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
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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

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.

Sample chapters available online at springer.com!

Available in November 2007
Patients with PG also demonstrate pathergy. This thin condition has been reported following a variety of surgical procedures, for example, thoracotomy or limb amputation. The systemic associations vary depending on the type of PG. Classical disease and periungual PG are associated more frequently with inflammatory bowel disease and/or arthritis. Cutaneous evolution (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 myelocytic leukemia or preleukemic conditions.

For cases 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 idiopathic PG. Infliximab (3–5 mg/kg every 6 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 (50–200 mg/day, assuming normal levels of glucagon), sulfasalazine, cyclosporine, thalidomide (100 mg/day), dapsone (100–200 mg/day), and acitretin (0.5–1 mg/kg/day). Neutrophilic dermatosis of the dorsal hands (NDDH), considered by some to be a separate disease entity, is regarded more commonly as a variant of either bowel inflammatory disease and atypical PG. NDDH is associated with the same underlying conditions as Sweet’s syndrome and atypical PG, and the management considerations are identical.

Bowel-associated neutrophilic dermatosis—arthritis syndrome was first recognized in the 1980s following gattex bypass surgery for morbid obesity. Fortunately, because of major alterations in surgical technique, this syndrome is rare. Monocytes are stimulated by colony-stimulating factor-1 and interleukin-1, which are often used. In patients with acute, idiopathic disease, the prognosis is generally good; many have only one episode. However, the course of patients with underlying leukemia or myelodysplasia follows that of the associated disease. Absent disease remission or a cure, recurrences are common.

**TABLE 25E-1. CLINICAL FEATURES OF THE PRINCIPAL ASSOCIATIONS.**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Wegener’s granulomatosis</th>
<th>Polyarteritis nodosa (PAN)</th>
<th>Henoch-Schönlein purpura (HSP)</th>
<th>Churg-Strauss syndrome (CSS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocyte sedimentation rate (ESR)</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Leukocytosis</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Protein S (&lt;1.5 mg/mL)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Renal involvement</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pulmonary involvement</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Cutaneous involvement</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Neutrophilic vasculitis</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Antineutrophil cytoplasmic antibodies (ANCAs)</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

**FIGURE 25E-1. Sweet’s syndrome.**

**FIGURE 25E-2. Histopathological findings in Sweet’s syndrome.**

CLINICAL FEATURES

There is substantial overlap in many of the clinical features of the AAVs. In some cases, distinguishing among two or more of these diseases on the basis of clinical features alone is difficult (Table 21E-1).

Upper Respiratory Tract and Ears

Although patients with the CSS or MPA may experience substantial ear, nose, or skin disease, this pattern of involvement is more characteristic of WG. More than 90% of patients with WG eventually develop upper airway or ear abnormalities. The nasal symptoms of WG include nasal pain and stuffiness, rhinorrhea, epistaxis, and blocked or brown nasal crusts. Nasal inflammation may lead to septal erosions, septal perforation, or, in many cases, nasal bridge collapse—the “valve-nose deformity” (Figure 21E-1). The distinction between active WG in the sinuses and secondary infections in the sinuses may be challenging (see Nosocomial Interventions section). In 60% to 75% of patients with the CSS, rhinitis is the earliest disease manifestation, typically appearing years prior to the development of full-blown sinusitis.

Pyoderma gangrenosum (PG) is a form of ulcerative skin disease. There are at least four clinical variants of PG, classical, staphylococcal, peristomal, and mucosal (3). The classical lesion is a rapidly progressing, punctate 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 dorsal hands (Figure 25E-4), extensor forearms, or face. The border of atypical PG is usually more superfi cial, often with a necrotic center (Figure 25E-4).

**TABLE 25E-2. ASSOCIATIONS WITH NEUTROPHILIC DERMATOSES.**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pyoderma gangrenosum (PG)</th>
<th>Rheumatoid arthritis (RA)</th>
<th>Bowel-associated dermatosis syndrome</th>
<th>Neutrophilic dermatosis of the dorsal hands</th>
</tr>
</thead>
<tbody>
<tr>
<td>Some</td>
<td>20%–25%</td>
<td>No</td>
<td>Yes</td>
<td>Occasional</td>
</tr>
<tr>
<td>Occasional</td>
<td>10% for superficial forms, 5% for classical PG</td>
<td>Yes, occasionally severe</td>
<td>No, but joint disease may stimulate RA</td>
<td>Occasional</td>
</tr>
<tr>
<td>25%–30%</td>
<td>15% for the superficial forms</td>
<td>No</td>
<td>No</td>
<td>15%</td>
</tr>
<tr>
<td>Rare</td>
<td>Rare</td>
<td>Possible</td>
<td>No</td>
<td>Rare</td>
</tr>
<tr>
<td>Occasionally</td>
<td>No</td>
<td>Possible</td>
<td>No</td>
<td>Possible</td>
</tr>
</tbody>
</table>

**FIGURE 25E-4. Atypical pyoderma gangrenosum, also known as neutrophilic dermatosis of the dorsal hands.**

**FIGURE 25E-5. Pyoderma gangrenosum.**

**FIGURE 25E-6. Histopathological findings in Sweet’s syndrome.**

**FIGURE 25E-7. Histopathological findings in Sweet’s syndrome.**

**FIGURE 25E-8. Histopathological findings in Sweet’s syndrome.**

**FIGURE 25E-9. Histopathological findings in Sweet’s syndrome.**

**FIGURE 25E-10. Histopathological findings in Sweet’s syndrome.**

Color figures depict cutaneous findings and histopathology.

Details musculoskeletal signs and symptoms.

Expanded chapter on the cutaneous manifestations of disease.
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
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Juvenile Idiopathic Arthritis - A. Clinical Features Daniel J. Lovell; B. Pathology and Pathogenesis Patricia Woe; C. Treatment and Assessment Philip J. Hashkes and Ronald M. Laxer; D. Special Considerations Carol B. Lindsay
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
Relapsing Polychondritis - Harvinder S. Luthra
Adult Onset Still's Disease - John M. Esdaile
Periodic Syndromes - John G. Ryan and Daniel L. Kastner
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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 diplomate 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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