Contents

Preface: Immunotherapy in Clinical Medicine  xiii
Nancy Misri Khardori and Romesh Khardori

Erratum  xv

Immunotherapy in Clinical Medicine: Historical Perspective and Current Status  421
Lokesh Shahani, Sushma Singh, and Nancy Misri Khardori

In humans, the immune system is a complex organ system involving cells and soluble mediators whose function is, essentially, protection. However, disequilibrium in this intricate system leads to disease in itself. To modulate these responses, immunotherapy is now the primary or adjunct treatment of many diseases. In addition, immunologic tests now diagnose several diseases.

Immunotherapy for Primary Immunodeficiency Diseases  433
Philip Wood

The 2 most commonly encountered primary immunodeficiency syndromes in adult practice are antibody deficiency disorders and hereditary angioedema. Immunologic therapy for these disorders has significantly improved patient management. Therapy with immunoglobulin leads to improvement in overall quality of life. With increasing survival rates and decreasing levels of life-threatening infections in patients with primary antibody deficiencies, disease complications are more commonly encountered. Treatment of these complications with monoclonal antibody therapy seems promising and is likely to increase in the future. More recently, several additional agents have become available, including novel drugs targeted at different elements of the disease process.

Immunotherapies in Infectious Diseases  455
Vivek Kak, Vidya Sundareshan, Jignesh Modi, and Nancy Misri Khardori

The development of an infection involves interplay between the host’s immune system and the virulence of the infecting microorganism. The traditional treatment of an infection involves antimicrobial chemotherapy to kill the organism. The use of immunotherapies in infections includes treatment options that modulate the immune response and can lead to control of infections. These therapies are expected to become more important therapeutic options with the increase in infections due to multidrug-resistant organisms and the increasing number of immunocompromised patients.

Immunotherapies in Rheumatologic Disorders  475
Anne V. Miller and Sriya K.M. Ranatunga

Over the past several decades, rheumatology has directed its focus to understanding and countering the immune dysregulation underlying autoimmune diseases with rheumatologic manifestations. Older therapies, effective though poorly understood, are being scrutinized anew and are
yielding the immune-modulating mechanisms behind their efficacy. New therapies, the “biologics,” are drugs tailored to address specific immune defects and imbalances. This article discusses the current standard and biologic immunotherapies of the rheumatic diseases, correlating our current understanding of their mechanisms with dysfunctions believed to be present in the major autoimmune syndromes, especially rheumatoid arthritis and systemic lupus erythematosus.

Immunotherapies in Neurologic Disorders 497
Donna Graves and Steven Vernino

Therapy for autoimmune demyelinating disorders has evolved rapidly over the past 10 years to include traditional immunosuppressants as well as novel biologicals. Antibody-mediated neuromuscular disorders are treated with therapies that acutely modulate pathogenic antibodies or chronically inhibit the humoral immune response. In other inflammatory autoimmune disorders of the peripheral and central nervous system, corticosteroids, often combined with conventional immunosuppression, and immunomodulatory treatments are used. Because autoimmune neurologic disorders are so diverse, evidence from randomized controlled trials is limited for most of the immunotherapies used in neurology. This review provides an overview of the immunotherapies currently used for neurologic disorders.

Immunotherapy in Inflammatory Bowel Disease 525
Jatinder P. Ahluwalia

Inflammatory bowel disease affects an increasing number of patients worldwide and is associated with significant morbidity. The dysregulation of the immune system with increased expression of proinflammatory cytokines and increased mucosal expression of vascular adhesion molecules play an important role in its pathogenesis. Strategies targeting TNF-alpha and alpha4-integrin have led to the development of novel therapies for treatment of patients with IBD. This article discusses the efficacy of immunologic agents currently approved for treating Crohn disease and ulcerative colitis and reviews the risks and challenges associated with their use.

Immunotherapy in Renal Diseases 545
Ajay Kher and Vijay Kher

Immunotherapy has been used for the treatment of renal diseases for a long time, and there has been significant progress in such treatment. This review focuses on the use of immunotherapy for the treatment of glomerular diseases. The use of immunosuppression in the treatment of minimal change disease, membranous nephropathy, primary focal segmental glomerulosclerosis, lupus nephritis, immunoglobulin-A nephropathy, anti-neutrophil cytoplasmic antibody–associated disease, and anti–glomerular basement membrane disease is discussed.

Immunotherapies in Dermatologic Disorders 565
Robyn S. Fallen, Collin R. Terpstra, and Hermenio C. Lima

Treatment modalities and therapeutic response experience support the use of immunotherapy in the treatment of many diseases in all fields of medicine. The aim of this article is to conduct and present a review of
literature on the use of immunotherapy in the treatment of skin diseases analyzing scientific literature available up to January 2012. Studies that presented evidence-based data were selected. The article discusses how blocking or reverting the effect of a specific immunologic disequilibrium can treat dermatoses and intends to transfer a large amount of immunotherapy knowledge into a historical perspective for physicians naive to immunotherapy practices.

The Use of Monoclonal Antibodies in Immune-Mediated Hematologic Disorders

Daan Dierickx, Emilie Beke, Timothy Devos, and André Delannoy

In this article, the evidence on the clinical use of monoclonal antibodies in the treatment of immune-mediated hematologic disorders is described. Insights into pathogenic mechanisms have revealed a major role of both B and T cells. Controlled trials have shown conflicting results, necessitating further research regarding pathogenesis, mechanism of action, and resistance. Although the use of more potent and specific monoclonal antibody therapy, mainly targeting costimulation signals, may improve response rates and long-term outcome, its use should be carefully balanced against potential side effects.

Immunotherapies in Diabetes Mellitus Type 1

Smita Gupta

Type 1 diabetes is an autoimmune disease that gradually destructs insulin-producing beta cells. Over the years, clinicians’ knowledge regarding the immunopathogenesis of this disease has greatly increased. Immunotherapies that can change the course of immune-mediated destruction and preserve and possibly regenerate the pancreatic beta cells seem to be promising in preclinical trials but so far have been unsuccessful in human studies. This article reviews the important immune interventions for type 1 diabetes that have been tried so far targeting the different stages of disease development and provides an insight into what the future might hold.

Immunotherapy in Miscellaneous Medical Disorders Graves Ophthalmopathy, Asthma, and Regional Painful Syndrome

Michael Gonzales, Carmel Fratianni, Chaitanya Mamillapali, and Romesh Khardori

In Graves ophthalmopathy, immunotherapy is offering an opportunity of reducing bad outcomes that lead to disfigurement and impairment of vision. These therapies are not perfect; however, we now have a chance to achieve better outcomes. In asthma, immune therapy using passive immunity targeting key proinflammatory cytokine/chemokines and medications of their effects has opened an avenue of research into a safe and durable therapy. Omalizumab appears to be safe and effective in clinical use. In regional pain syndrome, immune mechanisms may be involved in sustaining long-standing pain, and IVIG may moderate pain sensitivity by reducing immune activation.