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## Preface

Alcoholic liver disease (ALD) and Nonalcoholic fatty liver disease (NAFLD) are among the most common causes of cirrhosis, liver failure, and liver cancer worldwide. Histologically, they resemble each other and they both share several common pathogenetic mechanisms. Over the last decade, steady progress has been made in almost all aspects of these two diseases, and this book reflects our attempt to integrate these new developments into existing disease pathogenesis and management paradigms. This book is developed as a state-of-the-art resource for medical students, clinicians, pathologists, clinical researchers, basic science investigators, and pharmaceutical industry worldwide. At the outset, we believed that a single book that includes both ALD and NAFLD would be highly desirable for various stakeholders, but organizing various chapters into a logical sequence turned out to be somewhat challenging. After much deliberation, we have decided to divide our book into multiple sections (e.g., epidemiology, pathogenesis, and clinical features) and then have both ALD and NAFLD chapters next to each other to make it easier for the readers. All contributors, who are experts in their respective areas, have done a masterful job with their chapters and we are indebted for their contributions.

Drs. Mariana Lazo and Mack Mitchell start the book with their review of the epidemiology and risk factors of ALD, followed by a detailed review of the epidemiology and risk factors of NAFLD by Drs. Zobair Younossi and Abhijit Chowdhury. These two chapters set the stage for two marvelous chapters on the pathogenesis of ALD (Drs. Gavin Arteel and David Crabb) and NAFLD (Dr. Jacquelyn Maher). Drs. Jun Xu and Hide Tsukamoto provide an outstanding review of various animal models for studying ALD, and Drs. Mariana Machado and Anna Mae Diehl have done an equally elegant job in describing a large number of animal models which have been developed in the recent past to investigate NAFLD. There have been several major developments in better understanding the genetic basis of these diseases (especially NAFLD), and Drs. Silvia Sookoian and Carlos Pirola have provided an in-depth review of the genetic basis of both ALD and NAFLD in a single chapter.

Moving to more clinical chapters, Dr. Craig McClain and colleagues review clinical features, disease modifiers, and natural history of ALD and alcoholic hepatitis, whereas Drs. Dawn Torres and Stephen Harrison describe in detail the clinical features, disease modifiers, and natural history of NAFLD. Currently, there are no approved therapies for either alcoholic hepatitis or nonalcoholic steatohepatitis (NASH), but there is tremendous interest among various stakeholders to develop novel and effective treatments

for these conditions. To conduct registration clinical trials that are needed for regulatory approval, we must have valid diagnostic criteria and therapeutic end points. The landscape in this area is rapidly evolving and Drs. Cheong, Stein, and Bataller describe state-of-the-art diagnostic criteria for various sub-phenotypes of ALD and therapeutic end points for various stages of clinical trials in individuals with various forms of ALD. The clinical trials' landscape for NAFLD and NASH has dramatically changed over the last 3 years, and there is an evolving consensus on "NASH without fibrosis" and "NASH with advanced fibrosis" as approvable indications from a regulatory standpoint. Also, clear-cut guidance from the regulatory agencies is becoming available with regard to primary end points for Phase 2 and Phase 3 clinical trials in NAFLD. Dr. Arun Sanyal, a pioneer in the field of NASH clinical trials, describes valid diagnostic approaches and clinical end points for treatment in NAFLD and NASH in Chap. 11.

Liver histology remains the gold standard for characterizing the severity of NAFLD and for diagnosing NASH, and there are recent studies showing the prognostic value of liver histology in individuals with alcoholic hepatitis. Drs. David Kleiner and Pierre Bedossa, two expert hepatopathologists, tackle the liver histology in ALD and NAFLD in a comprehensive fashion. NAFLD and ALD are strongly associated with hepatic and extrahepatic malignancies, and Drs. Vasilis Vasilou and Sam Zakhari thoroughly cover hepatic and extrahepatic malignancies in ALD, whereas Drs. Fabio Nascimbeni and Vlad Ratziu describe the putative mechanisms and risk factors of malignancies in NAFLD with a special emphasis on the risk of hepatocellular carcinoma in individuals with non-cirrhotic NAFLD.

Alcoholic hepatitis continues to carry significant morbidity and mortality and unfortunately no new effective therapies have been developed for this condition in nearly 3 decades. The role and timing of liver transplantation for individuals with acute alcoholic hepatitis remain controversial and geographically variable. Dr. Szabo and Dr. Jan Petrasek comprehensively describe existing and emerging therapies, novel targets, and the role of liver transplantation for individuals with various forms of ALD. As stated before, there is tremendous interest in developing effective pharmacological agents for NASH and there has been an explosion of Phase 2 and Phase 3 trials in this space. Drs. Samer Gawrieh and Naga Chalasani review various treatments including lifestyle modification, bariatric surgery, and new compounds to treat liver disease and coexisting comorbidities in individuals with NAFLD. Last but not the least, Drs. Hannah Awai and Jeffrey Schwimmer provide a comprehensive review of NAFLD in children, a growing problem with substantial disease burden.

As research is progressing rapidly in these two disorders, we suspect some important articles that have just been published may be missing in this book. Regrettably, such omissions are unavoidable due to lengthy editing and publishing process involved in developing a multiauthored textbook. Nonetheless, we hope this book provides an updated, broad, and practical review of all aspects of ALD and NAFLD.

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