Primer on the Rheumatic Diseases

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

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- 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.

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. The pathergy test, performed by puncturing the skin with a needle, allows for the evaluation of the ultrarapid development of a visible lesion at the site of the puncture. The pathergy test is positive in approximately 30% of patients with PG, whereas it is negative in patients with other cutaneous disorders, such as psoriasis.

PG occurs as a deep ulcer near the site of a stoma, often occurring as a more superficial lesion, often on the dorsal hands (Figure 25E-4), extensor forearms, or face. The PG: classical, atypical, peristomal, and mucosal (3). The mucosal 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, painless ulcer, most often on the leg, with a violaceous, undermined (overhanging) border (Figure 25E-3). 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 may appear bullous, leading to clinical confusion with Sweet’s syndrome. Peristomal PG occurs as a deep ulcer near the site of a stoma, usually created after gastrointestinal or perinomary 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 of the Primary Antineutrophil Cytoplasmic Antibodies

#### Table 25E-1: Clinical Features of the Primary Antineutrophil Cytoplasmic Antibodies

<table>
<thead>
<tr>
<th>Feature</th>
<th>Wegener’s Granulomatosis</th>
<th>Polyarteritis Nodosa</th>
<th>Churg-Strauss Syndrome</th>
<th>Goodpasture’s Syndrome</th>
<th>Henoch-Schönlein Purpura</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age onset</td>
<td>Infants</td>
<td>Adolescents</td>
<td>Adults</td>
<td>Infants</td>
<td>Adolescents</td>
</tr>
<tr>
<td>Nephritis</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Pericarditis</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Pleuritis</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Renal manifestations</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Cough</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Chest pain</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Fever</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

| Table 25E-2: Infectious Mimickers | PG syndromes, also known as neutrophilic dermatoses of the dorsal hands. | Infectious mimickers are not common but include deep fungal infections, for example, Blastomycosis, Sporotrichosis, and deep mycosis. The lesion is most often on the leg, with a violaceous, undermined (overhanging) border (Figure 25E-3). 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 may appear bullous, leading to clinical confusion with Sweet’s syndrome. Peristomal PG occurs as a deep ulcer near the site of a stoma, usually created after gastrointestinal or perinomary 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.

### Infectious Mimickers

- **Sweet’s syndrome**
  - Neutrophilic infiltration of the skin, typically involving the head and neck, and often associated with fever, malaise, and leukocytosis.
  - Characterized by recurrent episodes of fever and inflammation.
- **Atypical PG**
  - Typically presents with a more superficial ulcerative lesion, often on the dorsal hands.
  - May mimic Sweet’s syndrome.

### Table 25E-1: Infectious Mimickers

<table>
<thead>
<tr>
<th>Infectious Mimickers</th>
<th>PG Syndrome, Also Known as Neutrophilic Dermatoses of the Dorsal Hands</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fungal infections</td>
<td>Yes</td>
</tr>
<tr>
<td>Mycobacterial infections</td>
<td>Yes</td>
</tr>
<tr>
<td>Bacterial infections</td>
<td>Yes</td>
</tr>
<tr>
<td>Viral infections</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### Figures

- **Figure 25E-1**: Sweet’s syndrome
- **Figure 25E-2**: Histopathological findings in Sweet’s syndrome.

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**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 25E-1).

**Upper Respiratory Tract and Ears**

- Although patients with the CSS or GPA may experience submucosal or, more commonly, superficial or purpura, this pattern of involvement is most 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 nasal or oropharyngeal ulceration. Nasal inflammation may lead to nasal obstruction, septal perforation, or, in many cases, nasal bridge collapse—the “vallecular deformity” (Figure 25E-3). The distinction between active WG in the nasopharynx and secondary infections in the sinuses may be challenging (see Neurological Interventions section).

- In 60% to 70% of patients with the CSS, rhinitis is the earliest disease manifestation, typically appearing years before the development of full-blown inflammatory manifestations. This is regarded more commonly as a variant of either Sweet’s syndrome or atypical PG. NDDH is associated with seronegative RA. In terms of histopathology, rheumatoid arthritis has a more extensive subcutaneous lymphoid infiltrate, and Sweet’s syndrome has a more prominent neutrophilic infiltrate. The distinction between active WG in the nasopharynx and secondary infections in the sinuses may be challenging (see Neurological Interventions section).

- NDDH is associated with seronegative RA. In terms of histopathology, rheumatoid arthritis has a more extensive subcutaneous lymphoid infiltrate, and Sweet’s syndrome has a more prominent neutrophilic infiltrate. The distinction between active WG in the nasopharynx and secondary infections in the sinuses may be challenging (see Neurological Interventions section).
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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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