

# Preface

*We ought not to set them aside with idle thoughts or idle words about 'curiosities' or 'chances'. Not one of them is without meaning; not one that might not become the beginning of excellent knowledge, if only we could answer the question — why is it rare or being rare, why did it in this instance happen?*

— James Paget (1882)

I had the good fortune of coming to Mount Sinai Medical Center (MSMC), New York to complete my training in medical genetics, after an initial period of grounding at the Mayo Clinic in Minnesota. At that time (1990), enzyme therapy for Gaucher disease (GD) was in clinical trials. As New York had a large Ashkenazi Jewish community and GD was a prevalent and well-characterized disorder in this population, patient recruitment would not be a problem. Furthermore, a physician at MSMC (Gregory A. Grabowski) had up to that point devoted most of his professional life to studying the disease. Thus, our group had anticipated being involved in the pivotal trials to evaluate the recombinant form of glucocerebrosidase (the enzyme deficient in GD). When Greg left for Ohio in 1991 to head the Division of Genetics at the Children's Hospital in Cincinnati, I took over the care of our GD patients and completion of the trials, which was then a collaborative effort between MSMC and Norman Barton and Roscoe O. Brady at the National Institutes of Health. Roscoe's role was both vital and of special interest,

as he had in the mid-60's delineated the enzyme deficiency that was shown to cause GD and proposed the feasibility of treatment by infusing the protein, isolated from human placenta, into patients. These initiatives were supported by Genzyme Corporation, and facilitated by Orphan Drug legislation (established in 1983).

Subsequently, I was involved in other GD-related studies delineating genotype–phenotype relationships, assessment of disease burden and mapping therapeutic profile in patients on enzyme therapy. Then as now, Robert J. Desnick, a leader in the field of lysosomal storage disorders (LSD), headed the Department of Human Genetics. In 1997, I moved to New York University to work with Edwin H. Kolodny whose interests included two other LSDs; specifically Tay-Sachs and Anderson-Fabry disease. The conjunction of these personalities and particular circumstances served as my introduction to the field, which to a large extent has defined my own professional life. These events were to also play a role in my personal life, as it enabled the happy occasion of meeting Derralynn A. Hughes, a hematologist at the Royal Free Hospital who was involved with caring for the London-based patients with GD and Anderson-Fabry disease. Derralynn and I were married in 2008, and at the time this book was written we have a daughter (Paloma).

Although my time at the Mayo Clinic was short, the individuals I met and the genuine spirit of mutual respect and high standard of patient care delivery I was to witness has formed a firm foundation, from which I was to draw the needed strength to confront the challenges I have subsequently had to deal with. In this regard, Virginia Michels was an excellent guide and teacher. More recently, Gilles Lyon, a French physician with whom Ed Kolodny and I co-authored a text entitled the *Neurology of Hereditary Metabolic and Molecular Diseases in Childhood* (2006), has been a source of inspiration.

I have been engaged in clinical practice and research in the field of LSDs for the past 20 years, and I was involved in several of the seminal trials to evaluate the safety and efficacy of various therapeutic options for several of these conditions. I believe this gives me a unique perspective, which I would now like to share with the readers of this book. Various investigators focus on different aspects in relation to LSDs, some are

primarily clinicians and others do only basic scientific investigations. Thus, most books on the subject tend to be multi-authored, and can be variable in scope and depth. I have attempted to fill what I perceive as a gap in the existing literature: information in a single textbook which can serve as a concise guide not only for the novice, but for the expert as well whose focus or interest may be narrower than my personal experience.

Rapid progress is underway; thus, knowledge regarding pathophysiology and treatment of the LSDs is constantly undergoing revision. I have tried my best to present the most up-to-date information on the subject as I understand it. I would appreciate any effort by the reader to call attention to inaccuracies or outdated information, so this can be addressed in future editions of this monograph.

In closing, I would like to inscribe this book to my parents, Jovito C. Pastores and Annie H. McCarthy; both were equally devoted to my upbringing and education. My parents passed away within a span of one year, shortly before and after my wedding. What I am I know confidently has come from my parents; what I hope for and will become I pray my wife and daughter will enable.

Also, I would like to express my gratitude to the patients who have entrusted their care to me, and have given me the opportunity to develop my clinical skills. My interactions with the patients and their extended families have helped to enrich my life in several ways, because it has allowed me to learn of cultures and traditions that have not been part of my own upbringing. In entrusting their care to me, it is my fervent hope that I have met with their expectations.

Thus far, it has been a great adventure and I look forward to participating in future studies to elucidate the pathophysiology of LSDs and the development of treatment. Through the years I have interacted with and learned from several colleagues, and I am most grateful for the privilege and their mentorship.