Inborn errors of development: the molecular basis of clinical disorders of morphogenesis


The third edition of David Smith's outstanding textbook, Recognizable patterns of human malformation, was published in 1982. It consisted of 652 pages with detailed descriptions and tables of over 250 malformation syndromes. It was, and remains, an excellent book. Yet it did not contain a single mention of molecular pathogenesis or an underlying mutational spectrum.

How times have changed. Now, thanks to extraordinary developments in molecular biology, it is the exception rather than the rule to encounter a syndrome for which there is not an available molecular handle. The diverse fields of molecular genetics and clinical dysmorphology have pooled their intellectual responses to burrow away at the mysteries of human development. Their triumphant emergence is elegantly encapsulated in this wonderful book.

The title is clearly derived from Garrod's original concept of "inborn errors of metabolism" and it is probably not too fanciful to surmise that the next edition will come with a pullout wall chart linking all the known molecular developmental cascades in the sort of multidirectional interconnected nightmarish diagram that is much beloved of biochemists. For the over 250 readers with any involvement with a syndrome with over 250 genes, clinical and genetic diagnostic strategies, and the management of renal and extra-renal manifestations.

What are the surprises? The first surprise, and a highlight of the book, is the third chapter, which is by Paul Winyard, and is entitled "Renal development". This provides a comprehensive yet readable summary of a complex field with relevance to the pathogenesis, and perhaps eventually the therapy, of many renal diseases. The first and second chapters are introductions to clinical genetics and renal physiology, respectively. These will be helpful to non-specialists.

A second surprise is the very complete chapter, written by Gough and Vile, on gene therapy for renal cancer, which provides a potential framework for gene therapy for other forms of renal disease. Perhaps future books of similar scope will be able to include chapters devoted to targeted small molecule therapies and renal regenerative therapy.

A third surprise is the inclusion of genetically complex renal diseases such as glomerulonephritis and membranous nephropathy, and genetically complex systemic disorders affecting the kidney, including hypertension, diabetes, and systemic lupus erythematosus. The genetic data underlying these diverse diseases are elegantly summarised in a chapter by Pows. Elucidating the genetic basis of these disorders will be a major challenge of the next phase of renal genetics research.

In summary, this comprehensive yet accessible text links genetics, pathogenesis, and clinical management. The reader can rapidly locate a single piece of information using the index, efficiently review a topic by reading a few paragraphs, or acquire a comprehensive introduction to a disease by reading an entire chapter. The genetics of renal disease will have broad appeal to paediatric and adult nephrologists, clinical and laboratory based geneticists, and basic scientists, highlighting the increasingly interdisciplinary nature of renal disease research.

I D Young

The genetics of renal disease


“The kidney inspires awe in all those who attempt to understand its functions.” This first sentence of chapter 2 of The genetics of renal disease perfectly captures the spirit of this book. Inherited renal disease is one of the most diverse, fascinating, and quickest growing areas of human genetics. Functional analyses of the genes associated with renal disease are leading to connections with many other scientific fields. For example, as is beautifully illustrated in colour plate 5 in this book, proteins now known to be directly involved in genetic renal disease are linked to the actin cytoskeleton, the endothelium, and basic cellular processes studied by laboratories not necessarily involved in renal disease.

The genetics of renal disease contains everything you might expect based on its title, and also some surprises. In the category of things you would expect are chapters devoted to each of the major genetic renal diseases, including Alport's syndrome, cystinosis, autosomal dominant polycystic kidney disease, autosomal recessive polycystic kidney disease, tuberous sclerosis complex, and von Hippel Lindau disease. An important feature is the broad scope of each chapter, most of which encompass aetiology and pathophysiology as well as clinical management. For example, the chapter on autosomal dominant polycystic kidney disease by Saggard-Malik and Somlo includes animal models of polycystic kidney disease, functional analyses of the PKD1 and PKD2 genes and proteins, mutation detection, and a flow diagram for the clinical evaluation of suspected intracranial aneurysm in autosomal dominant polycystic kidney disease. The chapter on autosomal recessive polycystic kidney disease by Guay-Woodford discusses animal and cell culture models, prenatal diagnosis, and clinical management. The chapter on von Hippel Lindau disease by Maher discusses the function of the von Hippel Lindau disease protein, clinical and genetic diagnostic strategies, and the management of renal and extra-renal manifestations.

E P Henske

do: 10.1136/jmg.2003.011924corr1


www.jmedgenet.com