Psoriasis
Don't miss the comorbidities

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Psoriasis has a complex aetiology that includes genetic and immunological components. Accepted comorbidities of psoriasis include psoriatic arthritis, cardiovascular disease, metabolic syndrome and depression. Psoriasis and its comorbidities have a significant impact on a patient's quality of life.

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KEY POINTS

- Psoriasis is a common condition characterised by erythematous, scaly patches and plaques.
- The aetiology and pathogenesis is complex and not fully understood; however, genetic and immune-related components play a key part.
- Accepted comorbidities of psoriasis include psoriatic arthritis, cardiovascular disease, metabolic syndrome and depression.
- Timely diagnosis and effective management of comorbidities are vital to limit morbidity and mortality. The role of the GP is central in co-ordinating care of patients with this complex condition.
- Comorbidities change over time, are associated with increased psoriasis severity and can occur secondary to treatments used.
- Psoriasis and its comorbidities have a huge impact on a patient's quality of life. Modifiable comorbidities should be treated aggressively.
- Referral of the patient to a dermatologist is recommended when the patient does not respond to conventional therapy.

Psoriasis is a common, chronic, noncontagious, multisystem autoinflammatory disease.[1] It is complex in its aetiology and pathogenesis and appears to be influenced by genetic and immune-related components.[2,3] Psoriasis affects between 2 and 3% of the population worldwide; it is seen less commonly in the tropics and in dark-skinned populations. The onset of disease can occur at any age; however, there is a probable bimodal distribution at 16 to 22 years and 57 to 60 years, with early-age onset being associated with more severe disease and an affected first-degree relative. Men and women are equally affected, with children less than 10 years of age contributing to more than 20% of all new cases.[4]

The characteristic form of psoriasis, psoriasis vulgaris, presents with erythematous, scaly papules and plaques (Figures 1a to c). Morphological variants include guttate (Figures 2a and b), palmoplantar (Figures 3a and b), erythrodermic (Figures 4a and b) and pustular (Figures 5a and b) psoriasis.[5] Disease severity is classified according to percentage of body surface involved combined with plaque thickness and scaling (Psoriasis Area and Severity Index [PASI] score), with moderate-to-severe disease being

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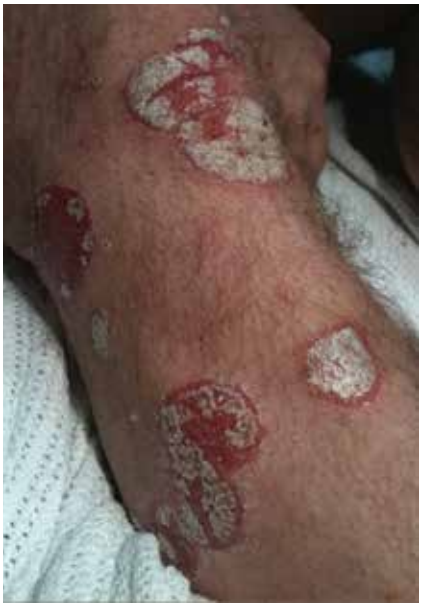
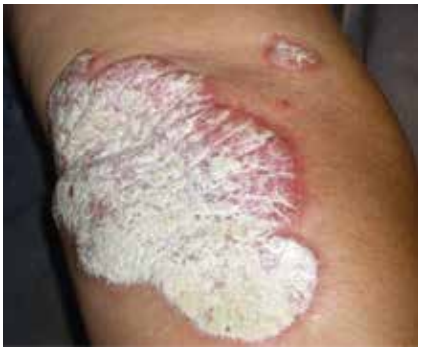
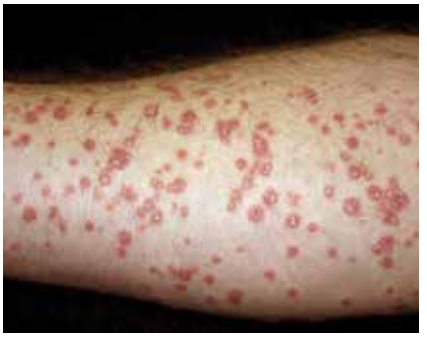
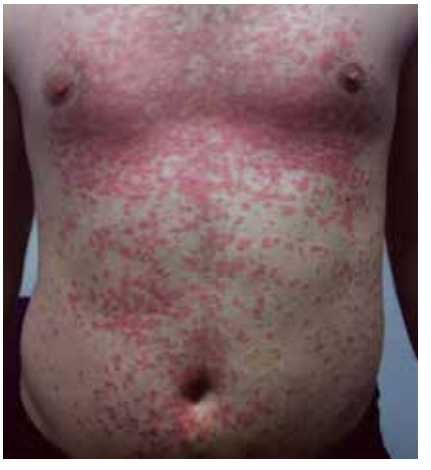


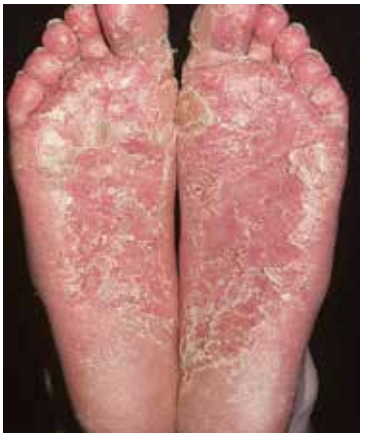


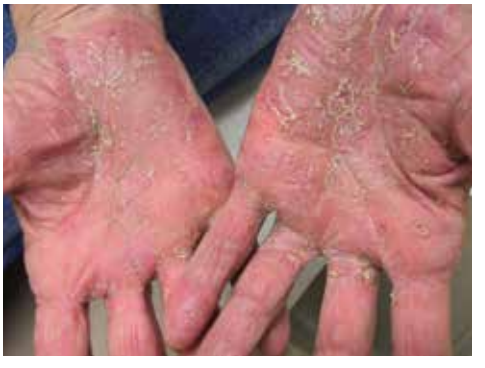
Figures 1a to c. Psoriasis vulgaris.





Figures 2a and b. Guttate psoriasis.





Figures 3a and b. Palmoplantar psoriasis.

defined as more than 10% body surface area affected.

Pathophysiology

Psoriasis is a complex disease that has a strong genetic background. The genetic basis of psoriasis has long been evident from high concordance rates in twin studies.[3] Major insights through genetic sequencing of patients with familial psoriasis have provided evidence that mutations in the *CARD14* and *IL36RN* genes are disease inducing. Further studies have identified numerous psoriasis susceptibility loci, implicating the human leucocyte antigen Cw6 (*HLA-Cw6*) gene with psoriasis heritability and early onset.[2] Genetic sequencing has also validated the importance of T lymphocytes, with the central importance of interleukin (IL) 17 and tumour necrosis factor (TNF) alpha now recognised in the pathogenesis of psoriasis.[3] Such information has led to the identification of treatment targets for effective biological therapies.

The underlying pathological mechanisms of triggers and initiators of psoriasis remain incompletely understood. However, a correlation between streptococcal throat infection and guttate psoriasis has been identified in patients with *HLA-Cw6* expression.[6] Furthermore, studies suggest that psychological stress may play a role in the exacerbation of psoriasis.[7]

Comorbidities associated with psoriasis

Psoriasis is a systemic autoinflammatory disorder associated with a number of comorbidities.[8] Autoinflammation is the dysregulation of the innate immune system, leading to propagation of inflammatory pathways. Autoinflammatory disorders are distinct from autoimmune diseases, which result from the proliferation of T lymphocytes and/or antibodies directed against self antigens.

The exact mechanisms behind the associations between psoriasis and its comorbidities are unclear; however, a common genetic background and acquired risk factors appear to link psoriasis to its

comorbidities. Epidemiological studies have shown that more severe disease accompanies a higher risk of significant comorbidities. The systemic inflammation in psoriasis contributes to continuation of the disease, as well as the development of comorbidities.[1] Accepted comorbidities of psoriasis include psoriatic arthritis, cardiovascular disease, metabolic syndrome, inflammatory bowel disease and depression.

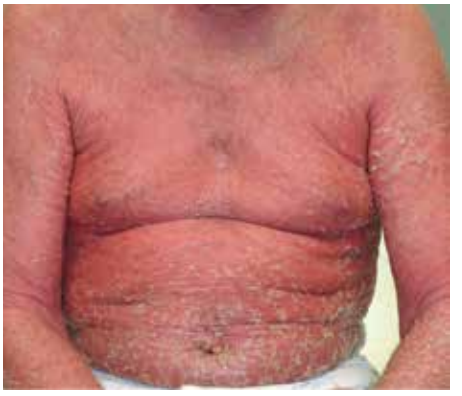
Psoriatic arthritis

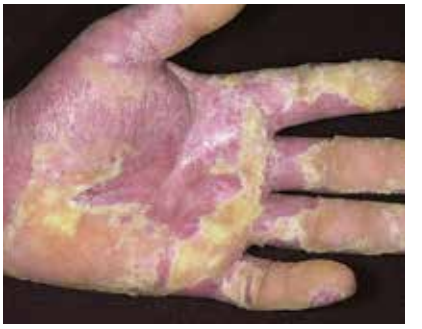
Up to 35% of patients with chronic plaque psoriasis have an associated spondyloarthropathy, the most common being dactylitis (Figure 6) and enthesitis – that is, inflammation at the site of insertion of tendon into bone (Figure 7).[9] Individuals with psoriatic arthritis (PsA) have more severe skin symptoms and a lower quality of life than patients with psoriasis but not arthritis.[10] PsA commonly develops after the onset of skin changes (in 6 to 18% of patients), but may also develop before.[11] PsA has a variable but chronic clinical course, and causes severe disability from destructive lesions in 20% of affected individuals. The skin manifestations of PsA may be mild and in some cases poorly recognised, with nail dystrophies often misinterpreted as fungal infections especially when affecting toes (Figures 8a and b).

Screening for PsA in patients with psoriasis is recommended, with involvement of a rheumatologist for definitive diagnosis. To meet the CASPAR (Classification Criteria for Psoriatic Arthritis) criteria for PsA, a patient needs to have inflammatory articular disease and score three or more points from the categories of psoriasis, nail dystrophy, a negative rheumatoid factor, dactylitis (Figure 6) and radiological evidence of juxtaarticular new bone formation.[12]

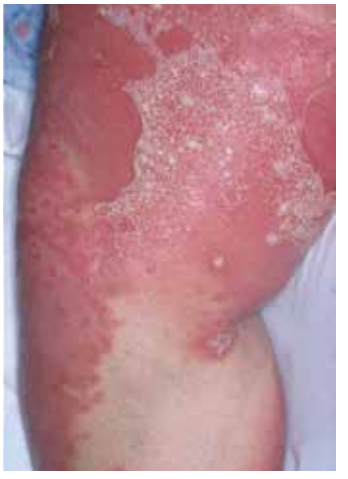
Cardiovascular disease

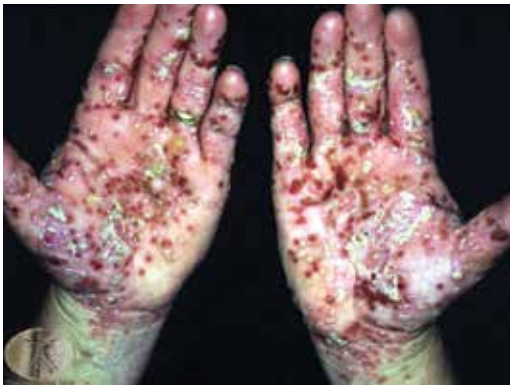
Psoriasis is strongly related to an increased risk of cardiovascular disease, including ischaemic heart disease, myocardial infarction (MI) and arterial/venous thrombosis.[13]





Figures 4a and b. Erythrodermic psoriasis.





Figures 5a and b. Pustular psoriasis.

Psoriasis is an independent risk factor for the development of an MI, especially in young people.[14] Both patients with mild and with severe psoriasis have been shown to have an increased risk of MI when compared with matched controls.[15] Underlying mechanisms include common genetic factors and risk factors for both conditions, specifically metabolic syndrome, obesity, a sedentary lifestyle, depression or anxiety and smoking. Control of these modifiable cardiovascular risk factors is essential in the management of patients with psoriasis, through guidance by the GP with a holistic approach to patient care. Recent evidence suggests that systemic therapy, particularly biological agents such as infliximab and etanercept, reduces mortality and morbidity.[9,16]

Metabolic syndrome

Psoriasis is associated with a higher prevalence and incidence of insulin resistance and diabetes. In particular, young patients with psoriasis and those with severe disease have a greater risk of developing diabetes.[16] It is thought that systemic inflammation in psoriasis promotes insulin resistance, which is an independent risk factor for type 2 diabetes.[17] Insulin

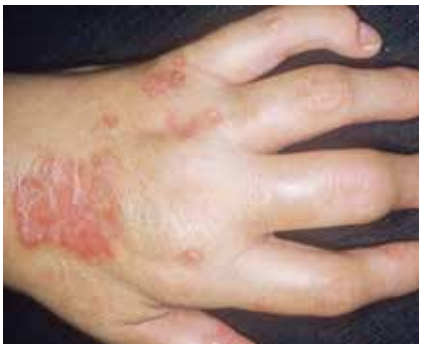


Figure 6. Dactylitis.

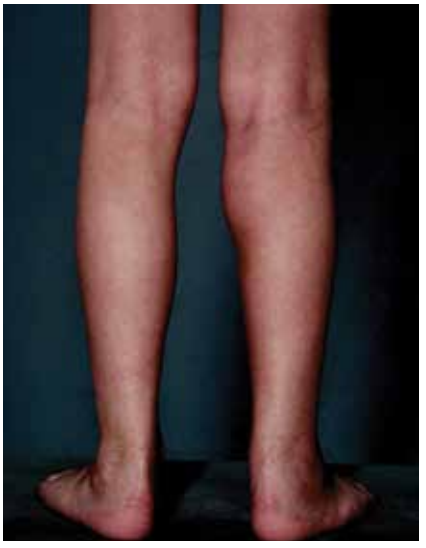


Figure 7. Enthesitis.

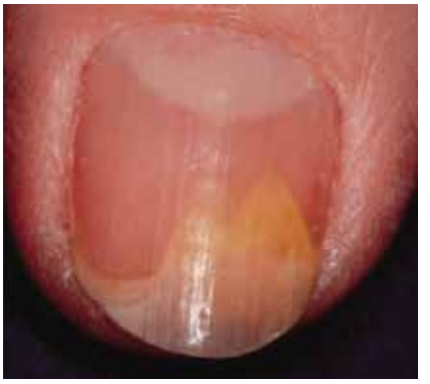
resistance is also related to endothelial dysfunction, an important component in the pathogenesis of atherosclerosis and coronary artery disease. In the authors' clinic more than 50% of patients with moderate-to-severe psoriasis are affected by the metabolic syndrome and more than 65% are obese as measured by body mass index (BMI). Obesity seems to be particularly treatment resistant in this cohort.

As part of the metabolic syndrome, psoriasis has a significant association with dyslipidaemia, a known risk factor for cardiovascular disease. Greater psoriasis disease severity is linked to a higher prevalence of dyslipidaemia.[18] Control and monitoring of blood lipid levels by dietary and medical means is important to reduce morbidity and mortality rates.

Obesity has long been associated with psoriasis in adult and now paediatric populations, with an increased BMI contributing to increased risk for disease development.[4,19] BMI and other measurements of adiposity are independent risk factors for the development of psoriasis and PsA.[20] Patients with psoriasis have a more than 50% increased odds of being obese compared with the general population.[21] Also, obese patients have been found to have a higher risk of developing more severe forms of psoriasis. Recent literature suggests that adipocytes and inflammatory macrophages play key roles in the disease processes of both obesity and psoriasis.[21] Activated macrophages stimulate adipocytes to secrete inflammatory mediators called adipokines that establish and maintain an inflammatory state in patients with obesity.[4] The increased visceral adipose tissue compartments in obese patients appear to be central in adipokine dysfunction.[20]

Depression

Psoriasis has a significant impact on quality of life and is associated with an increased prevalence of depression, anxiety, suicidal ideation and substance misuse.[22] Up to 60% of patients with psoriasis have depression, which is comparable with the prevalence in patients with cancer, chronic obstructive pulmonary disease, ischaemic heart disease and diabetes.[10,22] Patients with psoriasis have increased rates of smoking and alcohol misuse, contributing to the worsening of psoriasis and cardiometabolic comorbidities.[8] Smoking has been shown to increase the likelihood of psoriasis onset and chronicity of the disease when it is established and to negatively affect treatment outcomes.[22] Recognition and treatment of psychological distress is important in patient management.



Figures 8a and b. Nail dystrophies: pitting and oil spotting.

Other comorbidities

Other comorbidities associated with psoriasis include inflammatory bowel disease, particularly Crohn's disease (CD), uveitis and skin cancer. The exact relation between psoriasis and inflammatory bowel disease is uncertain and is currently being investigated.[23] Patients with psoriasis have a 2.9 times higher risk of developing CD, and patients with CD are seven times more likely than the normal population to develop psoriasis.[24,25] Non-infectious uveitis has been reported to occur in 7 to 10% of patients with psoriasis, and as many as 7 to 25% of those with psoriatic arthritis. Biological therapy with adalimumab is effective in patients with both uveitis and psoriasis.[26] The association of psoriasis with nonmelanoma skin cancer is related to previous treatment with phototherapy.

Investigations

A diagnosis of psoriasis is usually based on a clinical history and examination. Patients with psoriasis should be screened for PsA by taking a thorough history of any early morning stiffness and joint symptoms, with review of inflammatory markers (i.e. C-reactive protein, erythrocyte sedimentation rate, rheumatoid factor). The Early Arthritis for Psoriatic Patients (EARP) questionnaire is a simple and fast tool that can help to identify PsA in the clinic setting (Box).[27]

On examination, the extent of body surface involvement should be noted. Measurements of adiposity (i.e. BMI, waist circumference, weight) are essential at each

THE EARLY ARTHRITIS FOR PSORIATIC PATIENTS QUESTIONNAIRE

The Early Arthritis for Psoriatic Patients (EARP) questionnaire is a simple and fast tool that can assist the identification of psoriatic arthritis in the clinic setting.

The total score is calculated by summing the number of 'yes' answers. An EARP score of ⩾3 is clinically significant.

- Do your joints hurt?
- Have you taken anti-inflammatory medication more than twice a week for joint pain in the past three months?
- Do you wake up at night because of low back pain?
- Do you feel stiffness in your hands for more than 30 minutes in the morning?
- Do your wrists and fingers hurt?
- Do your wrists and fingers swell?
- Does one finger hurt and swell for more than three days?
- Does your Achilles tendon swell?
- Do your feet and ankles hurt?
- Do your elbows and hips hurt?

patient review and provide a good opportunity to introduce the patient to the possibility of lifestyle changes that may reduce cardiovascular morbidity. Components of the metabolic syndrome and cardiovascular disease risk factors should be identified and investigated at the first consultation and monitored at subsequent reviews. Any bowel symptoms should be investigated if present. Baseline blood test results, including full blood count and renal and liver function, should be obtained before systemic therapy is used.

Treatment options

Treatment options for psoriasis include the following and are listed in order of increasing specificity.

- **Topical therapies:** corticosteroids alone or in combination with vitamin D analogues
- **Narrow band** ultraviolet B phototherapy
- **Systemic therapies:** acitretin, methotrexate, cyclosporin
- **Biological agents:** etanercept, infliximab, adalimumab, ustekinumab
- **Newer agents:** oral apremilast (phosphodiesterase-4 inhibitor), secukinumab (biological agent), brodalumab (biological agent).

Considerations for management

Consideration of comorbidities associated with psoriasis is vital when reviewing each patient. Comorbidities change over time, are associated with increased psoriasis severity and can occur secondary to treatments used for psoriasis. Psoriasis and its comorbidities have a huge impact on a patient's quality of life. Modifiable comorbidities should be treated aggressively. Close patient monitoring, potentially with the involvement of a multidisciplinary team, is essential for those with moderate-to-severe disease and those with significant comorbid disease.

Entry on a national registry (Australian Psoriasis Registry at www.psoriasis.asn.au) for all patients on systemic therapies (including biological agents) is now available and encouraged. Data are entered by centres providing such treatment.

Numerous support groups for patients with psoriasis exist within Australia and internationally. Engagement of patients with support groups has shown to improve patient satisfaction, education, treatment compliance and overall psychological wellbeing.[28,29] The chronicity and recalcitrance of this condition makes patients vulnerable to the variously marketed over-the-counter products, many of which are ineffective and cause unnecessary harmful side effects. Support groups may have the additional potential to assist by providing realistic advice, orientating towards education and encouraging necessary lifestyle changes. Psoriasis Australia (www.psoriasisaustralia.org.au) is one such organisation.

Resources for rural GPs

Tele-Derm offers an invaluable opportunity for rural GPs to engage in holistic care through a co-operative approach that transcends barriers between rural, remote, regional and tertiary centres. The service provides support, advice and valuable rapid information about new and emerging therapies. It is available online at www.acrrm.org.au/tele-medicine.

Conclusion

Psoriasis is a common yet complex multisystem autoinflammatory disease. Accepted comorbidities of psoriasis include psoriatic arthritis, cardiovascular disease, metabolic syndrome and depression. The role of the GP is central in co-ordinating care of patients with this complex condition. Psoriasis and its comorbidities have a huge impact on a patient's quality of life. Modifiable comorbidities should be treated aggressively. MT

References

A list of references is included in the website version (www.medicinetoday.com.au) and the iPad app version of this article.

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