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Neuromuscular Disorders

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Contents

The colour plate section can be found facing page 228.

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Series Foreword

The genesis for this book series started with the proposition that, increasingly, physicians want direct, useful information to help them in clinical care. Textbooks, while comprehensive, are useful primarily as detailed reference works but pose challenges for uses at point of care. By contrast, more outline-type references often leave out the "how's and whys" – pathophysiology, pharmacology – that form the basis of management decisions. Our goal for this series is to present books, covering most areas of neurology, that provide enough background information for the reader to feel comfortable, but not so much to be overwhelming; and to combine that with practical advice from experts about care, combining the growing evidence base with best practices.

Our series will encompass various aspects of neurology, the topics and specific content chosen to be accessible and useful. *Neuromuscular Disorders* by R. Tawil and S. Vance, covers the commonly seen areas of acquired and inherited conditions of muscle, nerve, and the neuromuscular junction, which we hope will appeal to students, trainees, experts and practicing neurologists alike. The editors are expert in their field and have recruited superb contributors to share their views on best treatment and management options.

Chapters cover critical information that will inform the reader of the disease processes and mechanisms as a prelude to treatment planning. Algorithms and guidelines are presented, when appropriate. "Tips and Tricks" boxes provide expert suggestions. Other boxes present cautions and warnings to avoid pitfalls. Finally, we provide "Science Revisited" sections that review the most important and relevant science background material. Bibliographies guide the reader to additional material.

We welcome feedback. As additional volumes are added to the series, we hope to refine the content and format so that our readers will be best served.

Our thanks, appreciation and respect goes out to our editors and their contributors, who conceived and refined the content for each volume, assuring a high quality, practical approach to neurological conditions and their treatment.

And our thanks also go to our mentors and students (past, present, and future), who have challenged and delighted us; and to our book editors and their contributors, who were willing to take on additional work for an educational goal; and to our publisher, Martin Sugden, for his ideas and support, for wonderful discussions, and for commiseration over baseball and soccer teams that might not quite have lived up to expectations.

We would like to dedicate the series to Marsha, Jake and Dan; and to Janet, Laura and David.

And to Steven R. Schwid, MD, our friend and colleague, whose ideas helped shape this project and whose humor brightened our lives; but who could not complete this goal with us.

Robert A. Gross
Jonathan W. Mink
Rochester, July 2011

Preface

Neuromuscular diseases include acquired and inherited conditions of muscle, nerve, and the neuromuscular junction. As neuromuscular clinicians, we recognize that having a familiarity with and an approach to these disorders is important for all physicians for several reasons. First, many of the acquired neuromuscular disorders are eminently treatable and some can present as emergencies. Consequently, early recognition of these disorders is important. Second, and equally important, modern medical management has significantly improved the quality of life of many individuals living with inherited neuromuscular disorders. Therefore, most inherited neuromuscular disorders are now considered chronic illnesses and early recognition of complications specific for certain neuromuscular conditions may lead to lifesaving interventions. Finally, the manifestations of neuromuscular diseases span several medical specialties including cardiology, pulmonology, and gastroenterology, and an integrated, multidisciplinary approach to the management of these patients has become a standard of care.

The challenge in writing this introductory textbook is to provide accessible, useful information about an ever more complex field of study. Our understanding of the inherited neuromuscular disorders has grown exponentially since the discovery in 1987 of the Duchenne gene. This explosion of molecular information has both simplified the diagnosis and management of certain neuromuscular disorders and complicated that of others. From a clinically based classification of a handful of diseases, we now have dozens of neuromuscular diseases defined by specific gene defects. Molecular genetics has allowed exact clinical definition for some entities, while blurring the clinical boundaries of others as mutations in different genes sometimes result in clinically indistinguishable conditions. Complicating matters is the realization that identical clinical presentations may be seen with acquired and hereditary disorders.

Despite the increasing complexity of molecular classifications, the diagnosis of neuromuscular disorders remains a singularly clinical exercise. Ancillary testing, short of DNA testing, helps to narrow the differential but rarely results in specific diagnoses. Moreover, genetic testing is not always available to practitioners and, therefore, an accurate history and careful exam remain critical in providing the most useful clues to direct the diagnostic workup. Even where DNA testing is widely available, the history and exam are essential in determining the most efficient and cost-effective use of DNA diagnostics. In many instances today, DNA testing will be the first test ordered to confirm the clinical suspicion, sparing the patient other unnecessary diagnostic tests.

This textbook is meant as an introductory volume for trainees and generalists alike, providing a practical framework to approach patients presenting with problems that localize to the neuromuscular system. Four chapters describe the clinical approach to the major neuromuscular disease categories including diseases of the motor neuron, nerve, neuromuscular junction, and muscle. The textbook covers the spectrum of neuromuscular disorders from the common to the esoteric. Each chapter contains text boxes highlighting relevant information regarding the diagnosis and management of individual disorders. The short bibliography at the end of every chapter provides relevant references for those interested in a more in-depth understanding of specific disorders.

We hope that the authors' tips and tricks and cautions prove to be valuable in clinical practice. With the increasing complexity of the neuromuscular field, making a specific diagnosis may not be achievable in some cases except in specialized academic centers. More relevant, however, is that better understanding of the neuromuscular disorders and their associated complications, result in improved patient care.

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Neuromuscular Diseases: Approach to Clinical Diagnosis

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Effective clinical diagnosis of neuromuscular disorders requires the thoughtful use of the physician's core clinical skills of history taking and examination. Hypotheses are generated based on the clinical presentation and history taking, and tested during the physical examination. Unique to neurosciences is the need for accurate localization within the nervous system, before arriving at the differential diagnosis and identifying the investigations needed to confirm the clinical diagnosis. Only then is confirmation of a clinical diagnosis possible. Once the determination is made that the history and exam are consistent with a disorder of the peripheral nervous system, the clinician has to decide if the presentation is a disorder of peripheral nerve, muscle, neuromuscular junction, or motor neuron. Complicating matters are neuromuscular disorders, such as amyotrophic lateral sclerosis (ALS) in which peripheral and central nervous system (CNS) signs and symptoms coexist. As a general rule, investigations are tailored to reflect the clinical reasoning process and the most likely diagnostic considerations. A diagnosis is important for different reasons in different circumstances and individuals. An accurate diagnosis directs treatment and management, permits a discussion of disease progression, potential complications, and, in certain cases, is required for peace of mind. The approach taken throughout this volume emphasizes a careful history and examination with an insightful approach to the use of newer imaging and molecular diagnostic techniques in arriving at a diagnosis.

History taking: generating hypotheses

The clinical presentations of neuromuscular disorders reflect dysfunction of the lower motor neuron and the peripheral aspects of the sensory and autonomic systems. Similar complaints may be non-neurological or seen with CNS disorders. The art of history taking, allowing the patient to tell his or her story, is a critical aspect in deciding if there is a neurological problem and, in particular, a neuromuscular disorder.

It is helpful to categorize symptoms as positive (e.g. cramping, twitching, stiffness, tingling, pins, needles, burning pain) or negative (e.g. weakness, loss of muscle, numbness, incoordination), recognizing that it is often negative symptoms that have ready correlates on examination. Conversely, examination may be entirely normal in a patient with only positive symptoms. Ask patients to clarify what a symptom means to

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