common of which is chronic plaque psoriasis, affecting 80% to 90% of patients with psoriasis. The hallmark of classic plaque psoriasis is well-demarcated, symmetric, and erythematous plaques with overlying silvery scale (**Figure 1**). Plaques are typically located on the scalp, trunk, buttocks, and extremities but can occur anywhere on the body. Patients might demonstrate nail involvement, which can present without concomitant plaques (**Figure 2**). Active lesions might be itchy or painful. Psoriasis can also present as an isomorphic response, where new lesions develop on previously normal skin that has sustained trauma or injury. The severity of disease can be helpful in guiding management and is classified as mild, moderate, and severe (**Table 2**).[1]

Evaluation and differential diagnosis. Less common variants of psoriasis include inverse psoriasis, pustular psoriasis, guttate psoriasis, erythrodermic psoriasis, and annular psoriasis (**Figures 3** to **6**). These variants can be differentiated from the common plaque type by morphology. Differential diagnoses include atopic dermatitis, contact dermatitis, lichen planus, secondary syphilis, mycosis fungoides, tinea corporis, and pityriasis rosea (**Table 3**). Careful observation often yields the diagnosis. For more atypical presentations, a skin biopsy might be helpful.

Table 1. Clinical manifestations of psoriasis

CLINICAL MANIFESTATION	CLINICAL FINDINGS
Plaque psoriasis	• Well circumscribed, erythematous, scaly plaques >0.5 cm in diameter, either as single lesions or as generalized disease • Classified further according to anatomic sites
• Flexural	• Also known as *intertriginous* or *inverse psoriasis* • Well circumscribed, minimally scaly, thin plaques localized to the skin folds (inframammary, axillary, groin, genital, natal cleft regions)
• Nail	• Can present without concomitant skin plaques • Pitting, distal onycholysis, subungual hyperkeratosis, oil drop sign, splinter hemorrhages, leukonychia, crumbling, red lunula • Nail involvement is a predictor of psoriatic arthritis
• Scalp	• One of the most common sites of psoriasis • Often difficult to treat
• Palmoplantar	• Localized to the hands and soles of feet • Confluent redness and scaling without obvious plaques to poorly defined scaly or fissured areas to large plaques covering the palm or sole
Other variants	
• Guttate	• Acute eruption of "dew-drop," salmon-pink, fine-scaled, small papules on the trunk or limbs • Can follow history of group A streptococcal pharyngitis or perianal group A streptococcus dermatitis
• Pustular	• Sheets of monomorphic pustules on painful, inflamed skin • Most commonly localized to the palms or soles
• Erythroderma	• Acute or subacute onset of generalized erythema covering 90% or more of the patient's entire body with little scaling • Might be associated with hypothermia, hypoalbuminemia, electrolyte imbalances, and high-output cardiac failure • Life-threatening emergency
• Annular	• Well demarcated erythematous scaly plaques with central clearing

Data from the Canadian Psoriasis Guidelines Committee.[1]

Figure 1. Plaque psoriasis is characterized by well-demarcated and erythematous plaques with silvery scale: *A) Plaque psoriasis on the elbow; B) Psoriasis on the trunk, marked by confluent red, well-demarcated, scaly plaques; C) Psoriasis on the dorsal foot and metatarsophalangeal joint with psoriatic nails showing dystrophy; D) Psoriasis in the postauricular area, which is a common site of involvement.*

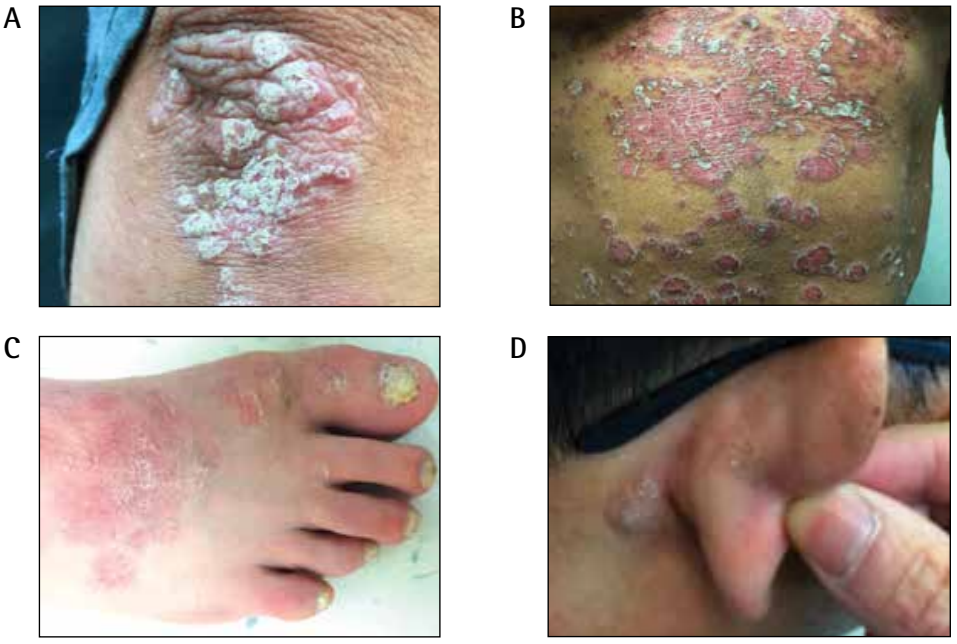


Figure 2. Patients with psoriasis might have nail involvement, which can present without concomitant plaques: *A) Psoriatic nails, consisting of pitting, distal onycholysis, subungual hyperkeratosis, and crumbling; B) Leukonychia and splinter hemorrhages; C) Distal onycholysis and oil drop sign.*

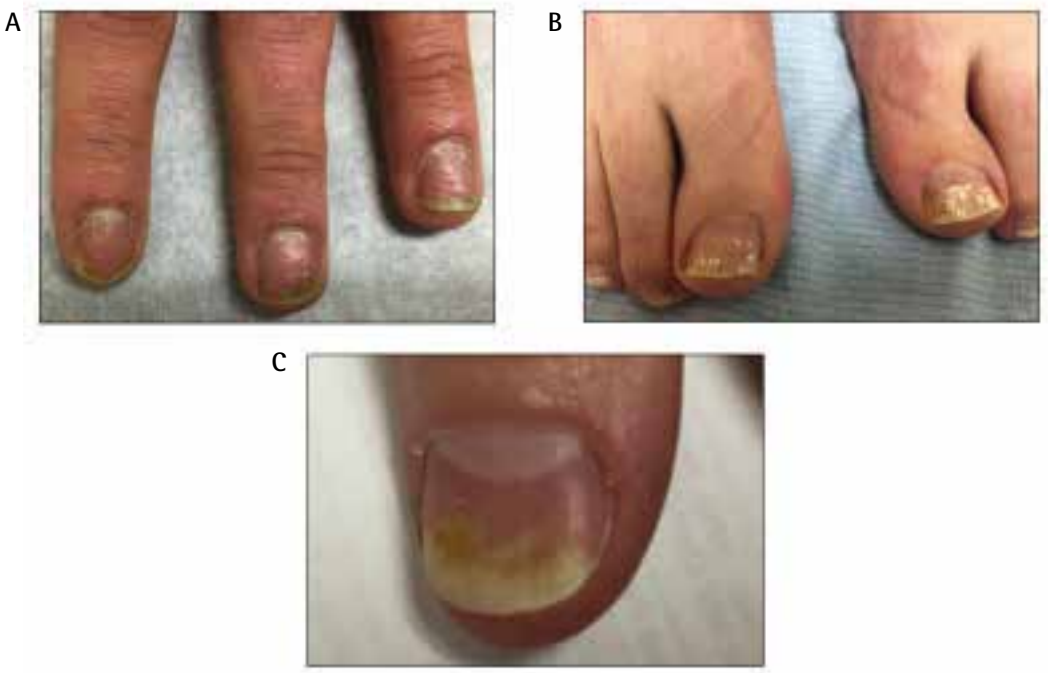


Table 2. Measures of disease severity

SEVERITY	MEASURES*
Mild	• < 3% BSA† • Disease with a minimal effect on the patient's QoL; patient can achieve an acceptable level of symptomatic control by routine skin care measures and topical therapy
Moderate	• 3% to 10% BSA† • Disease that cannot be, or would not be expected to be, controlled to an acceptable degree by routine skin care measures or disease that substantially affects the patient's QoL, either because of the extent of the disease, physical discomfort (pain or pruritus), or location (eg, the face, hands, feet, or genitals)
Severe	• > 10% BSA† • Disease that cannot be, or would not be expected to be, satisfactorily controlled by topical therapy and that causes severe degradation of the patient's QoL

BSA—body surface area, QoL—quality of life.
*These are definitions for clinical practice, as applied in the Canadian guideline. The Psoriasis Area and Severity Index is another measure of disease severity, based on BSA, erythema, induration, and scaling.
†The size of a single hand is estimated to be 1% BSA.
Data from the Canadian Psoriasis Guidelines Committee.[1]

Figure 3. Annular psoriasis on the back: *Annular psoriasis is characterized by well-demarcated, erythematous, and scaly plaques with central clearing.*

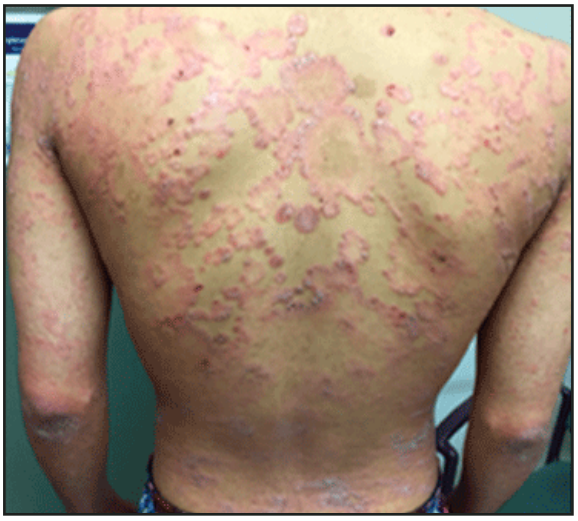
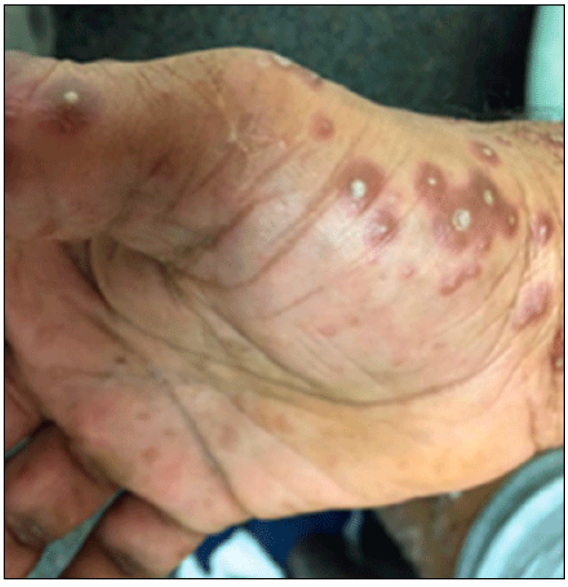


Figure 4. Pustular psoriasis on the palm



Associated comorbidities. There is increasing evidence that psoriasis is a disease of systemic inflammation with ramifications for multiple organ systems. Thus, patients with psoriasis should receive appropriate therapy for psoriasis and management of comorbid conditions to improve long-term outcomes.

Psoriatic arthritis: Psoriatic arthritis affects approximately 30% of patients with psoriasis.[7] The skin disease most commonly precedes the joint disease by about a decade, ranging from 7 to 12 years.[8] Psoriatic arthritis is now known to be a more severe disease than previously recognized.[9] Studies have shown that almost 47% of patients can develop erosive disease within the first 2 years.[10] The presentation of arthritis can vary. A common feature is dactylitis, in which the entire digit becomes swollen, often called a *sausage digit*. Psoriatic arthritis can affect small joints and large joints, presenting as joint swelling—either oligoarticular or polyarticular. Psoriatic arthritis can also affect the axial skeleton, presenting as inflammatory back pain. Recent literature tells us that the sooner the inflammatory process is halted, the more likely patient function, radiologic damage, and long-term prognosis will improve considerably.[8] Despite this, psoriatic arthritis is often overlooked; 30% of patients with known psoriasis followed at dermatology clinics were found to have undiagnosed psoriatic arthritis.[11] Patients with scalp psoriasis, nail

Figure 5. Guttate psoriasis, which developed 12 d after onset of streptococcal pharyngitis

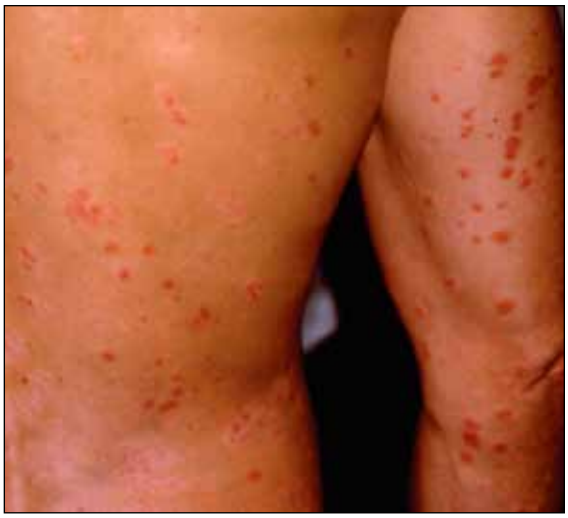


Figure 6. Approaching erythrodermic psoriasis

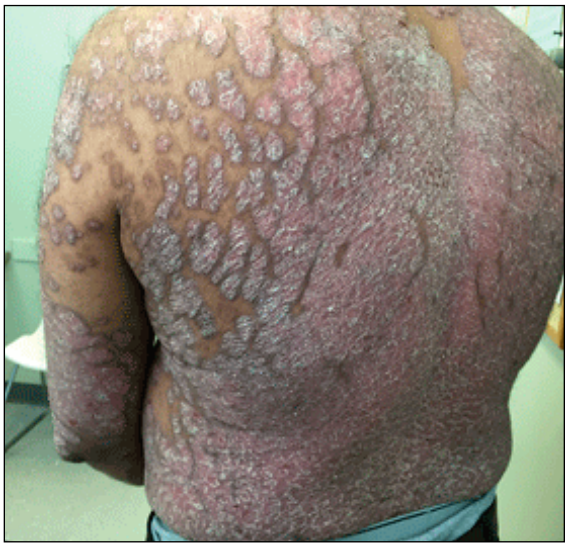


Table 3. Differential diagnoses and distinguishing clinical features

DIFFERENTIAL DIAGNOSES	DISTINGUISHING CLINICAL FEATURES
Atopic dermatitis	• Predominant symptom of pruritus and typical morphology and distribution (flexural lichenification in adults and older children; facial and extensor papules and vesicles in infancy)
Contact dermatitis	• Patches or plaques with angular corners, geometric outlines, and sharp margins dependent on the nature of the exposure to the irritant or allergen
Lichen planus	• Violaceous lesions and frequent mucosal involvement
Secondary syphilis	• Copper-coloured lesions and frequent involvement of palms and soles
Mycosis fungoides	• Irregularly shaped lesions with asymmetric distribution, peculiar colour, and wrinkling due to epidermal atrophy
Tinea corporis	• Fewer lesions with annular configuration
Pityriasis rosea	• Tannish-pink, oval papules and patches with "Christmas tree" configuration on trunk with sparing of the face and distal extremities

features of psoriasis, and intergluteal or perianal disease have a higher risk of psoriatic arthritis.[12] Although we should have a high index of suspicion for all patients, special attention should be paid to patients with these features. Early detection is key. Many of the therapies currently available for the skin component of the disease are also highly effective in the treatment of joints.

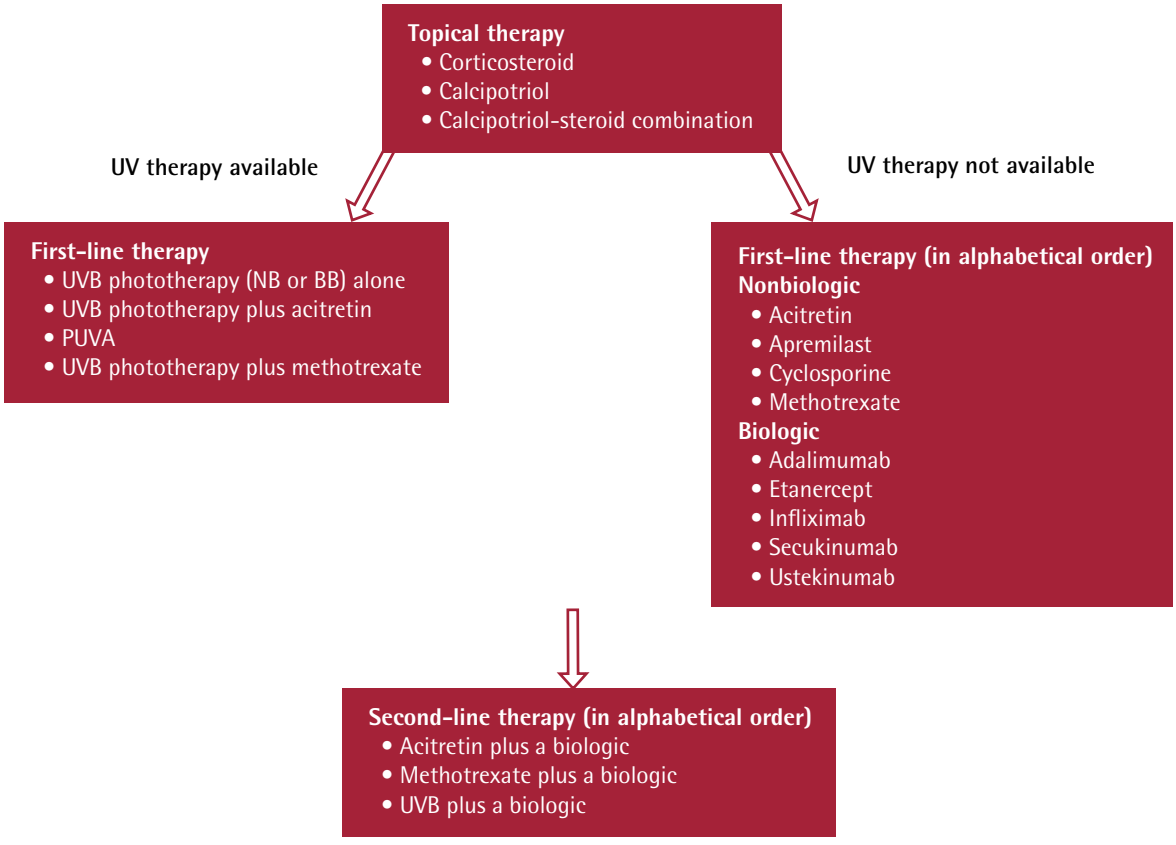
Cardiovascular disease and diabetes: Psoriasis has also been linked to increased risk of cardiovascular disease and diabetes in an observational study with 78 061 women and a cross-sectional study with 3236 patients with psoriasis.[13,14] Other population-based studies have also shown a strong association between psoriasis and metabolic syndrome (odds ratio of 3.58, P=.008).[15]

Malignancy: Psoriasis has also been associated with a low but elevated risk of non-Hodgkin lymphoma and cutaneous T cell lymphoma in a study of 2718 patients with psoriasis (odds ratio of 2.95, 95% CI 1.83 to 4.76).[16]

Psychiatric illness: Psychiatric illnesses, including depression (prevalence of up to 60%) and anxiety, can also commonly accompany psoriasis. This warrants assessment of the psychosocial well-being of patients, and clinicians should consider psychological interventions as needed.[17]

Management. Although there is no cure for psoriasis, there are multiple effective treatment options (**Figure 7**). Topical therapy is the standard of care for treatment

Figure 7. Treatment algorithm for healthy adult men with chronic plaque psoriasis (> 5% BSA) without psoriatic arthritis



BB—broadband, BSA—body surface area, NB—narrowband, PUVA—psoralen plus UVA, UV—ultraviolet.

of mild to moderate disease. A large proportion of patients would benefit from topical therapy, which can be initiated at the primary care level. If topical agents do not elicit an adequate response or if they are not practical owing to the affected body surface area, these patients can be referred for assessment by a dermatologist, at which point systemic therapy with topical adjuncts might be more suitable. Presence of psoriatic arthritis might also call for systemic therapies in collaboration with a rheumatologist.

Topical therapy

Corticosteroids: Considered the cornerstone of topical treatment, corticosteroids are often well tolerated and effective for patients with mild psoriasis.[18] Despite widespread use for more than half a century, large RCTs and head-to-head comparisons are rather limited. A Cochrane review of 177 RCTs, however, showed that corticosteroids performed at least as well as vitamin D3 analogues, with standardized mean differences ranging from -0.89 (95% CI -1.06 to -0.72) to -1.56 (95% CI -1.87 to -1.26) for potent and very potent corticosteroids, respectively.[19] Overall, topical steroids in various formulations, strengths, and combinations are efficacious initial therapy for rapid control of symptoms. For instance, salicylic acid, a keratolytic agent, can be combined with steroid therapy to help treat plaques with thicker scales, for better penetration of medication. Although uncommon, long-term use is complicated by possible side effects of local skin changes, tachyphylaxis, and hypothalamic-pituitary-adrenal axis suppression.[1]

Vitamin D3 analogues: Calcipotriol, a vitamin D3 analogue, is a first-line topical agent for treatment of plaque psoriasis and moderately severe scalp psoriasis.[1] It reduces symptoms by modulating keratinocyte proliferation and differentiation, and by inhibiting T lymphocyte activity. Multiple randomized trials have shown calcipotriol to be safe and efficacious for patients with mild plaque psoriasis and not inferior to most corticosteroids with respect to efficacy.[20,21] Further, a Cochrane meta-analysis of 177 RCTs showed that vitamin D3

analogues are more effective than all other topical medications, except the most potent of corticosteroids; standardized mean difference ranged from -0.7 (95% CI -1.04 to -0.30) to -1.66 (95% CI -2.66 to -0.67) for twice-daily becocalcidiol and once-daily paricalcitol, respectively.[19] Given their efficacy and safety profile, vitamin D3 analogues are commonly used as monotherapy or, more often, as combination therapy. Side effects include mild irritant dermatitis and rarely hypercalcemia with excessive use. These agents should not be used in combination with salicylic acid or before phototherapy.

Combination products: Combination of calcipotriol and betamethasone dipropionate was shown to be more effective for psoriasis than either monotherapy alone in a Cochrane review of 177 RCTs.[19] Clinical trials have also demonstrated reduced incidence of adverse events with concomitant or sequential use of vitamin D3 analogues and topical corticosteroids.[22] Based on a systematic review of 6 RCTs with 6050 patients, the mean reduction in Psoriasis Area and Severity Index score at 4 weeks was 74% with combination therapy, compared with 59% and 63% with calcipotriol and betamethasone dipropionate, respectively.[23] The combination gel is well tolerated and can be applied once daily, avoiding the facial, genital, and flexural areas.

Systemic therapy

Phototherapy: Phototherapy is a mainstay treatment of moderate to severe psoriasis, especially in psoriasis that is unresponsive to topical agents.[1] It is available as psoralen plus UVA, broadband UVB, and narrowband UVB (NB-UVB). Owing to its efficacy and safety advantages, as shown in multiple RCTs,[24] NB-UVB therapy is often used as first-line treatment. In fact, NB-UVB therapy can be given to almost any patient, including children and pregnant women. There is no evidence that NB-UVB increases the risk of skin malignancy.[25] Despite its safety, limited availability of phototherapy centres (fewer than 50 centres across Canada) and the need for frequent visits (3 times a week for 3 months initially) renders this option extremely inconvenient for patients.

Acitretin: Acitretin is a synthetic retinoid indicated for treatment of moderate to severe psoriasis. Its role as an adjunctive therapy to other systemic agents has been well documented to enhance efficacy, lower doses, and reduce occurrence of side effects.[26-28] However, large robust trials studying its efficacy and safety as monotherapy are lacking. Common side effects include mucocutaneous dryness, arthralgia, gastrointestinal upset, and photosensitivity. This medication can sometimes cause transaminitis and elevated triglyceride levels. Acitretin is a potent teratogen that is best avoided in women of childbearing age and potential; it is recommended that women not get pregnant for 3 years after discontinuing the medication.[29]

Methotrexate: Methotrexate is an inhibitor of folate biosynthesis, used for its cytostatic and anti-inflammatory properties in the treatment of moderately severe to severe psoriasis, as well as psoriatic arthritis.[1] Despite substantial clinical experience with this drug, large robust studies of its efficacy and safety are extremely limited. One randomized, double-blind, placebo-controlled study showed 75% improvement in Psoriasis Area and Severity Index score in almost 40% of patients with methotrexate, compared with 18.9% of patients with placebo at 16 weeks.[30] A well-known side effect is hepatotoxicity.[31] Other more common side effects include nausea, vomiting, diarrhea, and fatigue.

Cyclosporine: Cyclosporine is a calcineurin inhibitor indicated for treatment of moderate to severe psoriasis.[1] There is also some evidence for its efficacy in psoriatic arthritis.[32,33] It has been shown to cause significant improvement or complete remission in 80% to 90% of patients within 12 to 16 weeks in a 1-year open, multicentre, randomized study with 400 patients.[34] Advantages over other systemic agents include rapid onset of action and less concern about myelosuppression or hepatotoxicity. Adverse effects include nephrotoxicity, hypertension, elevated triglyceride levels, gingival hyperplasia, tremors, hypomagnesemia, hyperkalemia, numerous drug interactions, and malignancies such as skin cancers and lymphoma.[35]

Biologic therapy: Biologics have emerged as highly potent treatment options in patients for whom traditional systemic therapies fail to achieve an adequate response, are not tolerated owing to adverse effects, or are unsuitable owing to comorbidities.[4] There is no single sequence in which biologics should be initiated or switched[4]; however, a meta-analysis of pivotal phase III studies has shown that infliximab might be the most efficacious, followed by ustekinumab, adalimumab, and etanercept.[36] Choice of therapy depends on clinical needs, benefits and risks, patient preferences, and cost effectiveness (around $20 000 to $25 000 a year on average). Previous randomized trials and retrospective studies have shown that biologic therapy was not associated with increased risk of malignancy or serious infection.[37,38]

Conclusion

Psoriasis is a multisystem inflammatory disease that is underdiagnosed and undertreated despite its prevalence and considerable effect on quality of life. Beyond skin and joint involvement, psoriasis is also associated with an array of important medical and psychiatric comorbidities that require timely therapy to improve long-term outcomes. Primary caregivers are well positioned to provide diagnosis and treatment of patients who seek initial evaluation at the primary care level. Patients with psoriasis for whom topical therapy fails can be referred to a dermatologist for further evaluation.

Dr Kim is a dermatology resident at the University of Ottawa in Ontario. **Dr Jerome** is Head of the Division of Rheumatology at the University of Toronto in Ontario. **Dr Yeung** is Lecturer in the Division of Dermatology at the University of Toronto.

Competing interests

Dr Yeung has been a speaker, consultant, and investigator for AbbVie, Allergan, Amgen, Astellas, Boehringer Ingelheim, Celgene, Centocor, Coherus, Dermira, Eli Lilly, Forward, Galderma, Janssen, Leo, Medimmune, Novartis, Pfizer, and Takeda. **Dr Jerome** has participated in advisory board meetings for AbbVie, Celgene, UCB, Amgen, and Novartis.

Contributors

All authors contributed to the literature review and analysis, and to preparing the manuscript for submission.

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