Therapy of Moderate-to-Severe Psoriasis
Second Edition, Revised and Expanded

edited by
Gerald D. Weinstein
Alice B. Gottlieb
Therapy of
Moderate-to-Severe Psoriasis
Second Edition, Revised and Expanded

edited by
Gerald D. Weinstein
University of California, Irvine
College of Medicine
Irvine, California, U.S.A.

Alice B. Gottlieb
University of Medicine and Dentistry of
New Jersey–Robert Wood Johnson Medical School
New Brunswick, New Jersey, U.S.A.
Preface

Over the years, psoriasis has challenged physicians to achieve better control of this disease. Patients, however, must cope with its chronicity, appearance, psychological burden, expense, time-consuming treatments, and problematic therapeutic responses. Many patients—and even some physicians—have concluded that little can be done for psoriasis, but this attitude ignores the many treatment advances developed in recent years. Now, at the beginning of the 21st century, we are entering an era of many new drugs related to the immunological basis of psoriasis.

The goal of this book is to provide guidelines on state-of-the-art clinical management of moderate-to-severe psoriasis utilizing the experience of a group of experts well known in each area. There is also a chapter highlighting recent advances in our understanding of the clinical manifestations, epidemiology, and pathogenesis of the disorder. Several chapters discuss immunological aspects of psoriasis and the new group of immunomodulators or “biologics.” The treatments covered include several types of ultraviolet B (UVB) phototherapy, photochemotherapy (psoralen/ultraviolet A; PUVA), methotrexate, retinoids, cyclosporine, and the first biologics likely to become available. Because pediatric patients and patients with psoriatic arthritis present special treatment problems, we have also included chapters on these patient populations. We hope that the reader will learn some new approaches to therapy or perhaps add some new wrinkles to old treatments that may improve the comfort of their patients.

We thank the distinguished clinicians who contributed to this book and especially the National Psoriasis Foundation (NPF) for sponsoring this
undertaking. The NPF is the major lay advocacy group for psoriasis patients in the United States and provides outstanding services in patient education and research support. We urge all of you to join the NPF and to encourage your patients to join and reap the benefits of this organization.

_Gerald D. Weinstein_
_Alice B. Gottlieb_
Introduction

The National Psoriasis Foundation is pleased to present *Therapy of Moderate-to-Severe Psoriasis: Second Edition, Revised and Expanded*, a powerful tool that can assist you in providing the best care for your psoriasis patients. Leading experts in psoriasis and psoriatic arthritis have recently updated the chapters from the first edition and offer a concise, useful overview of the most commonly prescribed therapies for these diseases. New to this edition are chapters on the immunobiology of psoriasis and several of the new biological therapies planned for psoriasis.

Treating psoriasis can be frustrating, for both the physician and the patient. The National Psoriasis Foundation believes that caring, knowledgeable medical staff, combined with membership in the Foundation, are a winning combination to help people successfully manage their psoriasis and psoriatic arthritis. The following patient guidelines complement the clinical information found in this book.

1. **WHY UNDERSTANDING THE PATIENT PERSPECTIVE IS SO IMPORTANT**

   Patients often have unrealistic expectations about how psoriasis treatment therapies should work, due to a lack of knowledge and widely conflicting information.
   No treatment is universally effective.
The amount of time physicians have to spend with each patient is shrinking.

Alone, each of these things is frustrating, but the combination creates a situation in which treating psoriasis successfully and instilling hope in patients seems impossible. The National Psoriasis Foundation is committed to making it easier for patients to live with psoriasis and psoriatic arthritis by providing award-winning educational materials, support services, and advocacy. We give patients what they need to cope with the physical and emotional challenges of their disease. And for physicians, we offer the most comprehensive, cutting-edge diagnosis and disease treatment information available.

II. BEYOND THE TREATMENTS—TIPS FOR PATIENT SUCCESS

Since 1968, the National Psoriasis Foundation has served more than a million people with psoriasis and psoriatic arthritis. We’ve heard thousands of stories of success as well as of disappointment. We know what patients are seeking when it comes to treatment, and we know what makes for a successful outcome in a patient’s eyes. Based on our extensive experience working with patients, and our involvement in research about their behavior, we offer the following tips.

A. Set Realistic Expectations

Addressing and clarifying patient expectations up front can have a dramatic impact on how patients view both their disease and you, the physician. Read these examples and ask yourself if they sound familiar.

A newly diagnosed patient walks into your office thinking you will dispense a cream that will make his “rash” go away permanently.

A patient tells you that the treatment you prescribed during her last visit doesn’t work—she used it for one week (not the month you prescribed) before giving up because of slow or inadequate results and now wants something that “works.”

A patient has been to 10 dermatologists in 20 years for his psoriasis, without ever finding an effective treatment that works—he thinks he’s tried everything but “everything” has actually been only an impressive array of topical steroids.

We have heard these stories, and so have you. Many patients don’t know the simple facts about their disease and have unrealistic expectations
about what their physician can and can’t do for them. Communicating the following key points can mean the difference between a compliant and optimistic patient and a frustrated and dissatisfied one.

- Explain that psoriasis is chronic—something they will likely have (on and off) for life, requiring lifelong management.
- Communicate that many treatment options are available and explain that you will work with them to find one that works best for them.
- Reinforce that although not every treatment is effective, compliance can mean the difference between no results and very good results, including clearance.

B. Understand the Psychosocial Impact and Treat with Compassion

Psoriasis creates a significant stigma for many patients. The emotional impact of the disease can range from embarrassment to extreme shame. Understanding how psoriasis affects patients emotionally is paramount to the success of the physician–patient relationship.

The number-one complaint from psoriasis patients about their dermatologist is not that the doctor didn’t “fix” their disease. Instead, patients feel most frustrated that their doctor didn’t listen or didn’t seem to care. Whether you are the first doctor they have seen for their psoriasis or the 20th, you can make a significant and valuable impact on how psoriasis patients view themselves, their disease, and you, the physician.

Here are a few simple things that demonstrate to your psoriasis patients that you care.

- Acknowledge and validate the patients’ feelings.
- Touch their skin—patients often tell us their physician never touched their psoriasis or even looked at their skin.
- Don’t imply that their disease is insignificant.
- Direct them to the National Psoriasis Foundation for additional support.

C. Partner with the National Psoriasis Foundation

The Foundation is the leading organization dedicated to improving the quality of life of people who have psoriasis and psoriatic arthritis. We can help make your job easier in a variety of ways.
1. Patient Education

www.psoriasis.org (The National Psoriasis Foundation’s Website).
(800) 723-9166, toll-free support for patients and medical professionals.
Easy-to-understand patient education on a variety of psoriasis-specific topics.

2. Emotional Support and Referrals

Patient education and support specialists to speak with patients and lead them to the appropriate resources: (800) 723-9166.
Programs that connect psoriasis patients—there is no better support than connecting with someone who knows exactly what you are going through.

3. Insurance Advocacy

The Foundation educates insurance companies about psoriasis and the need for adequate and prompt reimbursement for appropriate therapies.
The Foundation creates individual appeals letters and illustrated educational materials designed to educate insurance companies.

4. Programs for Medical Professionals

Annual meeting for chief residents to train dermatologists about psoriasis early in their careers.
Training sessions on effective phototherapy techniques.
Insightful information from medical experts in the Psoriasis Forum, a newsletter for National Psoriasis Foundation professional members.

D. Stay Educated

The National Psoriasis Foundation wants to be your partner in patient care. We hope that you find this manual helpful. We will continue to support you as we head into an exciting time of new hope and possibility for the psoriasis and psoriatic arthritis community.

For information about professional membership please contact the National Psoriasis Foundation at (800) 723-9166, or visit www.psoriasis.org

Thank you for partnering with us to improve the quality of life of people with psoriasis and psoriatic arthritis.
Contents

Preface iii 
Introduction National Psoriasis Foundation v
Contributors xi

1. An Overview of Psoriasis 1
   Gerald D. Weinstein and M. Alan Menter

2. Topical Agents in the Treatment of Moderate-to-Severe Psoriasis 29
   Kristina P. Callis and Gerald G. Krueger

3. The Art and Practice of UVB Phototherapy for the Treatment of Psoriasis 53
   John Koo, Grace Bandow, and Steven R. Feldman

4. Systemic and Topical PUVA Therapy 91
   Warwick L. Morison

5. Therapy of Moderate-to-Severe Psoriasis with Methotrexate 115
   Gerald D. Weinstein
6. Systemic Retinoids
   *Paul S. Yamauchi, Dalia Rizk, Tanya Kormeili, Rickie Patnaik, and Nicholas J. Lowe*

7. Cyclosporine in the Treatment of Severe Psoriasis
   *Charles N. Ellis and Madhu Battu*

8. Combination, Rotational, and Sequential Therapy
   *Mark Lebwohl*

9. Pediatric Psoriasis
   *Peggy Lin and Amy S. Paller*

10. Psoriatic Arthritis
    *Dafna D. Gladman*

11. Immunobiologicals for Psoriasis: Using Targeted Immunotherapies as Pathogenic Probes in Psoriasis
    *Alice B. Gottlieb*

12. Etanercept for Treatment of Psoriasis and Psoriatic Arthritis
    *Alice B. Gottlieb*

13. Alefacept to Treat Psoriasis
    *Gerald G. Krueger and Kristina P. Callis*

14. Infliximab in the Treatment of Psoriasis
    *Alice B. Gottlieb*

15. Treatment of Psoriasis Using Efalizumab
    *Craig L. Leonardi*

*Index*
Contributors

**Grace Bandow, M.D.** Clinical Research Fellow, Department of Dermatology, University of California, San Francisco, San Francisco, California, U.S.A.

**Madhu Battu, B.A.** University of Michigan Medical School, Ann Arbor, Michigan, U.S.A.

**Kristina P. Callis, M.D.** Clinical Research Fellow, Department of Dermatology, University of Utah Health Sciences Center, Salt Lake City, Utah, U.S.A.

**Charles N. Ellis, M.D.** Professor and Associate Chair, Department of Dermatology, University of Michigan Medical School, Ann Arbor, Michigan, U.S.A.

**Steven R. Feldman, M.D., Ph.D.** Professor of Dermatology, Pathology, and Public Health Sciences, Wake Forest University School of Medicine, Winston-Salem, North Carolina, U.S.A.

**Dafna D. Gladman, M.D., F.R.C.P.C.** Professor of Medicine, University of Toronto, and Senior Scientist, Toronto Western Research Institute, and Centre for Prognosis Studies in the Rheumatic Diseases, University Health Network, Toronto Western Hospital, Toronto, Ontario, Canada

**Alice B. Gottlieb, M.D., Ph.D.** W. H. Conzen Chair in Clinical Pharmacology, Professor of Medicine, and Director, Clinical Research Center, Univer-
University of Medicine and Dentistry of New Jersey—Robert Wood Johnson Medical School, New Brunswick, New Jersey, U.S.A.

John Koo, M.D.  Professor and Vice Chair, Department of Dermatology, University of California, San Francisco, San Francisco, California, U.S.A.

Tanya Kormeili, M.D.  Clinical Research Specialists, Santa Monica, and Division of Dermatology, UCLA School of Medicine, Los Angeles, California, U.S.A.

Gerald G. Krueger, M.D.  Professor, Cumming Presidential Endowed Chair, Department of Dermatology, University of Utah Health Sciences Center, Salt Lake City, Utah, U.S.A.

Mark Lebwohl, M.D.  Professor and Chairman, Department of Dermatology, Mount Sinai School of Medicine, New York, New York, U.S.A.

Craig L. Leonardi, M.D.  Clinical Associate Professor, Department of Dermatology, St. Louis University School of Medicine, St. Louis, Missouri, U.S.A.

Peggy Lin, M.D.  Department of Pediatrics, Children’s Memorial Hospital and Northwestern University Feinberg School of Medicine, Chicago, Illinois, U.S.A.

Nicholas J. Lowe, M.D., F.R.C.P.  Clinical Research Specialists, Santa Monica, and Clinical Professor, Division of Dermatology, UCLA School of Medicine, Los Angeles, California, U.S.A.

M. Alan Menter, M.D.  Chief, Division of Dermatology, Baylor University Medical Center, Dallas, Texas, U.S.A.

Warwick L. Morison, M.D., F.R.C.P.  Professor of Dermatology, Johns Hopkins Medical School, Baltimore, Maryland, U.S.A.

Amy S. Paller, M.D.  Chair, Division of Dermatology, Children’s Memorial Hospital and Professor of Pediatrics and Dermatology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, U.S.A.

Rickie Patnaik, M.D.  Clinical Research Specialists, Santa Monica, and Division of Dermatology, UCLA School of Medicine, Los Angeles, California, U.S.A.

Dalia Rizk, M.D.  Clinical Research Specialists, Santa Monica, and Division of Dermatology, UCLA School of Medicine, Los Angeles, California, U.S.A.
Contributors

Gerald D. Weinstein, M.D.  Professor and Chairman, Department of Dermatology, University of California, Irvine, College of Medicine, Irvine, California, U.S.A.

Paul S. Yamauchi, M.D., Ph.D.  Clinical Research Specialists, Santa Monica, and Division of Dermatology, UCLA School of Medicine, Los Angeles, California, U.S.A.
I. INTRODUCTION

Psoriasis has traditionally been considered an inflammatory skin disorder of unknown etiology producing red scaly patches of mere cosmetic nuisance to patients. However, with recent knowledge gleaned from the immunopathogenesis and genetics of psoriasis together with what may be termed the biological revolution in therapy, all of which will be discussed in later chapters, psoriasis now has to be considered a dynamic, genetic, immunological, systemic disorder manifesting on the body surface as well as in the joints in a significant proportion of patients. Patients and dermatologists alike thus need to shift their focus from considering psoriasis as a mere skin disease likely to be controlled with topical therapy to a condition no different from other immune-mediated disorders such as Crohn’s disease, rheumatoid arthritis, and lupus erythematosus, all of which have a vast range of clinical manifestations. Just as the full spectrum of these disorders of the immune system need to be carefully considered, so too does psoriasis need a careful clinical evaluation, taking into account the extent of disease, the form of the disease, and quality of life issues for each individual patient as well as the potential for coexistent psoriatic joint disease. All of this, particularly on an initial patient visit, will not be accomplished in a 5–10 min patient encounter. It will require time and dedication from the physician and his or her support staff to improve patient compliance as well as the disappointment factor.
currently prevalent in the psoriatic population. Never has psoriasis been so much at the forefront; the buzz among researchers, clinicians, and indeed patients with the advent of new therapies, is palpable. It behooves us as dermatologists to rise to the challenge, refocus our energies and thought processes to the treatment of this most prevalent of all immune-mediated diseases, and take center stage along with our rheumatology and gastroenterology colleagues in biotechnology, target-based therapeutics. Certainly, we will continue to utilize the full therapeutic armamentarium currently available to us, as will be discussed later in this chapter. The explosion of this new knowledge, and with it new therapeutics, will enable patients and physicians alike to tailor therapy to individual forms of psoriasis as well as to individual patient needs.

II. CLINICAL MANIFESTATIONS

Psoriasis is defined by the Committee on Guidelines of Care and the Task Force on Psoriasis of the American Academy of Dermatology as follows: “A chronic skin disease that is classically characterized by thickened, red areas of skin covered with silvery scales” (1). The extent of skin involvement can range from discrete, localized areas to generalized body involvement. The joints, nails, and mucous membranes may also be affected with the disease. “Psoriasis has a tremendous range of phenotypic variability,” with a range of clinical manifestations from mild disease with a few isolated discoid plaques to multiple different morphological variants together with more serious forms of the disease involving major portions of the body surface, and, finally, coexistent psoriatic joint disease. Psoriasis may be symptomatic throughout one’s lifetime, may progress with age, or may wax and wane in severity. The disease may be readily apparent to others and cause functional impairment, disfigurement, and emotional distress out of all proportion to the actual extent of clinical disease. When severe, in the judgment of the patient, the effects of psoriasis can have a deleterious impact on work performance, social performance and acceptability, sexual function, and mental health. The diagnosis of psoriasis is normally relatively easy to make, although conditions such as cutaneous T-cell lymphoma (CTCL), mycosis fungoides, eczema, tinea infections, and secondary syphilis may occasionally cause confusion and should be considered in the differential diagnosis, particularly when patients’ conditions fail to respond to traditional antipsoriatic therapy. A full medical, family, and personal history is likewise important (Table 1). The classic morphological variants are noted in Table 2.

While psoriasis normally remains true to form during one’s lifetime with discoid plaques predominating, the whole range of morphological
Overview

Table 1  Important Factors in Patient’s History

<table>
<thead>
<tr>
<th>Medical history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic scaling of the ears</td>
</tr>
<tr>
<td>Coexistent or previously diagnosed immune-mediated diseases</td>
</tr>
<tr>
<td>Long-standing “dandruff”</td>
</tr>
<tr>
<td>Atopy</td>
</tr>
<tr>
<td>Pruritus ani or vulvae</td>
</tr>
<tr>
<td>Associated joint problems</td>
</tr>
<tr>
<td>Family history</td>
</tr>
<tr>
<td>Atopy</td>
</tr>
<tr>
<td>Psoriasis</td>
</tr>
<tr>
<td>Rheumatological disorders</td>
</tr>
<tr>
<td>Precipitating factors</td>
</tr>
<tr>
<td>Antecedent infections, particularly streptococcal</td>
</tr>
<tr>
<td>Stress (physical, emotional, or metabolic)</td>
</tr>
<tr>
<td>Medications (see Table 7)</td>
</tr>
</tbody>
</table>


subtypes may present in an individual patient either simultaneously or progressively with increasing age. Thus patients with palmar–plantar psoriasis may have no other clinical evidence of psoriasis, may have coexistent flexural psoriasis, or may have classic discoid plaque psoriasis involving a few anatomical sites or major portions of the body surface area. In addition, erythrodermic psoriasis also classically shows severe palmar–plantar involvement. It is likely that as we unravel the genetics of psoriasis (see below), this

Table 2  Morphological Variants of Psoriasis

<table>
<thead>
<tr>
<th>Localized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generalized</td>
</tr>
</tbody>
</table>