Psoriasis: The Future

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KEYWORDS

• Drug safety • Phenotypical variants • Personalized medicine • Psoriatic arthritis • Systemic disease • Biosimilars

KEY POINTS

- Personalized or stratified medicine will become increasingly important.
- The cost-effectiveness of treatments will be ever more germane to health care providers.
- Psychological comorbidities and their management will be an integral part of psoriasis management.
- The identification of, and management plans for, subpopulations of patients with psoriasis will become important aspects of clinical practice.

INTRODUCTION

The articles that constitute this detailed review of psoriasis have each focused on specific areas of interest in this fascinating disease which affects 120 million people globally. The authors have assimilated specific areas of interest discussed in prior articles with their personal views into a coherent "The Future" review of interest to clinicians and researchers alike. The scope and interest of this final article is what is anticipated to change the landscape of both our understanding of psoriasis and implications for therapy by 2020.

We are fortunate to have a full range of therapeutic options available for our patients with psoriasis, ranging from topicals to phototherapy to systemic and biological agents. Scientific research, in which our International Psoriasis Council (IPC) members are committed to maintaining their leading role, will, we believe, drive the optimal use, cost-effectiveness, and safe utilization of this spectrum of therapies allied to new agents in the pipeline.

MANUSCRIPT

The preceding articles in this issue of *Dermatologic Clinics* devoted to psoriasis have detailed the full extent of this complex, immune-mediated, genetic disorder and included measurements of outcome used in clinical trials and clinical practice. In addition, the life cycle stages of this lifelong disease from childhood to old age are reviewed, as are the significant comorbidities associated with psoriasis.

Will it be possible in the future to assess each patient with psoriasis *ab initio* from a genetic perspective, building on a new molecular taxonomy for the disease so that appropriate therapy can be tailored to the individual thereby affording them a normal lifestyle? The IPC's proposal toward completing the genetic map of psoriasis is, we believe, one of the most important current research projects likely to change our understanding of the disease. The intricacies of protein variants may enable targeting of specific therapies to the wide spectrum of psoriasis phenotypes (**Figs. 1–8**) with a significantly higher likelihood of clinical success.

Disclosures: See last page of article.

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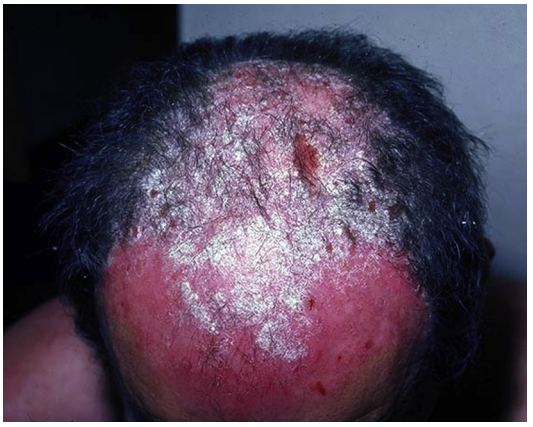

Fig. 1. Scalp psoriasis.

This task is not easy; witness the 18-year gap following the discovery of the first locus for psoriasis (PSORS2) outside MHC by modern genetic technology in 1994[1] before CARD 14, an epidermal regulator of nuclear factor–kappa B, was shown to be the specific protein involved.[2]

THE CLINICAL SPECTRUM OF PSORIASIS (PHENOTYPICAL VARIANTS)

Understanding the diverse clinical phenotypes of psoriasis,[3] the complex genetic architecture that determines them, and their mutual relationship to the pathogenesis of the disease is a daunting task and one that has significant implications for future patient care. Although most new therapeutic agents introduced over the past decade have been biological agents for moderate to severe psoriasis,[4] the need for new topical and small molecule oral agents for milder disease is paramount. This latter category of patients comprises at a minimum 75% of the total number of patients worldwide (ie, 90 million). Our most potent topical agent for treating this large group of patients, clobetasol propionate, was introduced more than 4 decades ago[5] and the newest, calcipotriol, 25 years ago. Thus, in the future, our ability to develop new classes of topical agents that are effective, cosmetically acceptable, and of low-frequency application are mandated. In addition, the use of specific topicals for defined areas of involvement (eg, flexures, including genitalia [frequently involved but seldom evaluated or discussed by clinicians and patients alike] and scalp) is currently very much a stochastic process that will necessitate new clinical and investigative approaches. Fortunately, there are a host of new topical agents in various stages of development with the likelihood of at least one or two of them emerging as important new classes for our patient population (**Box 1**).

When considering the future of systemic therapies, it is interesting to note that methotrexate, like clobetasol propionate, was also introduced more than 4 decades ago and is still the first-line systemic agent used for psoriasis worldwide despite only showing effectiveness in 40% to 45% of patients.[6] Cost obviously plays a very significant role in methotrexate retaining its leadership position. However, targeting methotrexate to specific patients with the potential of an optimized response and with lower toxicities is a definitive future need. Likewise, the introduction of new methotrexate-based molecules is emerging with a recent phase 1 study of an aminopterin (the original precursor of methotrexate) enantiomer showing superior absorption and tolerability with less accumulation in cerebral spinal fluid.[7] Phase 2 studies are in the late stages of development.

Future oral as well as biological therapies have been well covered in prior articles with a great deal of excitement surrounding the oral, small molecule technologies, such as apremilast and tofacitinib, and the three interleukin (IL)-17 inhibitors brodalumab, ixekizumab, and secukinumab.

Appropriate comparator studies with the IL-17 inhibitors against the three tumor necrosis factor

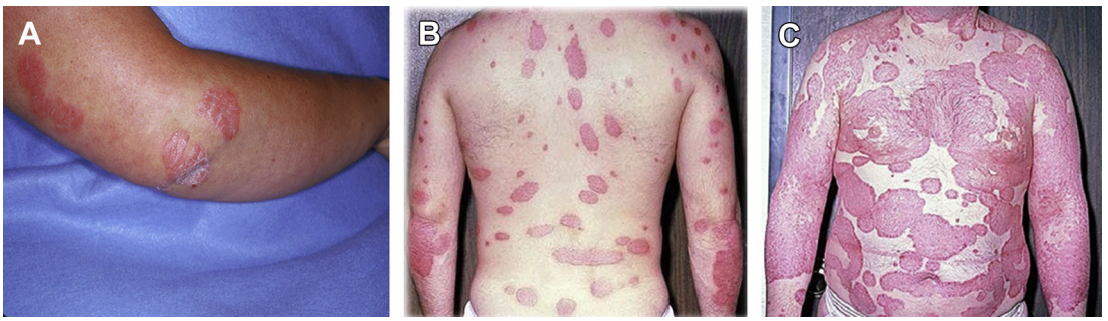

Fig. 2. Plaque psoriasis. (*A*) Mild. (*B*) Moderate. (*C*) Severe.