Alagille Syndrome

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Editors

Alagille Syndrome

Pathogenesis and Clinical Management

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I dedicate this book to my parents for their unfailing support and encouragement and to Maya and Anika who keep me going with their love and laughter.

Binita M. Kamath

I dedicate this book to the memory of my mother Joan, for her constant love and support.

Kathleen M. Loomes

Preface

Alagille syndrome (ALGS) is a fascinating disorder that challenges us to comprehend multi-organ disease, molecular genetics, and developmental biology. Our understanding of this disorder has blossomed since its first description almost 50 years ago. We now appreciate that there are two disease-causing genes associated with ALGS and the phenotypic spectrum encompasses at least eight organ systems. The advances in elucidating the genetics of this condition have actually improved our understanding of intrahepatic bile duct development. This explosion of knowledge is encapsulated in the following book. We have the privilege of having the amalgamated knowledge from the experts and leaders in ALGS. Each author is a respected and recognized authority in his or her field that has been especially handpicked for the topics presented. Currently, there is no textbook entirely devoted to the pathophysiology and management of ALGS. This textbook is designed to provide a comprehensive and current overview of the important issues specific to the field of ALGS. Care of these patients and their multisystem disease can be quite complex, and materials have been collected from the most current, evidence-based resources, providing an overview of all aspects of ALGS, from the developmental and genetic perspectives, to liver transplantation, to the most innovative, molecular advances that will launch our management of this complex disease forward in the near future.

Gaps in knowledge about ALGS challenge us for the present and future. Specific understanding about how *JAG1/NOTCH2* mutations lead to bile duct paucity, why some patients have resolution or stabilization of their cholestasis, the identification of genetic modifiers, and the lack of specific targeted therapies, to name a few, remains unknown. Finally, issues surrounding nomenclature also persist. Daniel Alagille described a condition characterized by hepatic involvement with multisystem disease – it may not be appropriate to describe an individual with no overt liver involvement as having ALGS, and we are lacking more detailed molecular-based terminologies that better reflect disease states.

On behalf of all the authors and ourselves, we sincerely hope this text will serve as a valuable and useful guide of better understanding and management strategies for those who are interested in providing the very best approaches to the care of our patients with ALGS.

Toronto, ON, Canada — Binita M. Kamath
Philadelphia, PA, USA — Kathleen M. Loomes

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