Introduction

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Abstract

Just like the first edition of this widely successful book the second edition provides latest updates of our understanding of pathophysiology, pathology, clinical presentation and treatment of heritable soft connective tissue diseases. In addition, new knowledge of not only structures but also of functions of basic components of connective tissues (e.g., collagen), and of organs such as tendons has been added as well. Moreover, readers will learn more about new syndromes and new subgroups of previously described syndromes and disorders as well. The authors are not only prominent investigators in their field, but they are also good writers and that should provide an additional incentive for interested readers.

Keywords

Ehlers- Danlos syndrome · Marfan syndrome · Joint hypermobility · Collagen and tendon structure and function · Transforming growth factor β · Cutis laxa · Collagen VI myopathies

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This volume represents a second edition of a widely successful and read book Progress in Heritable Soft Connective Tissue Diseases. The content was revised and updated with inclusion of newly identified syndromes and variations of already more or less characterized disorders. Marfan and Ehlers-Danlos syndromes are the best known and studied conditions included in this group of diseases. The first description of Ehlers-Danlos syndrome appeared first in Hippocrates' writing (Airs, Waters and Places) in 400 BC (Parapia and Jackson 2008). It was not until the seventeenth century when sporadic accounts were published in medical literature. Finally, the syndrome was named after Edward Lauritz Ehlers and Henri-Alexander Danlos provided more comprehensive and systematic descriptions of several patients suffering with joint hypermobility and skin fragility more than a century ago (Parapia and Jackson 2008). Marfan syndrome, a more common condition than Ehlers-Danlos syndrome, was named after Antoine Marfan who published the first case report of possible Marfan syndrome in 1896 (Marfan 1896).

The difference in knowledge about the pathogenesis, biochemistry, genetics of these two and related disorders between then and now has widened as it will become obvious upon reading this volume. However, this does not take anything away from the contribution of past physicians as they applied their ingenuity, clinical astuteness

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and close attention to seemingly unrelated details. On the contrary, they are providing examples how to approach new unknown phenomena. Though the roster of authors has changed to some extent, the quality of chapters has not. The topics have been revised or updated, and some were expanded as necessary.

The first chapters are more general, concentrating more on the physiology, structure and biochemistry of normal soft tissues. That should help in understanding of the pathophysiology of these disorders, many of them related to each other in more than one ways.

Chapters 2 and 3 discuss primarily collagen and tendon structure and function. Though most of tendon disorders and injuries encountered by millions of people on daily basis are non-hereditary in nature, many of the disorders described in this volume (Marfan, Ehlers-Danlos, cutis laxa etc) affect musculoskeletal system (and mainly tendons) to great degree. Chapter 2 informs mostly on collagen structure and structural components, as well as on the interface between structure and biomechanical behavior. Chapter 3 deals with changes and adaptations of structure, not just collagens, but of extracellular matrix with time and development. Moreover, Connizzo et al. interpret the functional changes in tendons through the glasses of bioengineering (Chap. 3). In this sense these two chapters are complementary. The several next chapters (Chaps. 4, 5 and 6) review the role of basic components of extracellular matrix in function of normal connective tissue and their contribution to pathophysiology of soft tissue diseases. Authors of Chap. 7 continue in this vein by concentrating on one growth factor, transforming growth factor β, which plays an outsized role in many disorders of soft connective tissues. Chapter 8 on Marfan syndrome expands this narrative, together with advances in Marfan management.

The Ehlers-Danlos category has grown to 13 bona fide members described in details in Chap. 9 together with related and enlarging group of joint hypermobility disorders. In addition, Chap 10 brings us up to date progress in Ehlers- Danlos syndrome due to abnormal metabolism of glycosaminoglycan chains attached to proteoglycans regulating assembly of collagens.

New entities are included as well, now we have not one but two syndromes associated with professor Bart Loeys (Chaps. 11 and 12). Advances in genetic analysis have greatly expanded our understanding of cutis laxa, and also added many new (and rare subtypes) (Chap 13) – it turns out that the complexity of cutis laxa has greatly expanded over the last several years. Numerous variations of cutis laxa and joint mobility disorders have been discovered taking advantage of recent advancements) in genetic analysis. We have acquired better understanding of pathogenesis and biochemical changes in some other, more established entities, such as Marfan and collagen VI myopathies where better management and treatment is on the horizon (Chaps. 8 and 14, respectively). In particular, antisense agents, cyclosporine A and autophagy stimulating drugs are being investigated for treatment of myopathies due to mutations in in the *COL6A1*, *COL6A2* and *COL6A3* genes (Chap. 14). Even in the case of connective tissues diseases in domestic animals some progress has been made. Warmblood fragile foal syndrome was added to the last chapter, and the section on equine degenerative suspensory ligament desmitis was substantially revised in Chap. 15.

All chapters were contributed by a group of distinguished and preeminent physicians and scientists, all of them not working "just" in the field but making new discoveries described by them. Most authors address clinical, biochemical or/and genetic similarities among the various entities and conditions, provide guidance how distinguish among them and properly diagnose patients. Readers will notice that seemingly there is an overlap among many of these disorders. And indeed, many of them, if not most are interconnected because of the prominent roles of TGFβ, of fibrillin microfibrils and collagen fibril assembly (and other molecules) playing in connective tissues physiology, and by extension in pathogenesis of many disorders described in the book. What I found particularly helpful that author(s) of each chapter bring their own per-

spective even when describing closely related mechanism of the disease. These observations from different point of view by each group of authors should help with diagnosis and management of such cases.

Last but not least, the chapters are very readable, more like detective stories than dry description of genetic/biochemical defects. I do hope that basic scientists and clinicians with similar and diverse interests alike will appreciate this volume and will be inspired by it to develop their research in the field.

We hope that you will find this volume not just informative, but also stimulating to ask questions about the basic science behind these syndromes and diseases, and perhaps even inspiring to pursue research on one or more topics elaborated on in this book. This volume should serve as a bridge between basic science and clinical disciplines, and as a reference book not only for established physicians, residents and medical students, but also for scientists whether they are well established investigators or graduate students.

I would like to thank all contributors for their hard work, especially during these unexpectedly difficult times. Special appreciation goes to Dr. Gonzalo Cordova, our editor at Springer Nature., for his kindness, patience and understanding why we had to request additional time to push back on the deadline. Now when all is done, let us say Cheers on work well done!!

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