Experimental Models for Renal Diseases

Pathogenesis and Diagnosis

Volume Editor

Guillermo A. Herrera  Tempe, Ariz.

76 figures, 27 in color, and 13 tables, 2011
Contents

VII  Foreword
   Herrera, G.A. (Tempe, Ariz.)

1  Overview of Models for the Study of Renal Disease
   Turbat-Herrera, E.A. (Tempe, Ariz.)

6  Mesangial Homeostasis and Pathobiology: Their Role in Health and Disease
   Herrera, G.A.; Turbat-Herrera, E.A.; Teng, J. (Tempe, Ariz.)

23 Parietal Epithelial Cells: Their Role in Health and Disease
   Romagnani, P. (Florence)

37 Role of Proximal Tubules in the Pathogenesis of Kidney Disease
   Nakhoul, N.; Batuman, V. (New Orleans, La.)

51 Kidney Microvasculature in Health and Disease
   Jen, K.-Y. (San Francisco, Calif.); Haragsim, L. (Oklahoma City, Okla.); Laszik, Z.G. (San Francisco, Calif.)

73 Renal Interstitial Fibrosis: A Critical Evaluation of the Origin of Myofibroblasts
   Barnes, J.L. (San Antonio, Tex.); Glass II, W.F. (Glen Allen, Va.)

94 Immunopathogenesis of Idiopathic Nephrotic Syndrome
   Zhang, S.; Audard, V.; Fan, Q.; Pawlak, A.; Lang, P.; Sahali, D. (Creteil)

107 Membranous Nephropathy
   Cybulsky, A.V. (Montreal, Que.)

126 Prospects and Perspectives on IgA Nephropathy from Animal Models
   Emancipator, S.N. (Cleveland, Ohio)

153 Infection-Related Glomerulonephritis
   Brodsky, S.V.; Nadasdy, T. (Columbus, Ohio)

161 Discovery of Genes Related to Diabetic Nephropathy in Various Animal Models by Current Techniques
   Wada, J. (Okayama); Sun, L.; Kanwar, Y.S. (Chicago, Ill.)

175 Glomerular Basement Membrane Disorders in Experimental Models for Renal Diseases: Impact on Understanding Pathogenesis and Improving Diagnosis
   Kashtan, C.E.; Segal, Y. (Minneapolis, Minn.)
183 Experimental Models of Lupus Nephritis  
Grande, J.P. (Rochester, Minn.)

198 Experimental Models of Membranoproliferative Glomerulonephritis, Including Dense Deposit Disease  
Vernon, K.A.; Pickering, M.C.; Cook, H.T. (London)

211 Experimental Models of Vasculitis and Glomerulonephritis Induced by Antineutrophil Cytoplasmic Autoantibodies  

221 Monoclonal Immunoglobulin Light and Heavy Chain Deposition Diseases: Molecular Models of Common Renal Diseases  
Ronco, P.; Plaisier, E.; Aucouturier, P. (Paris)

232 Renal Amyloidosis: Current Views on Pathogenesis and Impact on Diagnosis  
Herrera, G.A.; Teng, J.; Turbat-Herrera, E.A. (Tempe, Ariz.)

247 Toward Understanding Renal Fanconi Syndrome: Step by Step Advances through Experimental Models  
Sirac, C. (Limoges); Bridoux, F. (Limoges/Poitiers); Essig, M. (Limoges); Devuyst, O. (Brussels); Touchard, G. (Poitiers); Cogné, M. (Limoges)

262 Light Chain-Mediated Tubulopathies  
Sanders, P.W. (Birmingham, Ala.)

270 HIV-Associated Nephropathy: Experimental Models  
Avila-Casado, M.C.; Fortoul, T.I. (Mexico City); Chugh, S.S. (Birmingham, Ala.)

286 Acute Kidney Injury: Lessons from Experimental Models  
Heyman, S.N. (Jerusalem); Rosenberger, C. (Berlin); Rosen, S. (Boston, Mass.)

297 Pathogenesis of Tubular Interstitial Nephritis  
Tanaka, T.; Nangaku, M. (Tokyo)

311 Obstructive Uropathy  
Truong, L.D.; Gaber, L. (Houston, Tex./New York, N.Y.); Eknoyan, G. (Houston, Tex.)

327 Renal Vasculature in Essential Hypertension: A Review of Some Contrarian Evidence  
Tracy, R.E. (New Orleans, La.)

337 Thrombotic Microangiopathies: From Animal Models to Human Disease and Cure  
Caprioli, J. (Ranica); Remuzzi, G. (Ranica/Bergamo); Noris, M. (Ranica)

351 Glomerular Repair: Present Status and Future Expectations  
Herrera, G.A.; Turbat-Herrera, E.A.; Teng, J. (Tempe, Ariz.)

363 Author Index

364 Subject Index
Foreword

Experimental Models for Renal Diseases: Impact on Understanding Pathogenesis and Improving Diagnosis

The need for this book became apparent as discussions with colleagues clearly indicated that our understanding of pathogenesis and ability to accurately classify and diagnose renal diseases has improved considerably in the last two decades thanks to basic and translational research efforts and that this information has not been collated and organized in a proper format making it available to students, diagnosticians, researchers and/or teachers of renal diseases. A single source in which to find this information presented in an up-to-date, succinct, yet comprehensive manner is not currently available. There are excellent textbooks addressing clinical diagnosis and pathology of renal diseases and in these there are, sometimes, incursions into pathogenesis, but generally not an in-depth discussion of how research has impacted our knowledge and understanding of the pathogenesis of renal diseases and/or improved our ability to diagnose and treat them.

I am satisfied to have assembled many of the world leaders in the various renal disorders to contribute to this book. These scientists have themselves contributed with their own research to the advancement of our understanding of renal diseases. Together we have condensed vast amounts of information into relatively short chapters due to the usual space constraints that are imposed by the publisher. This is only possible when the writer’s understanding of the subject matter is clear and comprehensive making it possible to synthesize the knowledge in an insightful fashion. In many instances, these collaborators have developed their careers making their own seminal contributions to the literature. To these giants in the field of renal diseases, I am forever indebted for the time they have spent collecting, organizing and presenting the material in a coherent and comprehensive manner while at the same time conveying the concepts in a superb fashion, making the material amenable to be used for didactic purposes.

The famous anthropologist Claude Levi-Strauss has said, ‘the scientific mind does not so much provide the right answers as to ask the right questions’, emphasizing that our understanding of scientific issues is continuously being challenged. It is only through persistent questioning that the so-called established ‘dogmas’ are tested and that eventually advances in science occur. If the wrong question is asked in the first place, undoubtedly the wrong answer will be obtained when the research is done. On the other hand, if the right question is asked, an answer of value (though not necessarily unequivocal or final), but one that will likely advance our knowledge will emerge. The authors of the chapters have excelled in their careers by persistently asking the right questions and, as a result, have discovered and clarified information, helping in this way to formulate our vision of the present and the future, as it pertains to the understanding of the pathophysiologic mechanisms involved in renal disorders.
Without their original and seminal contributions to the various subjects, scientific progress would have been thwarted. Undoubtedly, without the efforts of these dedicated scientists, the treatment and management of patients with renal disorders would have been adversely affected. I feel honored to join them in sharing with the readers new knowledge. In doing so, we are able to explore some unique perspectives in the various subjects that I have carefully selected with our readers in mind. In some chapters, some controversial subjects are discussed with views expressed that indicate how these issues stand today. One of the purposes of doing this is to show our readers areas of future potential research interest.

It is the intent of all contributors that this book be used by students of various disciplines, clinicians and investigators alike and by all those trying to correlate basic research information with clinical issues and value the uniqueness of the translational approach to study renal diseases. At the end of many of the chapters, a summary of its contents is provided. This is often accomplished with a chart to facilitate the understanding of the information and to make it most useful for didactic purposes.

The initial chapters in the book discuss basic concepts and principles of renal tissue reactions to injurious agents using a specific cell/compartment approach. Since the patterns of tissue reaction are limited and different injurious agents lead to similar tissue alterations, understanding these is crucial to conceptualize pathogenesis in a logical fashion. I believe this to be a necessary preamble to discussing the specific entities. Although it is impossible to avoid some repetition, I have tried to minimize this during the editing process.

In this the era of molecular biology, disease processes associated with renal diseases have become much better understood. Specific steps in pathogenic cascades that can be controlled or modulated have been discovered. The elucidation and conceptualization of the complexity of cell reactions and tissue responses has advanced considerably and there is now a sophisticated understanding of molecular pharmacokinetics.

New therapeutic interventions are now possible as a result of the fact that sound and thorough mechanistic processes have been dissected in many diseases. New therapeutic interventions have been designed with these molecular pathways in mind. New therapies have improved the treatment of these diseases considerably thanks to the basic researchers and clinical scientists that have contributed so much to decipher key pathogenetic events that can be targeted by appropriate drugs. The ultimate beneficiaries of all this hard work are undoubtedly the patients who can now be treated based upon scientifically sound data rather than empirically. As a result, these patients now enjoy improved prognoses with longer, healthier lives.

It should be mentioned that the level of sophistication of the knowledge that patients command today in regards to their diseases is truly commendable. Patients have rather unrestricted access to information in the web to study; they can analyze research data generated by basic and translational research, including those obtained through carefully designed clinical trials conducted in relation to their specific ailments. Today many patients are very well informed and expect health care practitioners to be up to date with the latest advances in the various fields. Therefore, it behooves physicians to keep abreast of developments in the research arena which translate to patient care. This can be a daunting task since pertinent information is proliferating at a very a fast pace, requiring careful analysis of the data and proper evaluation of its meaning and significance in terms of clinical relevance.

I have tried to make this book a concise source where one can obtain most of the valuable information currently available regarding the topics addressed. I hope the readers find this book a useful reference and, above all, a resource for learning, conceptualizing and/or reviewing concepts related to the pathophysiology of renal diseases. My expectation is that this book can also be useful for teaching about the exciting and ever changing field of renal diseases.
Dedication

This book is dedicated to my wife Dr. Elba A. Turbat-Herrera who has been a source of inspiration and encouragement for me in good and bad times, and who has always believed in me. She has insatiably worked at my side as a close collaborator. Her innovative ideas have been crucial for the development and advancement of the research endeavors that we have conducted over the last 30 years. Without her, my career could have never matured. Our relationship has been a unique interactive professional experience that I have valued very much.

I also dedicate this book to my three grandsons: Athanasius Joseph, Linus Cyril and Elias More Brown who may one day read this book and use it as an inspiration to dabble in the world of science and medicine. Perhaps this book will engender or fuel in them the desire to make their own contributions to the scientific world.

Guillermo A. Herrera, MD
Tempe, Arizona, USA
May, 2010