Preface VII

Rat Models of Chronic Renal Failure
Gretz, N.; Waldherr, R.; Strauch, M. (Mannheim): The Remnant Kidney Model . 1
Uremia by Renal Cortex Electrocoagulation in the Rat 29
Metabolic Consequences 34
Jongejan, H.T.M.; Provoost, A.P. (Rotterdam): X-Ray-Induced Chronic Experimental
Renal Failure 40
El Nahas, A.M. (Sheffield): Masugi Nephritis: A Model for All Seasons 49
van Goor, H. (Groningen); Diamond, J.R. (Hershey, Pa.); Grond, J. (Groningen):
Renal Disease Induced in Rats by Puromycin Aminonucleoside 68
Gretz, N.; Strauch, M. (Mannheim): The Adriamycin Model 82
Kasiske, B.L.; O’Donnell, M.P.; Keane, W.F. (Minneapolis, Minn.): The Ohese
Zucker Rat Model of Chronic, Progressive Glomerular Injury 90
Provoost, A.P.; De Keijzer, M.H. (Rotterdam): The Fawn-Hooded Rat: A Model for
Chronic Renal Failure 100
Gretz, N.; Haisch, S.; Baur, S.; Bauss, F. (Mannheim); Bachmann, S.; Waldherr, R.
(Heidelberg); Strauch, M. (Mannheim): Models of Polycystic Kidney Disease
in the Rat 115
Chung, O.; Rohmeiss, P.; Gretz, N. (Mannheim); Unger, Th. (Heidelberg): The
Transgenic mRen2 Rat 124
Chung, O.; Rohmeiss, P.; Sponer, G.; Strauch, M.; Gretz, N. (Mannheim): Renal
Involvement in Spontaneous Hypertensive Rats 129
Mann, J.F.E.; Luft, F.C. (Erlangen): Hypertension-Induced Models of Nephrosclerosis
in the Rat 141
Kempe, H.P.; Engelmann, K. (Heidelberg); Gretz, N. (Mannheim); Hasslacher, C.
(Heidelberg): Models of Diabetes for Studying Diabetic Nephropathy 148
Harris, K.P.G. (Leicester): Models of Obstructive Nephropathy 156
Contents VI

Steinhausen, M.; Endlich, K. (Heidelberg): The Hydronephrotic Kidney: A Model to Study Renal Microcirculation 169

Pathophysiology of Progression of Chronic Renal Failure:
Influencing and Confounding Factors
Fogo, A. (Nashville, Tenn.): Growth Factors Promoting Progression in Renal Failure 184
Kriz, W.; Hackenthal, E.; Münter, K.; Nagata, M.; Nobiling, R. (Heidelberg);
Sakai, T. (Tokyo): The Isolated Perfused Rat Kidney: A Model to Study Glomerular Mesangial Failure 202
Bouby, N.; Bankir, L. (Paris): Role of Urine Concentration in the Progression of Renal Failure 216
Nephrotoxic Serum Nephritis: Possible Role of Intraglomerular Proteinases in Progressive Glomerulosclerosis 226
Westenend, P.J. (Nijmegen); Grond, J.; Weening, J.J. (Groningen): Strain and Species Differences in Experimental Models of Progressive Glomerulosclerosis 236
Zeier, M. (Heidelberg); Gretz, N. (Mannheim): The Influence of Gender on the Progression of Renal Failure 250
The Impact of Carbohydrate on the Progression of Renal Failure 258
Rayner, H.C.; Walls, J. (Leicester): Lipids and Progression of Renal Failure 273
O'Donnell, M.P.; Kasiske, B.L.; Keane, W.F. (Minneapolis, Minn.): Effects of Dietary Fatty Acids on Experimental Renal Disease 289
Barsotti, G.; Cupisti, A.; Moriconi, L.; Giovannetti, S. (Pisa): Effects of Dietary Protein and Phosphorus Restriction on Proteinuria and Glomerular Size in 5/6 Nephrectomized Rats 297
Matthias, S.; Ritz, E.; Mall, G. (Heidelberg): Effects of 1a,25 Dihydroxyvitamin D3 on Compensatory Renal Growth in the Growing Rat 302
Drescher, P.; Strauch, M.; Gretz, N. (Mannheim): Consequences of Acidosis following 5/6 Nephrectomy 310

Measurement of Blood Pressure and Glomerular Filtration Rate
Kiihnle, H.F.; Linzmeier, P.; Doerge, L. (Mannheim): Determination of Glomerular Filtration Rate in Rats 331

Subject Index 337
Animal models resulting in chronic renal failure are important research tools in order to gain insight into pathophysiological processes leading to terminal renal failure. Furthermore, the efficiency of treatment modalities like dietary or drug interventions can be checked for their ability to slow or halt progression. Animal models, however, are only reasonable research tools if they are well characterized, i.e. their course and peculiarities are known. Otherwise, their use might result in considerable artifacts or they may even be misused. In addition, it should be kept in mind that it is ethically questionable to perform animal experiments when the studies are useless or even unnecessary as the animal model used was not suitable to solve the question. Animal models might even be misused in order to obtain a certain result, if an animal model has features especially suited to solve a certain 'question', while the features of the models are not known to the scientific community. The aim of this book is to present a variety of experimental and genetic models of chronic renal failure in a way that their advantages, disadvantages and their special features become obvious to researchers, enabling them to choose the right model exhibiting the features needed for their research. Beside these rat models, the book contains a number of papers discussing factors which are influencing or potentially confounding the pathophysiology of progression of chronic renal failure, i.e. the outcome of the models. Finally, the measurement of blood pressure and glomerular filtration rate are discussed in detail. This book does neither give a survey on models of acute renal failure nor of renal replacement therapy in animals. The reader may find a survey of these models in the CRC Handbook of Animal Models of Renal Failure [1]. We also did not address the problem of peritoneal dialysis in animals, a field in which considerable progress has been made recently [2]. The problem of interstitial renal disease models is not addressed either. Yokozawa et al. [3] reported that they could induce chronic renal failure in rats by feeding excess adenine. This model exhibited biochemical signs of chronic renal failure and histologically crystal-induced interstitial fibrosis. Longterm biochemical data covering more than 60 days, however, are missing. Furthermore, several methods to produce chronic pyelonephritis have been devised [4-6]. Progressive renal failure, however, could not be induced by any of these models. Another model also not addressed in this book is that of lupus nephritis, which has been evaluated by Huston and
Steinberg [7].

Beside the discussion of induced chronic renal failure, special emphasis has been put on analyzing and evaluating genetic models resulting in chronic renal failure. An extensive discussion of available data is given for the BB rat, the Brattleboro rat, the Dahl rat, the Fawn-hooded rat as developed from the E3, the obese Zucker rat, polycystic kidney disease rats, SHR, and Transgenic mRen 2 rats. In addition to the development of terminal renal failure, the occurrence of focal segmental glomerular sclerosis or the resistance to it is discussed for several rat strains.

As animals developing spontaneous renal failure seem to be more suitable than chemically or mechanically induced models, there is a growing need to analyze other rat strains for their long-term outcome with respect to renal function. To us, the Osborne-Mendel rat having hypertension and fairly high cholesterol levels but very low triglyceride concentrations seems to be an interesting candidate for future research. But also other inbred strains like the Lewis, the Long-Evans, the Fischer 344, and the Brown Norway rat might be of interest. This might be especially true as some of these animals have fairly high plasma renin concentrations. Thus, a long-term analysis is needed.

Another model that could be of future interest is that of erythropoietin-induced loss of renal function, which is probably due to the rise in blood pressure in these animals. Whether this phenomenon is strain-independent has not been analyzed yet.

The editors want to express their gratitude to all contributors to this book. Financial support, which was gratefully appreciated, was given by the Deutsche Forschungsgemeinschaft (grant No. 4850/7/91), the Forschungsschwerpunktprogramm des Landes Baden-Württemberg (Forschungsschwerpunkt Niere und Hochdruck), the Zentrum für Medizinische Forschung, Klinikum Mannheim, and the Verein zur Förderung Nephrologischer Forschung Mannheim, e.V. The help of Mrs. Sigrid Redies and Dr. Marianne Gretz in preparing this volume is gratefully acknowledged.

The editors want to express their hope that this volume will not only be helpful for young researchers to get started with animal experiments, but also for well-read members of the scientific community as a tool for analyzing published data and better understanding research papers published in this field.
References