Primer on the Rheumatic Diseases

Edited by: John H. Klippel, John H. Stone, Leslie J. Crofford, Patience White

- A tradition of excellence for more than 70 years continues
- Presenting the best translational guide to over 100 rheumatic diseases

revised and EXPANDED

13th EDITION
Primer on the Rheumatic Diseases

Edited by John H. Klippel, Arthritis Foundation, Atlanta, GA, USA
Coeditors: John H. Stone, Massachusetts General Hospital, Boston, MA, USA; Leslie J. Crofford, University of Kentucky, Lexington, KY, USA; Patience White, Arthritis Foundation, Washington, DC, USA

Primer on the Rheumatic Diseases is one of the most prestigious and comprehensive texts on arthritis and related diseases, including osteoarthritis, rheumatoid arthritis, osteoporosis, lupus and more than 100 others. It offers medical students and physicians a concise description of the current science, diagnosis, clinical consequences, and principles of management. New and expanded chapters heighten the translational nature of this edition. Students, trainees, and practicing clinicians all need a standard textbook that can change with the times and reflect recent strides taken in understanding and treating rheumatic disease. The Primer fills that need.

12th ed. published by the Arthritis Foundation, 2001

13th ed. 2007. 724 p. 124 illus., 111 in color. Softcover
ISBN 978-0-387-35664-8 ➤ $79.95

New to the 13th Edition:

► New chapters entitled “Clinical Immunology” and “Applied Genetics”, designed to heighten the translational nature of the book.
► A section devoted entirely to juvenile inflammatory arthritis, with individual chapters on “Clinical Features”, “Pathology and Pathogenesis”, “Treatment and Assessment”, and “Special Considerations”.
► Separate chapters on ankylosing spondylitis and the reactive and enteropathic arthropathies, once lumped together (with psoriatic arthritis) as “seronegative spondyloarthropathies”.
► A tripling of the text devoted to psoriatic arthritis, an acknowledgement of the substantial treatment advances in that disorder.
► Individual chapters (and more than doubling of the allotted text) to the metabolic and inflammatory myopathies, once included in the same chapter.
► Reorganization of the vasculitis section along more rational and all-inclusive lines, with a chapter entitled “ANCA-Associated Vasculitis” that addresses together Wegener’s granulomatosis, microscopic polyangiitis, and the Churg-Strauss syndrome, disorders with striking similarities but important contrasts.
► Thoroughly-illustrated chapter related to the cutaneous manifestations of musculoskeletal disease.
► A clinically-focused textbook that addresses the full spectrum of rheumatic disease.
Patients with PG also demonstrate pathergy. Thus, this condition has been reported following a variety of surgical procedures, for example, thoracotomy or fistu- lotomy. The systemic associations vary depending on the type of PG. Classical disease and peristomal PG are associated more frequently with inflammatory bowel disease and/or arthritis. Careful evaluation (or inflammatory bowel disease is warranted in cases of peristomal PG) even when the stoma was created for other reasons (e.g., following cancer surgery). In contrast, atypical pyoderma gangrenosum is found more frequently in the setting of myelophthisic leukemias or pre-leukemic conditions.

In 60% to 70% of patients with the CSS, allergic rhinitis (90%) (80%) is present. Nasal congestion and nasal obstruction are prominent symptoms. Patients with PG often have allergic rhinitis and atopy. Nasal congestion may contribute to the development of PG. Patients with PG often have nasal pain and stuffiness, rhinitis, epistaxis, and nasal deformities. Nasal deformities may include a deviated nasal septum or a saddle-nose deformity. Patients with PG also demonstrate pathergy. Thus, atypical pyoderma gangrenosum, also known as neutrophilic dermatosis of the dorsal hands, is a form of ulcerative skin disease. There are at least four clinical variants of PG associated with an underlying disease (e.g., inflammatory bowel disease or RA), treatment of the primary condition often leads to improvement in PG. Prednisone (1 mg/kg/day) is generally the first line of therapy for ulcerative PG. Infliximab (3–5 mg/kg every 8 weeks following two initial doses 2 weeks apart) is also an effective therapy for PG, even in the absence of inflammatory bowel disease. Other therapies employed in PG include dapsone (100–200 mg/day assuming normal levels of thiamine methyltransferase—(TMST), and macrolide antibiotic model (14–15 mg b.i.d.).

Pyoderma gangrenosum (PG) is a form of ulcerative skin disease. There are at least four clinical variants of PG, classical, staphylococcal, parapsilosis, and mucosal (3). The classical lesion is a rapidly progressing, pustular ulcer, most often on the leg, with a violaceous, undermined (overhanging) border (Figure 25E-1). Atypical PG occurs as a more superficial lesion, often on the oral mucosa (Figure 25E-2), external foramina, or face. The border of atypical PG may appear bluish, leading to clinical confusion with Sweet’s syndrome. Perianal PG occurs as a deep ulcer near the site of a stoma, usually created after gastrointestinal or perianal surgery. Finally, mucosal PG is associated with ulcerations that can resemble simple aphthous or vegetative lesions. Mucosal PG must be differentiated from Behçet’s disease.

### CLINICAL FEATURES

<table>
<thead>
<tr>
<th>Feature</th>
<th>Sweet’s Syndrome</th>
<th>Pyoderma Gangrenosum (PG)</th>
<th>Rheumatoid Neutrophilic Dermatitis</th>
<th>Bowel-Associated Dermatitis Syndrome</th>
<th>Sweet’s Syndrome of the Dorsal Hands</th>
</tr>
</thead>
</table>

| Table 21C-3: CLINICAL FEATURES OF THE PRIMARY ANTINEUTROPHIL CYTOPLASMIC ANTIBODIES | | | | | |
|---|---|---|---|---|
| **Signs and symptoms** | **WEGENER’S GRANULOMATOSIS** | **SWEET’S SYNDROME** | **PYODERMA GANGRENOSUM (PG)** | **SWEET’S SYNDROME OF THE DORSAL HANDS** |
| Nasal polyps | Rare | No | Rare | Rare |
| Nasal crusting | No | Yes | No | No |
| Erosive rhinitis | Yes | No | Yes | No |
| Eosinophilic tissue infiltrates | Rare | No | Rare | No |
| Sinusitis | Rare | No | Yes | No |
| Osteitis | Rare | No | Rare | No |
| Erythema migrans | Rare | No | Rare | No |
| Ankle swelling | Rare | No | Rare | No |
| Rheumatoid factor | Rare | No | Rare | No |
| ANCA positivity | 80%–90% | 70% | 50% | 60%–70% |

### Expanded chapter on the cutaneous manifestations of disease

**TABLE 25.4: COMPARATIVE STUDIES OF CLINICAL FEATURES IN SWEET’S SYNDROME, PYODERMA GANGRENOSUM, AMPHITHELIONIC ARTHRITIS, AND BOWEL-ASSOCIATED DERMATITIS**

<table>
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<th>Sweet’s Syndrome</th>
<th>Pyoderma Gangrenosum (PG)</th>
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<tbody>
<tr>
<td>Pustules</td>
<td>Occasional</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Ulceration</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Mucosal injury</td>
<td>Rare</td>
<td>Yes</td>
<td>Yes</td>
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<td>Rare</td>
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<td>Yes</td>
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<td>Rare</td>
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<td>Yes</td>
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<tr>
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<td>Rare</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Bowel involvement</td>
<td>Rare</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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</tbody>
</table>

| **FIGURE 21C-1** | | | |
|---|---|---|
| Sweet’s syndrome of the dorsal hands | | | |

**COLOR FIGURES**

Color figures depict cutaneous findings and histopathology.

**TABLE 21C-4: COMPARATIVE STUDIES OF CLINICAL FEATURES IN SWEET’S SYNDROME, PYODERMA GANGRENOSUM, AMPHITHELIONIC ARTHRITIS, AND BOWEL-ASSOCIATED DERMATITIS**

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| **FIGURE 21C-2** | | | |
|---|---|---|
| Histopathological findings in Sweet’s syndrome. | | | |

**Details musculoskeletal signs and symptoms**
Table of Contents

- Public Health and Arthritis: A Growing Imperative - Patience H. White and Rowland W. Chang
- Evaluation of the Patient - A. History and Physical Examination David B. Robinson and Hani S. El-Gabalawy; B. Laboratory Assessment Kerstin Morehead; C. Arthrocentesis, Synovial Fluid Analysis, and Synovial Biopsy Kenneth H. Fye; D. Imaging of Rheumatologic Diseases William W. Scott, Jr., William J. Didie, and Laura M. Fayad
- Signs and Symptoms of Musculoskeletal Disorders - A. Monarticular Joint Disease H. Ralph Schumacher and Lan X. Chen; B. Polyarticular Joint Disease Sterling West; C. Neck and Back Pain David Borenstein; D. Regional Rheumatic Pain Syndromes Joseph J. Biundo, Jr.; E. The Fibromyalgia Syndrome Dina Dadabhoy and Daniel J. Clauw
- Molecular and Cellular Basis of Immunity and Immunological Diseases - Kevin Elias, Richard Siegel, and John J. O'Shea
- Genetics and Disease - James Kelley and Robert P. Kimberly
- Rheumatoid Arthritis - A. Clinical and Laboratory Manifestations Christopher V. Teihlirian and Joan M. Batton; B. Epidemiology, Pathology, and Pathogenesis Jean-Marc Waldenburger and Gary S. Firestein; C. Treatment and Assessment Alyce M. Oliver and E. William St. Clair
- Juvenile Idiopathic Arthritis - A. Clinical Features Daniel J. Lovell; B. Pathology and Pathogenesis Patricia Woo; C. Treatment and Assessment Philip J. Hashkes and Ronald M. Laxer; D. Special Considerations Carol B. Lindsley
- Psoriatic Arthritis - A. Clinical Features Dafna D. Gladman; B. Pathology and Pathogenesis Christopher Ritchlin; C. Treatment and Assessment Philip J. Mease
- Ankylosing Spondylitis - A. Clinical Features Désirée Van der Heijdt; B. Pathology and Pathogenesis Juergen Braun; C. Treatment and Assessment John C. Davis, Jr.
- Reactive and Enteropathic Arthritis - Robert D. Inman
- Osteoarthritis - A. Clinical Features Paul Dieppe; B. Pathology and Pathogenesis Francis Berenbaum; C. Treatment Leena Sharma
- Gout - A. Clinical Features N. Lawrence Edwards; B. Epidemiology, Pathology, and Pathogenesis Hyon K. Choi; C. Treatment Robert A. Terkeltaub
- Calcium Pyrophosphate Dihydrate, Hydroxyapatite, and Miscellaneous Crystals Geraldine McCarthy
- Systemic Lupus Erythematosus - A. Clinical and Laboratory Features Jill P. Buyon; B. Epidemiology, Pathology and Pathogenesis David S. Pisetsky; C. Treatment and Assessment Susan Manzi and Amy H. Kao
- Antiphospholipid Syndrome - Michelle Petri
- Systemic Sclerosis - A. Clinical Features Maureen D. Mayes; B. Epidemiology, Pathology, and Pathogenesis John Varga; C. Treatment and Assessment Maya H. Buch and James R. Seibold
- Idiopathic Inflammatory Myopathies - A. Clinical Features Robert L. Wortmann; B. Pathology and Pathogenesis Lisa G. Rider and Frederick W. Miller; C. Treatment and Assessment Chester V. Oddis
- Metabolic Myopathies - Alan N. Baer
- Sjögren’s Syndrome - Troy Daniels
- Vasculitides - A. Large Vessel Vasculitis and Polymyalgia Rheumatica Cornelia M. Weyand and Jörg J. Goronzy; B. Polyarteritis Nodosa Keith T. Rott; C. The Antineutrophil Cytoplasmic Antibody–Associated Vasculitides: Wegener’s Granulomatosis, Microscopic Polyangiitis, and the Churg-Strauss Syndrome John H. Stone; D. Immune Complex–Mediated Vasculitis Philip Seo; E. Miscellaneous Vasculitis (Behcet’s Disease, Primary Angiitis of the Central Nervous System, Cogan’s Syndrome, and Erythema Elevation Diutium) Kenneth T. Calamia and Carlo Salvarani; F. Kawasaki’s Disease Barry L. Myones
- Relapsing Polychondritis - Harvinder S. Luthra
- Adult Onset Still’s Disease - John M. Esdaile
- Periodic Syndromes - John G. Ryan and Daniel L. Kastner
- Complex Regional Pain Syndrome - Geoffrey Littlejohn
- Sarcoidosis - Edward S. Chen
- Storage and Deposition Diseases - Duncan A. Gordon
- The Amyloidoses - Pasha Sarraf and Jonathan Kay
- Neoplasms of the Joint - Andrew J. Cooper, James D. Reeves, and Sean P. Scully
- Heritable Disorders of Connective Tissue - Reed Edwin Pyeritz
- Bone and Joint Dysplasias - William A. Horton
- Osteonecrosis - Thorsten M. Seyler, David Marker, and Michael A. Mont
- Paget’s Disease of Bone - Roy D. Altman
- Osteoporosis - A. Epidemiology and Clinical Assessment Kenneth G. Saag; B. Pathology and Pathophysiology Philip Sambrook; C. Treatment of Postmenopausal Osteoporosis Nelson B. Watts
- Rehabilitation of Patients with Rheumatic Diseases - Thomas D. Beardmore
- Psychosocial Factors in Arthritis - Alex Zautra and Denise Krueszewski
- Self-Management Strategies - Teresa J. Brady
- Pain Management - John B. Winfield
- Therapeutic Injections of Joints and Soft Tissues - Juan J. Canoso
- Non-Steroidal Anti-inflammatory Drugs - Leslie J. Crofford
- Glucocorticoids - Frank Buttgereit and Gerd-Rüdiger Burmester
- Operative Treatment of Arthritis - Joseph A. Buckwalter and W. Timothy Ballard
- Complementary and Alternative Therapies - Erin L. Arnold and William J. Arnold
From the Foreword

The 13th edition of the Primer on the Rheumatic Diseases is an extraordinary handbook for clinical care. The Primer will educate trainees, update established clinicians, and help health care providers from all walks of the profession provide better care for patients with arthritis and rheumatic diseases. I congratulate the editors on their superb work. In addition, the multiple contributors — many of whom are members of the American College of Rheumatology — should be thanked for their scholarly contributions to the Primer.  

Michael E. Weinblatt, MD, Professor of Medicine, Harvard Medical School, Brigham and Women’s Hospital, Boston, MA, USA

About the Editors

John H. Klippel, M.D. is the President and Chief Executive Officer of the Arthritis Foundation. He previously served as a Senior Investigator in the Arthritis and Rheumatism Branch (NIH) (1976-1987), Clinical Director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) (1987-1999), and Medical Director of the Arthritis Foundation (1999-2003). He is a diplomat of the American Board of Internal Medicine and a fellow of the American College of Physicians and the American College of Rheumatology. His honors and awards include the Surgeon General’s Exemplary Service Award, Distinguished Clinical Teacher Award (NIH Clinical Center), Directors Award (NIH Clinical Center) and the Burroughs-Wellcome Visiting Professor Award from the Royal Society of Medicine in London.

He received a bachelor’s degree from Bowling Green State University and a doctor of medicine degree from the University of Cincinnati College of Medicine. He completed his residency in internal medicine at Yale-New Haven Hospital and his fellowship in rheumatology at the National Institutes of Health and the University of California at San Diego.

John H. Stone, M.D., M.P.H., co-founded and directed the Vasculitis Center at Johns Hopkins University. Dr. Stone attended Harvard Medical School before training in internal medicine at Johns Hopkins and performing his rheumatology fellowship at the University of California-San Francisco. While on the faculty at Johns Hopkins, Dr. Stone served as the Principal Investigator for first randomized clinical trial in Wegener’s granulomatosis in the U.S. and organized the Rituximab in ANCA-Associated Vasculitis trial. From 2002 to 2006, Dr. Stone served as the Deputy Director for Clinical Research at the Johns Hopkins Bayview Medical Center. He was named a Hugh and Renna Cosner Scholar in the Cosner Program on Translational Research (2005). Dr. Stone became Deputy Editor for Rheumatology at UpToDate in 2006 and is an Associate Physician at the Massachusetts General Hospital.

Leslie J. Crofford, M.D. is an active member of the American College of Rheumatology, serving previously as a member of the Committee on Research and Chair of the Committee on Journal Publications. She is currently Vice-President of the American College of Rheumatology Research and Education Foundation and sits on the Executive Committee of the College. Dr. Crofford was elected to the American Board of Internal Medicine for Rheumatology in 2002 and is currently serving her second term. She is on the Board of Trustees of the Ohio River Valley Chapter of the Arthritis Foundation and has served on the Medical and Scientific Committee of the National Arthritis Foundation. Dr. Crofford is active as a clinical rheumatologist and has been named as one of America’s Top Doctors.

Patience White, M.D. is the chief public health officer of the Arthritis Foundation. In addition to her work there, she is a professor of medicine and pediatrics at the George Washington University School of Medicine and Health Sciences and teaches a Health Policy seminar for Stanford University at the Stanford in Washington campus in Washington DC.
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Primer on the Rheumatic Diseases
Klippel, J.H.; Stone, J.H.; Crofford, L.e.J.; White, P.H. (Eds.)
2008, XIX, 721 p., Softcover