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Editors

Difficult To Treat Asthma

Clinical Essentials

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Humana Press

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To Mom and Dad, my teachers for life.

Sandhya Khurana

I would like to dedicate this book to my wonderful loving family, Shanta, Mateo, and Diego.

Fernando Holguin

Foreword

The title of this book has been carefully chosen and is both apt and appropriate. The term "difficult asthma" incorporates the many reasons why asthma continues to be poorly controlled in the majority of patients, even those considered to have mild or moderate disease, which could be well controlled with currently available, effective, and very safe medications, particularly inhaled corticosteroids (ICS). Difficult asthma is uncommonly severe asthma, which does not respond adequately to conventional doses of the range of asthma medications that are available.

The difficulty in obtaining well-controlled asthma is reflected in the range of chapters that address the challenges that both health care providers and patients face in managing asthma. As the Editors, Drs. Khurana and Holguin correctly identify, *"whether people with asthma gain and maintain control over their condition depends not only on the availability of effective drugs, but also multiple patient and healthcare provider behaviors*". Paramount among these is poor adherence to maintenance medications, particularly ICS, where milder patients, who are asymptomatic most of the time, perceive no immediate benefit.

Other important reasons for poor asthma control, which are comprehensively covered in the book, include a range of comorbidities that asthmatics can experience, sometimes related to other clinical manifestations of atopic disease, particularly allergic rhinitis, or rhinosinusitis, or gastroesophageal reflux, or a range of others, such as persistent allergen or occupational; cigarette smoking; psychopathology; and importantly an incorrect diagnosis of asthma, usually because objective measurements, such as spirometry, were not used to establish the diagnosis.

Once these considerations for difficult to control asthma have been addressed, there remain a small percentage of patients (perhaps 5–8%) who have severe, refractory asthma. This has been best defined by the ATS/ERS Task Force on Severe Asthma as "*asthma that requires treatment with high dose inhaled corticosteroids plus a second controller and/or systemic corticosteroids to prevent it from becoming "uncontrolled" or that remains "uncontrolled" despite this therapy."*

Over the past decade, great strides have been made in understanding the complexities of the pathobiology of severe asthma and, as a result, in developing new treatment approaches to help manage it. One extremely important insight was that

all severe refractory asthma is not the same. Two quite distinct phenotypes have been identified, which determine the response to the new treatment approaches. These are T_2-high asthma, characterized by persistent airway eosinophilia, and elevated exhaled nitric oxide levels, likely driven by Th2 cells and Type 2 innate lymphoid cells (ILC2), and non-T_2-high asthma (sometimes called "non-eosinophilic" asthma), where an absence of airway eosinophils and sometimes an increase in airway neutrophils is the characteristic phenotypic feature. It is quite likely that more distinct phenotypes will be described over time.

The new treatment approaches for severe refractory asthma are very well described in this book, including the use of biomarkers to help identify which patients would benefit from which treatment approach and the magnitude of benefit and risk each of these treatment approaches provide.

There are, in addition, chapters about clinical situations where asthma can even be more difficult to manage. These are in childhood, in obese patients, and during pregnancy. Each of these constitutes a different series of clinical challenges for the health care provider, the patient, and their family.

The management of patients with difficult asthma requires a team approach, which most importantly involves the patients, and (especially for childhood asthma) their family. This is particularly important for patients with severe refractory asthma, where referral to a clinical setting with expertise in the management of severe disease is available.

Finally, while there have been many important advances in asthma management over the past decade, there is still much to learn. This is particularly true for the origins of asthma, its pathobiology, and the reasons for asthma being easy to manage in some patients and very difficult in others. These contributions in "*Difficult to Treat Asthma: Clinical Essentials*" have summarized the current state of knowledge extremely well, but also look to the future and identify where further progress needs to be made.

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Preface

The last decade has ushered a new and exciting era in asthma. With increasing recognition of its heterogeneity and complex pathophysiology, asthma is no longer a "*one-size-fits-all*" disease. Novel therapies targeting treatable traits have made personalized medicine a reality, bringing with it the promise of much awaited respite to those who are suffering. Selecting the best evidence treatment requires an understanding of disease mechanisms, familiarity with available therapies, and appreciation of factors that make asthma truly "*difficult.*"

Our vision, when creating this volume, was a practical and ready-to-use resource for any provider taking care of patients with *difficult to treat* asthma. "*State of the science*" reviews on different facets of the disease are authored by renowned experts who are leaders in the field and have spent years in the study and practice of asthma. We hope that those treating patients with severe or difficult asthma will find this book useful. We are grateful to our authors, friends, and colleagues, who gave generously of their expertise, time, and effort. Without them, this book would not have been possible.

Rochester, NY, USA — Sandhya Khurana
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