Psoriasis: a brief overview

Authors: Antony Raharja, Satveer K Mahil and Jonathan N Barker

Psoriasis is a clinically heterogeneous lifelong skin disease that presents in multiple forms such as plaque, flexural, guttate, pustular or erythrodermic. An estimated 60 million people have psoriasis worldwide, with 1.52% of the general population affected in the UK. An immune-mediated inflammatory disease, psoriasis has a major genetic component. Its association with psoriatic arthritis and increased rates of cardiometabolic, hepatic and psychological comorbidity requires a holistic and multidisciplinary care approach. Psoriasis treatments include topical agents (vitamin D analogues and corticosteroids), phototherapy (narrowband ultraviolet B radiation (NB-UVB) and psoralen and ultraviolet A radiation (PUVA)), standard systemic (methotrexate, ciclosporin and acitretin), biologic (tumour necrosis factor (TNF), interleukin (IL)-17 and IL-23 inhibitors) or small molecule inhibitor (dimethyl fumarate and apremilast) therapies. Advances in the understanding of its pathophysiology have led to development of highly effective and targeted treatments.

Introduction
Psoriasis is a lifelong immune mediated inflammatory skin disease, associated with morbidities such as psoriatic arthropathy, psychological, cardiovascular and hepatic diseases. In 2014, the World Health Organization recognised psoriasis as a serious non-communicable disease and highlighted the distress related to misdiagnosis, inadequate treatment and stigmatisation of this disease. The Global Burden of Disease Study estimated that psoriasis accounted for 5.6 million all-age disability-adjusted life-years (DALYs) in 2016, at least three-fold that of inflammatory bowel disease.

Epidemiology
Psoriasis affects both males and females, with earlier onset in females and those with a family history. Its age of onset shows a bimodal distribution with peaks at 30–39 years and 60–69 years in men, and 10 years earlier in women.

Key points
Psoriasis is a chronic immune-mediated inflammatory skin disease with multiple phenotypically distinct subtypes eg plaque, flexural, guttate, pustular or erythrodermic.
Psoriasis has a major genetic component, with heritability estimated to be 60–90%.
High-impact and difficult-to-treat psoriasis sites include scalp, face, nails, genitalia, palms and soles.
Recognition and management of comorbidities (such as psoriatic arthritis, psychological, cardiovascular and hepatic diseases) is an essential part of holistic care for individuals with psoriasis.

Treatments for psoriasis include topical therapies (vitamin D analogue and corticosteroids), phototherapy (narrowband ultraviolet B radiation (NB-UVB) and psoralen and ultraviolet A radiation (PUVA)), conventional systemic agents (methotrexate, ciclosporin and acitretin), targeted biologics (tumour necrosis factor (TNF), interleukin (IL)-17 and IL-23 inhibitors) and oral small molecule inhibitors (dimethyl fumarate and apremilast).

KEYWORDS: psoriasis, plaque, pustular, multimorbidity, biologic

DOI: 10.7861/clinmed.2021-0257
Psoriasis is a chronic inflammatory skin condition that affects the skin and can also cause inflammation in other joints. It is characterized by red, raised areas on the skin (plaque psoriasis), which can be itchy or sore. Other forms of psoriasis include pustular psoriasis and guttate psoriasis. Psoriasis is often associated with other chronic conditions, such as obesity, cardiovascular diseases, and depression. The disease is thought to be caused by a combination of genetic and environmental factors, and the severity can vary from person to person. Treatment options include topical medications, phototherapy, systemic medications, and biologic drugs. Early treatment is important to prevent skin damage and reduce the risk of joint damage.
ciclosporin and acitretin). NB-UVB has largely superseded PUVA due to risks of skin cancer with cumulative doses of PUVA.\textsuperscript{21} Methotrexate works by inhibiting lymphocytes via multiple mechanisms including dihydrofolate reductase inhibition, aminomimidazole carboxamide ribotide transformylase (AICARTase) blockade and adenosine accumulation. Its most serious adverse effect is bone marrow suppression. Other potential complications of treatment include nausea, pneumonitis, hepatitis, liver fibrosis and teratogenicity. Methotrexate is usually taken orally every week. Subcutaneous formulation causes less gastrointestinal side effects and is more efficacious due to higher bioavailability.\textsuperscript{22} Ciclosporin is a calcineurin inhibitor and has a rapid onset of action, but may cause hypertension and irreversible renal toxicity. Acitretin is an oral retinoid that promotes keratinocyte differentiation. Its possible side effects include dry skin, hair loss, hyperlipidaemia and hepatotoxicity. Methotrexate and acitretin are contraindicated in pregnancy.\textsuperscript{23} For disease refractory to methotrexate and/or ciclosporin or where second-line therapies are not suitable, biologic therapies or oral small molecule inhibitors may be considered.

Biologics are monoclonal antibodies or soluble receptors that target proinflammatory cytokines. They have had a dramatic impact on outcomes in moderate–severe disease. Multiple biological therapies are approved for use in moderate–severe psoriasis such as TNF (adalimumab, etanercept, infliximab and certolizumab), IL-12/23p40 (ustekinumab), IL-17 (ixekizumab and secukinumab) and IL-17 receptor (brodlimab) inhibitors. There is no single ‘best’ agent and the choice of biologic needs to be tailored to the needs of each patient.\textsuperscript{24,25} Currently, this is primarily influenced by clinical information eg psoriasis factors (disease phenotype and presence of PsA and outcomes of previous biological treatment), comorbidities (demyelinating disease and inflammatory bowel disease), drug-specific factors (dosing frequency) and lifestyle considerations (conception plans).\textsuperscript{26} Genomic information has the potential to guide effective deployment of therapies in the future, and this is a field of active research.\textsuperscript{26}

Although highly effective, biologics require regular subcutaneous or intravenous administration. Oral small molecule inhibitors including apremilast (phosphodiesterase 4 inhibitor) and dimethyl fumarate are licensed for use in moderate–severe psoriasis, and trials are ongoing for small molecules blocking tyrosine kinase 2 in the Janus kinase (JAK) – signal transducer and activator of transcription proteins (STAT) pathway.

Pustular psoriasis

Pustular psoriasis is a distinct phenotype characterised by sterile pustules, which can either be acute generalised (generalised pustular psoriasis (GPP)) or limited to digits (acrodermatitis continua of Hallopeau (ACH)) or palms and soles (palmoplantar pustulosis (PPP)). GPP can present acutely with a widespread eruption of superficial pustules and erythematous skin. Patients may be unwell with fever, and blood tests typically show neutrophilia and elevated inflammatory markers.\textsuperscript{21} While GPP can be life-threatening, localised pustulosis can also severely impact on day-to-day activities.

Despite a burgeoning arsenal of treatment for plaque psoriasis, effective treatment for pustular psoriasis remains an area of high unmet need. PPP and ACH are notoriously recalcitrant to the treatments used in plaque psoriasis. Potent topical steroids with occlusion are first line. PUVA may be considered in palmoplantar pustulosis but systemic treatments are frequently required.\textsuperscript{26} For acute severe GPP, ciclosporin or infliximab may be required for its rapid onset of action. Advances in our understanding of the pathogenic role of IL36RN mutations in GPP have also led to the development of IL-36 receptor inhibitors, with trials ongoing.\textsuperscript{28,29}

Conclusion

In summary, psoriasis is a common inflammatory skin condition that is predominantly genetically determined and is associated with significant medical and psychosocial comorbidities. Advances in the understanding of its pathophysiology have led to an increasing number of therapeutic options that could dramatically improve the lives of individuals with psoriasis.

Funding

Satveer K Mahil and Jonathan N Barker are partly supported by the National Institute for Health Research Biomedical Research Centre at Guy’s and St Thomas’s NHS Foundation Trust and King’s College London.

Satveer K Mahil is funded by a Medical Research Council Clinical Academic Research Partnership award (MR/T02383X/1).

References


Address for correspondence: Prof Jonathan N Barker, St John’s Institute of Dermatology, King’s College London, 9th Floor Tower Wing, Guy’s Hospital, London SE1 9RT, UK. Email: jonathan.barker@kcl.ac.uk