

Summaries Weinberg: Treatment of Psoriasis

Summary

Alissa Cowden and Abby S. Van Voorhees

Introduction: History of psoriasis and psoriasis therapy

This chronicle of psoriasis begins in ancient times when psoriasis, leprosy, and other inflammatory skin disorders were thought to be the same condition. The identification of psoriasis as a distinct entity did not occur until the 19th century, when clinical descriptions distinguished it from other cutaneous disorders. Histopathologic descriptions in the 1960s and 1970s shed some light on the pathophysiology of psoriasis, but many aspects of the disease remain unknown to this day.

Given the lack of understanding of its pathophysiology, early psoriasis therapies were discovered serendipitously. Chance observations by early clinicians of psoriatic improvement in patients prescribed medications for other conditions led to advancements in therapy. As our understanding of the possible mechanisms of psoriasis grew, this serendipity evolved into detailed targeting of specific immunological processes. The rich history of psoriasis serves as inspiration for continued investigation into the pathophysiology and treatment of the disease.

Keywords: psoriasis, history of psoriasis, psoriasis treatment, medical history, historical therapy, anthralin, UV therapy, corticosteroid, methotrexate, retinoids, cyclosporine, vitamin D analogues, biologic therapy

Summary

Marissa D. Newman and Jeffrey M. Weinberg

Pathophysiology of psoriasis

Psoriasis is regarded as a disease of dysregulated immunity and inflammation in genetically susceptible individuals. A disruption in the balance of innate immune cells (including natural killer T lymphocytes, Langerhans cells and neutrophils) and acquired or adaptive immune cells (including mature CD4⁺ and CD8⁺ T lymphocytes) results in the excessive production of cytokines, chemokines and growth factors. These proinflammatory mediators increase the expression of adhesion molecules (which direct leukocytes to the skin), T cell activation and differentiation, keratinocyte proliferation and angiogenesis. Such factors are directly responsible for the inflammatory infiltrate observed on histologic specimens and the psoriatic phenotype of hyperkeratotic erythematous plaques. This chapter will review the pathophysiology of psoriasis through noteworthy developments in the past 25 years including serendipitous observations, reactions to therapies, clinical trials and animal model systems that have shaped our view of the disease process in the skin and joints.

Keywords: psoriasis, pathophysiology, immunity, cytokine, T lymphocyte, CD4⁺ T cell, CD8⁺ T cell, type 1 helper T (T_H1) cells, type 2 helper (T_H2) cells, natural killer T cells, antigen presenting cell, TNF-alpha, IL-2, PSORS 1

Summary

Allison J. Brown and Neil J. Korman

Psoriasis and psoriatic arthritis: a clinical review

Psoriasis is a common, systemic, inflammatory disease with genetic features that can be disabling not only because of skin involvement but also because of concomitant joint disease. The course of the disease is generally a lifelong, relapsing, remitting condition with an insidious onset. Five clinical variants are commonly recognized: chronic plaque psoriasis, which accounts for 90% of disease, guttate psoriasis, pustular psoriasis, erythrodermic psoriasis, and inverse psoriasis. In addition to its effect on the skin and joints, psoriasis may be associated with other systemic manifestations that are important to recognize. It is essential for the physician to recognize that psoriasis can have a major impact on a patient's quality of life, which may not correlate with physician measured disease severity. A broad base of knowledge of the clinical features and other disease associations of both psoriasis and psoriatic arthritis is important so that the most effective mode of therapy can be selected for these patients.

Summary

Paru R. Chaudhari, Dana K. Stern and Mark G. Lebwohl

Topical Therapy I: Corticosteroids and Vitamin D Analogs

Topical therapy is the first-line of treatment for mild to moderate psoriasis. The following two chapters will describe the available topical therapies for psoriasis, providing insight into the progress that has been made for treatment of the disease. This chapter will focus on the most widely used topical regimens, topical corticosteroids and vitamin D analogs, while the subsequent chapter will examine additional topical therapies used to treat psoriasis.

Keywords: psoriasis, topical corticosteroids, vitamin D analogs, combination therapy, calcipotriol

Summary

Paru R. Chaudhari, Dana K. Stern and Mark G. Lebwohl

Topical therapy II: retinoids, immunomodulators, and others

Use of topical therapy for mild and moderate psoriasis continues to be a mainstay of treatment. The previous chapter introduced topical corticosteroids and vitamin D analogs as the most common therapies for psoriasis (see Table 1). Here the newly available topical retinoids and immunomodulators, along with the traditional therapies of tars, anthralin, and salicylic acid, will be discussed in detail.

Keywords: psoriasis, topical retinoids, tazarotene, combination therapy, topical immunomodulators, pimecrolimus, tacrolimus, tars, Goeckerman regimen, anthralin, salicylic acid, non-steroidals

Summary

Rahat S. Azfar and Abby S. VanVoorhees

Ultraviolet and laser therapy

The history, various modalities, and future directions of phototherapy and photochemotherapy in the treatment of psoriasis are discussed.

Keywords: broadband, narrowband, UVB, Ingram, Goeckerman, balneophototherapy, reUVB, UVA, photochemotherapy, psoralen, RepUVA, UVA, UVA1, Excimer, PDL

Summary

Edward M. Prodanovic and Neil J. Korman

Traditional systemic therapy I: methotrexate and cyclosporine

Many medications have been discovered for the treatment of psoriasis, with methotrexate and cyclosporine being the earliest treatment options. They are complex structures that have shown efficacy, but both carry possible side effects and complications.

Summary

Sejal K. Shah and Jeffrey M. Weinberg

Traditional systemic therapy II: retinoids and others (hydroxyurea, thiopurine antimetabolites, mycophenolic acid, sulfasalazine)

Systemic agents, including oral retinoids, hydroxyurea, thiopurine antimetabolites, mycophenolic acid, and sulfasalazine, are commonly used to treat generalized psoriasis. Although they are efficacious, their potential adverse effects require close monitoring. These agents can be used either alone or in combination therapy. In addition, they can be used as rotational or sequential therapies.

Keywords: plaque-type psoriasis, generalized psoriasis, oral retinoids, acitretin, Soriatane, hydroxyurea, azathioprine, Imuran, 6-thioguanine, mycophenolic acid, mycophenolate mofetil, CellCept, Myfortic, sulfasalazine, Azulfidine

Jeffrey M. Weinberg

Biologic therapy for psoriasis: an overview of infliximab, etanercept, adalimumab, efalizumab, and alefacept

Psoriasis is a chronic skin disorder that affects approximately 2% of the US and European population. Over the last several years, one of the major focuses in psoriasis research has been the development of biologic therapies for this disease. The aim of these therapies is to provide selective, immunologically directed intervention with fewer side effects than traditional therapies. The goal of this article is to update the progress of the tumor necrosis inhibitors which are available, or under investigation, for clinical use in psoriasis: infliximab, etanercept, and adalimumab, as well as the T-cell-targeted therapies efalizumab and alefacept.

Keywords: psoriasis, biologic, infliximab, etanercept, adalimumab, efalizumab, alefacept

Summary

Maria R. Robinson and Neil J. Korman

Biologic and oral therapies in development for the treatment of psoriasis

Over the last several years, advances in understanding the pathogenesis of psoriasis have provided a framework for the development of novel, targeted therapies. These therapies, which to date include targets against tumor necrosis factor alpha and T-cell activation, appear to be safe and effective as short term treatments of patients with psoriasis. Several new psoriasis therapies are in development, including small molecules, monoclonal antibodies and fusion proteins. The small molecules are oral therapies and include a calcineurin inhibitor, a fumaric acid derivative, and a phosphodiesterase inhibitor. Monoclonal antibodies targeting interleukins -12/23, CD80 and a novel tumor necrosis factor antagonist are also under development. Here, we review these therapies, including their mechanisms of action and any available safety and efficacy data. To date, targeted therapies appear to be a valuable new treatment option for patients with moderate to severe psoriasis. However, additional long term analyses assessing their safety and efficacy are needed to elucidate what role they will play in the treatment of psoriasis.

Summary

Amanda B. Sergay, Matthew Silvan and Jeffrey M. Weinberg

Quality of life issues in psoriasis

Psoriasis is a chronic disease with physical, psychosocial, and economic implications that commonly interfere with patients' daily functional capacity, and consequently, their quality of life. Since psoriasis can affect some patients with mild disease to the same degree as those with very severe disease, it is necessary to evaluate the physical manifestations and the health-related quality of life (HRQOL) when assessing the disease's overall impact.

Although none of the treatments for psoriasis are curative, significant improvement in HRQOL has been observed with many of the available modalities. In addition to pharmacological intervention, it is clear the goal of treatment should aim to increase patients' feelings of control over their disease process, to encourage expression of emotions, and to educate about the disease. Meaningful improvement in psoriasis necessitates awareness of the range of problems these patients face: the cutaneous manifestations including pain and pruritus, and the physical, psychosocial and economic impact the disease has on a patient's quality of life.

Keywords: Health-related quality of life (HRQOL), Dermatology Life Questionnaire (DLQI), disability, work productivity, depression, stigmatization, biologics, psychological intervention, patient-centered care, advocacy groups

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