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
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.

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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 spondyloarthopathies”.
► 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.

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Patients with PG also demonstrate pathergy. This thin condition has been reported following a variety of surgical procedures, for example, thoracotomy or fasci
tomy. The systemic associations vary depending on the
PG. The clinical disease and peripheral PG are
associated more frequently with inflammatory bowel disease and/or arthritis. Cutaneous vasculitis or infl
flammatory bowel disease is warranted in cases of peritoneal
PG, even when the stoma was created for other reasons
(eg, following cancer surgery). In contrast, atypical systemic vasculitis or PG is found more fre
quently in the setting of myeloproliferative or pro
liferating conditions.

The diagnosis of PG is one of exclusion. Although
bipheny should be performed to exclude other condi
tions, PG does not have a distinctive histopathology. B

Because of the importance of including diseases in
termediate—periarteritis nodosa—PG is almost always
performed as part of the excisional, despite the pos
sibility that the site will extend through pathergy. Cultures of the lesions following skin biopsy is essential. Infections with Staphylococcus aureus or streptococci also include deep
fungal infections, for example, Histoplasmosis, coccidioidomycosis, blastomycosis, and cryptococcosis, as well as aspergillosis, horn, and mycobacterial disease. In addition, atypical pyoderma gangrenosum is found more fre
quently in the setting of myeloproliferative or prolif
erating conditions.

The systemic associations vary depending on the
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mia—Crohn’s disease—iatrogenic disease—solid tumors—drug-induced disease—Sjögren’s syndrome

Although patients with the CSS or MPA may experi
ence gastrointestinal or genitourinary fistulae, PG occurs as a deep ulcer near the site of a stoma,
usually created after gastrointestinal or genitourinary
operations. Atypical pyoderma gangrenosum, also known as neutrophilic dermatosis of the bowel tract,
monocyte colony-stimulating factor (CSF), interferon gamma (IFN-γ), and interleukin-12 (IL-12) 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 leuke
mia—Crohn’s disease—iatrogenic disease—solid tumors—drug-induced disease—Sjögren’s syndrome

There is a relationship between the cutaneous features of the AAVs. In some cases, distinguishing among two or more of these diseases on the basis of cutaneous features alone is difficult (Table 21C-3).

Color figures depict cutaneous findings and histopathology

Details musculoskeletal signs and symptoms

Expanded chapter on the cutaneous manifestations of disease

PG. Pyoderma gangrenosum (PG) is a form of ulcerative
skin disease. There are at least four clinical variants of
PG: classical, atypical, peristomal, and mucosal (3). The
classical lesion is a rapidly progressing, purplish ulcer,
most often on the leg, with a violaceous, undermined
border (Figure 25E-3). Atypical PG occurs as a more superfi cial lesion, often on the oral
mucosa (Figure 25E-4), extension forearms, or face. The
border of atypical PG may appear bullous, leading to
clinical confusion with Sweet’s syndrome. Periarticular
PG occurs as a deep ulcer near the site of a stoma,
usually created after gastrointestinal or genitourinary
surgery. Mucosal PG is associated with ulcerations
that can resemble simple aphthae or vegetative
lesions. Mucosal PG must be differentiated from
Bichet’s disease.

### TABLE 21C-3. CLINICAL FEATURES OF THE PRIMAL ASSOCIATIONS

<table>
<thead>
<tr>
<th>Feature</th>
<th>Wegener’s Granulomatosis</th>
<th>Churg-Strauss Syndrome</th>
<th>microscopic polyangiitis</th>
<th>Henoch-Schönlein purpura</th>
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</thead>
<tbody>
<tr>
<td>Acute polyarthritis</td>
<td>90%</td>
<td>40%</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Acute posterior</td>
<td>80%</td>
<td>50%</td>
<td>50%</td>
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<tr>
<td>Acute purpura spontanea</td>
<td>PR3 + MPO</td>
<td>PR3 + MPO</td>
<td>PR3 + MPO</td>
<td>PR3 + MPO</td>
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<tr>
<td>Functional hematuria</td>
<td></td>
<td></td>
<td>50%</td>
<td>50%</td>
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<tr>
<td>Leukocytoclastic vasculitis (renal biopsy positive)</td>
<td></td>
<td>50%</td>
<td>50%</td>
<td>50%</td>
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<tr>
<td>Cutaneous vasculitis</td>
<td>50%</td>
<td>50%</td>
<td>50%</td>
<td>50%</td>
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<tr>
<td>Eyelid granulomatous</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Ocular involvement</td>
<td>50%</td>
<td>50%</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Cutaneous vasculitis</td>
<td>50%</td>
<td>50%</td>
<td>50%</td>
<td>50%</td>
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<tr>
<td>Oral ulceration</td>
<td>50%</td>
<td>50%</td>
<td>50%</td>
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<tr>
<td>Nephrotic syndrome</td>
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<tr>
<td>Renal vasculitis (renal biopsy positive)</td>
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<tr>
<td>Leukocytoclastic vasculitis</td>
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<tr>
<td>Neutrophilic granulomatous</td>
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</table>

**Color figures depict cutaneous findings and histopathology**

**Details musculoskeletal signs and symptoms**

**Expanded chapter on the cutaneous manifestations of disease**

**There is a relationship between the cutaneous features of the AAVs. In some cases, distinguishing among two or more of these diseases on the basis of cutaneous features alone is difficult (Table 21C-3).**

### Upper Respiratory Tract and Ears

Although patients with the CSS or MPA may experi
ence substantial ear, nose, or sinus disease, this pattern of disease is not as 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, rhinitis, and loss of smell. Nasal inflammation may lead
to nasal polyps, septal perforation, or, in some cases,
Barnes, collapse—the “valve-like deformity” (Figure 21C-3). The distinction between active WG in the sinuses and secondary infections in the sinuses may
be challenging (see Nonmedical Interventions section).

In 60% to 70% of patients with the CSS, allergic
rhinitis develops, and about 50% develop upper
respiratory tract disease. In 80% of patients with the CSS, upper respiratory tract disease—nasal polyps,
histopathologic (H
drastic) findings in Wegener’s granulomatosis.

**Figure 25E-1**

Histiopathologic findings in Sweet’s syndrome.

**Figure 25E-2**

**Figure 25E-3**

bullous dermatitis in Wegener’s granulomatosis.

**Figure 25E-4**

Atypical pyoderma gangrenosum, also known as neutrophilic dermatosis of the bowel tract.

**Figure 25E-5**

Pyoderma gangrenosum is in a patient without an associated syndrome.

**Figure 25E-6**

Powdered gangrenosum is in a patient without an associated syndrome.
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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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