



Foreword to 1st Edition

The medical model of disease, which has served the practice of medicine well, proposes that a cause of disease – no matter what the cause or the disease – initiates a deviant process – called pathogenesis – which culminates in manifestations of the disease. The manifestations are its taxonomy and from them one initiates another process leading to diagnosis. Correct treatment depends upon diagnosis. All error in, or an absence of, diagnosis leaves manifestations naked, pathogenesis is not reversed and cause continues to initiate the disease.

This book is about diagnosis. The necessary or sufficient causes of the diseases described here are mutations in genes responsible for important steps in the metabolic mosaic that underlies health. Garrod recognized that inborn errors of metabolism are manifestations of biochemical individuality. The importance of this observation was recognized by biologists but they made little impression on the practitioners of medicine during Garrod's lifetime. Even today, the inborn errors of metabolism are believed to be rare encounters in medicine and likely never to be seen in a typical medical practice. How wrong it would be to see things that way in 1996. The inborn errors of metabolism induce disease manifestations in every organ and at every life interval from the fetus to the geriatric patient, and they are ubiquitous in their appearance, with little regard for the qualifications of the physician – generalist or specialist.

It is a sign of the times that this book is called *Physician's Guide* ... Such a book is something Garrod might have hoped for but was realist enough not to expect its appearance in his library. Even in the half century since Garrod's death in 1935 few physicians have experienced the excitement in diagnosis of an hereditary metabolic disease. A generation ago an enterprising publishing firm sponsored a series of advanced monographs for practitioners; those that dealt with problems affecting patients in large numbers with overt clinical problems that could be addressed by readily available resources and technologies did well and went into further editions; those devoted to genetic and metabolic themes did not. The present adventurous text implies that the times have changed.

Whereas screening programs have become widely established to detect selected inherited metabolic diseases long before the clinical signs appear,

the majority of diseases discussed in *Physician's Guide* will present first to the practising physician; he or she will identify the patient's disease first; it will be a challenge, and that is why the clinical features of these diseases are given prominence first here.

Why would already overworked editors and authors be willing to devote their time to preparing the texts, tables and appendices that comprise *Physician's Guide*? May I offer these reasons?

- In aggregate, the inborn errors are indeed not rare, they are prevalent and they involve an increasingly large number of humans requiring intensive, often lifelong, health care. Accordingly, diagnosis to set them on the right path is important.
- The methods of diagnosis described in this book will also be those used to monitor treatment and management of the patient's disease.
- The inborn errors of metabolism constitute a group of diseases about which there is an enormous amount of information; more in fact than for almost any other set of diseases. Such knowledge is beneficial to practitioner and patient.
- Should one still believe that the inborn errors of metabolism are esoteric, consult any major general textbook of pediatric or general medicine, or the *Oxford Medical Companion*, second edition. All of the former describe these problems; the latter – a vastly informative encyclopedia about the science and the practice of medicine – has a fine entry on the inborn errors of metabolism. The topic has found numerous harbors in the medical seascape.

The core of information common to each chapter of the *Physician's Guide* comprises:

- The major clinical and chemical signs initiating the diagnostic journey. In many cases they are translated into diagnostic algorithms. Perhaps they will be translated further into versions accessible on CD-ROM.
- Simple tests, both those that serve screening programs and those that can be done at the bedside, in physicians' offices or in nonspecialist laboratories. This information will replace a number of well-worn manuals and publications of a generation ago.
- Special tests done primarily at referral centers and whose interpretation is part of the *Physician's Guide's* lode of information. Useful practical matters such as how to collect and store the particular sample are described.
- Phenotype tests, primarily at chemical and biochemical levels (metabolites and enzymes) are emphasized. Genetic information is provided to indicate how much genetic and allelic heterogeneity may be associated with the phenotype. A later edition of this book may expand into the area of mutation detection and DNA diagnostics, but at present the phenotype tests are robust and remain powerful.

- The authors have also gone beyond diagnosis to provide useful information about initial and emergency treatments.

The *Physician's Guide* is a work of dedication and if there is fairness in the scheme of things it will find a place on many a practitioner's shelf. Those who use it will no longer be limited to a small group of specialists – I repeat, because diagnosis and care of the patient with hereditary metabolic disease is expanding beyond that small original community of practitioners into all medical specialties, and into internal medicine as the child patients grow into adulthood, thanks to advances in diagnosis and treatment. Accordingly, this book will not only be a guide, it will be a companion and it will complement very nicely the other major texts in the field.

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