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Preface: Pediatric Rheumatology **xiii**

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Principles of Inflammation for the Pediatrician **225**

Alessia Omenetti, Sabrina Chiesa, and Marco Gattorno

The immune system consists of 2 branches: *innate* and *adaptive*. The former represents the first line of host defense during infection and plays a key role in the early recognition and protection against invading pathogens. The latter orchestrates elimination of pathogens in the late phase of infection and leads to the generation of immunologic memory. Innate and adaptive immunity should not be considered separate compartments. Innate and adaptive immune responses represent an integrated system of host defense. The authors review the mechanisms driving the induction and perpetuation of the inflammatory responses observed during pathogen-associated, autoimmune, and autoinflammatory diseases.

Approach to the Child with Joint Inflammation **245**

Roberta Berard

Arthritis is manifested as a swollen joint having at least 2 of the following conditions: limited range of motion, pain on movement, or warmth overlying the joint. This article discusses an approach to the evaluation of a child with arthritis of one (mono) or several (poly) joints.

Laboratory Testing in Pediatric Rheumatology **263**

Jay Mehta

In children, laboratory evaluations can assist in the screening of patients for inflammatory disorders, confirm diagnoses, allow for monitoring of disease activity and response to therapy, and suggest prognoses and risk of morbidities associated with rheumatic diseases. This review provides an overview of the usefulness and interpretation of both the commonly ordered tests ordered by the general pediatrician as well as those frequently used in the pediatric rheumatology clinic for diagnosis and disease monitoring. Studies discussed include the complete blood count, acute phase reactants, autoantibodies, serum complement, urinalysis, streptococcal antibody tests, and commonly used genetic studies.

Rheumatologic Emergencies in Newborns, Children, and Adolescents **285**

Jonathan D. Akikusa

This article presents five clinical scenarios in which the initial manifestations of pediatric rheumatic diseases constitute life-threatening medical emergencies. It is intended as a problem-oriented guide for pediatricians to assist in the recognition of rheumatologic differentials in children presenting with critical illness and provides an approach to their initial investigation and management.

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Juvenile idiopathic arthritis (JIA) encompasses a complex group of disorders with arthritis as a common feature. This article provides the pediatrician with a review of the epidemiology, classification, clinical manifestations, and complications of JIA. It also provides an update on the current understanding of the cause of JIA and recent developments in management and a recent review of the long-term outcome in JIA.	
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Cytokine storm syndromes (CSS) are a group of disorders representing a variety of inflammatory causes. The clinical presentations of all CSS can be strikingly similar, creating diagnostic uncertainty. However, clinicians should avoid the temptation to treat all CSS equally, because their inciting inflammatory insults vary widely. Failure to identify and address this underlying trigger results in delayed, inoptimal, or potentially harmful consequences. This review places the hemophagocytic syndromes hemophagocytic lymphohistiocytosis and macrophage activation syndrome within a conceptual model of CSS and provides a logical framework for diagnosis and treatment of CSS of suspected rheumatic origin.	
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Kathryn S. Torok	
Pediatric scleroderma includes 2 major groups of clinical entities, systemic sclerosis (SSc) and localized scleroderma (LS). Although both share a common pathophysiology, their clinical manifestations differ. LS is typically confined to the skin and underlying subcutis, with up to a quarter of	

patients showing extracutaneous disease manifestations such as arthritis and uveitis. Vascular, cutaneous, gastrointestinal, pulmonary, and musculoskeletal involvement are most commonly seen in children with SSC. Treatment of both forms targets the active inflammatory stage and halts disease progression; however, progress needs to be made toward the development of more effective antifibrotic therapy to help reverse disease damage.

Pediatric Vasculitis

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Pamela F. Weiss

Childhood vasculitis is a challenging and complex group of conditions that are multisystem in nature and often require integrated care from multiple subspecialties, including rheumatology, dermatology, cardiology, nephrology, neurology, and gastroenterology. Vasculitis is defined as the presence of inflammation in the blood vessel wall. The site of vessel involvement, size of the affected vessels, extent of vascular injury, and underlying pathology determine the disease phenotype and severity. This article explores the classification and general features of pediatric vasculitis, as well as the clinical presentation, diagnostic evaluation, and therapeutic options for the most common vasculitides.

Kawasaki Disease

425

Rosie Scuccimarri

Kawasaki disease is a systemic vasculitis and the leading cause of acquired heart disease in North American and Japanese children. The epidemiology, cause, and clinical characteristics of this disease are reviewed. The diagnostic challenge of Kawasaki disease and its implications for coronary artery outcomes are discussed, as are the recommended treatment, ongoing treatment controversies, concerns associated with treatment resistance, and the importance of ongoing follow up.

Autoinflammatory Syndromes

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Philip J. Hashkes and Ori Toker

There has been an expansion of the autoinflammatory syndromes due to the discovery of new diseases related to mutations in genes regulating the innate immune system and the knowledge gained from these diseases as applied to more common nongenetic inflammatory conditions. Autoinflammatory syndromes are characterized by unprovoked (or triggered by minor events) recurrent episodes of systemic inflammation involving various body systems, which are often accompanied by fever. Inflammation is mediated by polymorphonuclear and macrophage cells through cytokines, particularly interleukin-1. This article reviews the clinical approach to patients with suspected autoinflammatory syndromes, several of the main and new (mostly genetics) syndromes, advances in treatment, and prognosis.

Approach to the Patient with Noninflammatory Musculoskeletal Pain

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Peter Weiser

Musculoskeletal pain is one of the most common presenting symptoms at the pediatrician's office. Etiology ranges from benign conditions to serious

ones requiring prompt attention. This article addresses entities that present as musculoskeletal pain but are not associated with arthritis. The most common nonarthritic conditions are benign limb pain of childhood (growing pains), hypermobility, overuse syndromes with or without skeletal abnormalities, malignancies, and pain amplification syndromes. The initial decision process, diagnosis, and treatment options for each of these conditions are discussed.

Immunodeficiency Diseases with Rheumatic Manifestations

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Troy R. Torgerson

Most clinicians associate primary immunodeficiency disorders (PIDDs) with susceptibility to frequent or severe infections. It is less commonly recognized, however, that PIDDs are frequently associated with autoimmune or rheumatologic manifestations. This review provides a synopsis of the rheumatic manifestations associated with immunodeficiencies in each of the major compartments of the immune system.

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