Foreword

I have had the good fortune of watching, from the very beginning, the explosive increase in knowledge of renal cystic disorders over the last five decades. My personal interest began when my elementary school chum, Ronnie Wilkerson, told me he had polycystic kidney disease (PKD), knowing that one day it would take his life. Ultrasound detection of cysts had just been applied to diagnose PKD patients at the University of Colorado School of Medicine in Denver. In 1974, Joseph Holmes M.D. made the initial presentation of what has become the largest cohort of affected individuals at a single site in the United States. Ronnie's name appears at an early position in that list. In his hour of need, however, there was no research to speak of except for long essays attempting to classify all of the inherited and acquired renal cystic disorders. These ended up becoming bewildering diatribes I have referred to, in a naughty mood, as "nattering nosology".

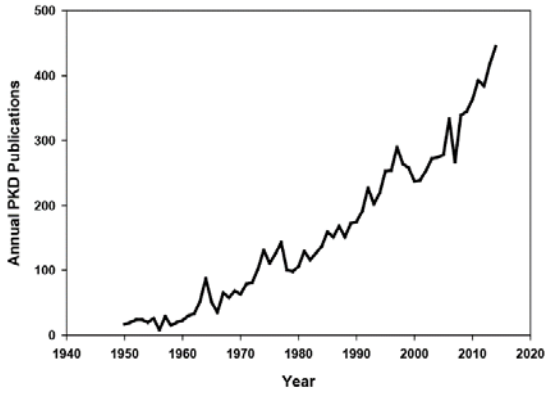
The first successful effort to move beyond descriptive accounts of the disease can be attributed to O.Z. Dalgaard, a Danish geneticist who in 1957 defined the genetics of autosomal dominant (ADPKD), thereby proving that the etiology of the condition was harbored in defective DNA. This provided a huge lead toward finding the cause of the disease. Lacking tools to localize the mutation and determine the molecular basis of cystic disorders, a few brave souls tried to learn something about the disease pathogenesis using classic physiology and pathology investigative approaches, now considered "blue collar".

In 1969, Kenneth Gardner M.D. collected cyst fluids from a single polycystic kidney, measured the electrolytes and osmolality in them, and discovered that some of the cysts continued to function as collecting ducts in spite of their massive dilatation. Prior to that renal cysts fell under the purview of radiologists who publically referred to them as "simple", and privately as "dull and a dead issue". With Jay Bernstein M.D. and Andrew Evan Ph.D., Gardner studied animals administered chemicals that caused acquired cysts to appear and, in doing so, discovered the important role that excessive cell proliferation plays in the development of a renal cyst. Frank Carone M.D. also explored the gross and micro-anatomy of cysts, finding abnormalities in the basement membranes and the renal interstitium.

I discovered, quite by accident, that normal renal tubules could secrete fluid, a new, and not especially welcome, function for normal kidney tubules. Wondering what to do with that unexpected discovery, I remembered Ronnie Wilkerson's cystic kidneys and I drew a connection between renal fluid secretion and the likelihood that it had something to do with how the fluid gets into renal cysts. In this new light I made it a quintet of "blue collar" scientists working on PKD.

In 1982, Joseph Breuning, a Kansas City business man, and I created the *Polycystic Kidney Research Foundation* to raise money in support of finding treatments and an eventual cure for PKD. In 1984, we invited every scientist and physician-scientist in the world who could spell polycystic to participate in a workshop to determine just how much useful information was in hand and where we needed to go to have the greatest impact. The first NIH-sponsored Program Project Grant emerged from the discussions in an atmosphere of excitement and camaraderie that motivated some exceptionally talented researchers among the attendees to join the intrepid band of PKD researchers.

From this modest beginning, PKD research has become a mainstream international field that enjoyed publication in 2012 publication of a large clinical trial showing that the blockade of vasopressin V2 receptors would slow the growth of cysts and reduce the rate of decline in glomerular filtration rate. And there certainly will be more trials and successes as detailed in this timely book, edited by Xiaogang Li. He has gathered PKD- focused scholars from all parts of the world to share their perspectives on the current diagnosis and treatment, the molecular mechanisms contributing to cyst formation and growth, and the extra-renal manifestations of PKD.



This is a volume that emphasizes new developments in the field. When one considers how much has been learned over the last four decades, compiled in the annual growth of PKD publications listed in PUB-MED (Figure), it is safe to say that it will be necessary to update this book within a few years.

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