Myasthenia Gravis and Related Disorders

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Preface

From the first clear clinical descriptions in 1879 by Wilhelm Erb and in 1893 by Samuel Goldflam, myasthenia gravis has evolved to become the best understood autoimmune disorder, serving as a model for understanding not only autoimmunity, but also synaptic function. The objective of *Myasthenia Gravis and Related Disorders* is to provide the clinician and the scientist a common source for the understanding of this complex disorder.

Myasthenia Gravis and Related Disorders begins with a discussion of neuromuscular junction structure and function as well as a detailed description of the acetylcholine receptor, the central target of pathology in myasthenia gravis. The neuromuscular junction, as recently as the late 1980s, could only be depicted as a cartoon of a nerve terminal with synaptic vesicles as circles and an undulating muscle surface. Now unfolding is an intricate machinery that coordinates the release of synaptic vesicles upon depolarization of the nerve and a beautiful architecture of numerous specialized proteins that underlies the postsynaptic surface. Although it was appreciated in the 1970s that autoantibodies to the acetylcholine receptor were the primary cause of myasthenia gravis, investigations have led to the characterization of the intricate T cell dependence and cytokine influences on autoantibody production. With this understanding has come the possible categorization of myasthenia gravis patients based on demographic characteristics, autoantibody profiles, and thymic pathology. Definition of genetic susceptibility loci will certainly lead to further refinement in patient subgroups. The new century should see treatments that will specifically target the autoimmune defect, which are further specialized on the individual patient's genetic profile.

Despite the advances in the basic sciences, myasthenia gravis remains a challenging disorder to recognize and treat, with patients frequently complaining of delays in diagnosis, complications of treatment, and poor response to therapies. Chapters detail information regarding the clinical presentation, diagnostic evaluation, and treatment of myasthenia gravis. Although thymectomy is widely accepted, its benefit in the light of modern immunosuppressive therapies has come into question and a chapter

discusses this controversy. The book concludes with a discussion of the most difficult to understand effects of myasthenia gravis, the psychological consequences of the disease. This subject is commonly neglected in myasthenia gravis texts but is becoming a focus of research. I include an appendix detailing recommendations of a Task Force of the Myasthenia Gravis Foundation of America for clinical research guidelines. These guidelines were a first step in knitting together the international community of investigators to adopt a common language to describe patients, treatments, and outcome. It is hoped that by the improvement of these recommendations, clinicians may study myasthenia gravis with the same rigor as their basic science colleagues.

Related to myasthenia gravis by clinical presentation or pathophysiology are the Lambert-Eaton syndrome, congenital myasthenias, and toxic neuromuscular junction disorders. A chapter discusses neuromyotonia because of its similarity in autoimmune pathology to myasthenia gravis and the occasional overlap of neuromyotonia with myasthenia gravis. Compared with myasthenia gravis, these diseases are only beginning to be defined at a molecular and immunologic level. Readers may be a bit surprised by the loss of "myasthenic" in referring to the Lambert-Eaton syndrome. This is done in deference to Vanda Lennon and Edward Lambert, who prefer this terminology.

All the authors have a personal relationship with myasthenia gravis, and this is appreciated in their writing, particularly that of Alfred Jaretzki and Robert Daroff. I hope this allows the reader to appreciate the human endeavor of not only medicine but scientific inquiry.

I thank all the contributing authors, in particular Robert Ruff and Robert Daroff, my long-time mentors, and I am indebted to Humana Press for making the book a reality. Appreciation is extended to the National Eye Institute at the National Institutes of Health, the Department of Veterans Affairs, and the Myasthenia Gravis Foundation of America for their support of my research as well as the research of many of the contributors. I also thank the Muscular Dystrophy Association for their support of neuromuscular research. To my patients who have given me more than I could ever return—thank you.

I dedicate this book to Janina Kaminski, my mother, and Linda Kusner, my wife.

Henry J. Kaminski, MD

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