Preface

The Power of one and the Power of Many: Patient Advocacy and its Influence on Rare Disease Research – Evolutionary and Revolutionary Factors

In this updated book, the Editors have invited John Forman to discuss patient advocacy in rare diseases through the actual history of a family affected by a rare disease. The Preface provides experiences and accomplishments of one family with heightening the awareness of a rare disease, mucolipidosis type III (ML3), following the birth of their first child. The necessity of the individual and the family to meet the needs of a family member has led many individuals to become the leader in the field to develop a research emphasis and provide information to the public on a specific rare disease. The role of patient advocacy in promoting research into rare diseases, like most aspects of our society, has changed over time. From volunteering, as largely passive subjects in studies, or donating samples for research, there have been evolutionary changes through many stages of development. Loose collections of families coalesced into support organizations and engaged with health professionals and researchers to promote disease knowledge, clinical care improvements, and a search for effective treatments or cures. Alongside this evolutionary growth in capacity and involvement, revolutionary changes spurred the impact of patient advocacy into new levels. One such change was the impact of human rights in society and the flow-on effect this had in the health field, with patients gaining explicit rights in consent in health care and research, plus rights to consultation on public policy.

The communications revolution from the 1990s meant patients could connect and share more easily with each other and build more effective advocacy groups while also gaining unprecedented access to medical and research information that had been effectively locked away from them. The move from passive recipients to active partners took some years to achieve. But this combination of evolutionary and revolutionary forces made it a present-day reality. The momentum continues, as patient advocacy moves from subject to participant, to partner, and then to financial supporter and leader in rare disease research. This Preface addresses a range of these issues in the context of one patient advocate's long-term commitment to research and better care for the very rare disease two of her children have. It offers a message of hope and encouragement that much more can be achieved through additional contributions by more patient advocates.

Introduction. When invited to write this Preface, I referred to the first edition where authors associated with NORD, the US National Organization for Rare Disorders, wrote about patient advocacy and research against a backdrop of the remarkable and inspirational work of Abbey Myers, the founder and first chief executive of NORD. I considered extending this theme by addressing some other high-profile advocates and their organizations and the far-reaching impact they had on research into a wide range of rare diseases. But many of those stories are likely well known to most readers of this chapter. Instead, I decided to focus on the work of just one patient advocate who is not so widely known, but has achieved significant accomplishments over the past 30 years. I believe her story is important as a recognition of what she has done largely "under the radar" for so long and the wide range of impacts her work has achieved. It is also important as a source of inspiration to others who may wish to work toward similar aims, but feel perhaps daunted by the

tasks or uncertain about their ability to make a difference in such a challenging and often mysterious area of activity. This could be especially so, if they do not have access to large sources of funds or lack knowledge of medical or scientific terms. She is, in my view, a fine example of what can be achieved with focus and determination and with very limited resources. I believe her story will also offer reassurance and support to many patient advocates who are operating at various points along the spectrum of advocacy activities. Not every advocate can aspire to nor reach the highest levels of achievement in research on their disease. The work of thousands who do unsung work at different levels remains vitally important to successfully progress in rare disease research.

In the Beginning. The parenting world of Jenny Noble and her husband Paul, living at the time in Nelson, New Zealand (NZ), had a very typical beginning with the birth of their first child Hayden, in 1981. What is still quite typical for many on the journey into the world of rare diseases was true for them too. Symptoms of a possible problem began when Hayden was just 5 years old, by which time Hayden had a brother David and a sister Sarah. The surprising fact for those times was the quick delivery of an accurate diagnosis after those first signs. Within 2 years, a correct diagnosis of mucolipidosis type III (ML3) was given, and as so often happens when the first child is diagnosed with an inherited disease, Sarah was soon found to be affected by the disease also, while David was not affected.

Lack of information and isolation were significant problems. There was no other family in New Zealand with the same disease, and in the pre-Internet age, it was very challenging to get information. In 1989, faced with significant surgery indicated and a range of other symptoms presenting, Jenny and Paul decided to borrow against their house and travel to an international meeting on MPS and related diseases (the closest umbrella gathering for ML3 families, researchers, and clinicians), to learn as much as they could about the disease and meet experts in the condition.

Making Connections and Finding Information. Finding at that meeting the doctor who first described this condition and, on that journey, finding others who had managed patients with the disease gave them important information about surgical options and risks, plus information about other complications to be expected with ML3. Some of this unpublished information was vital to the surgery facing their family and allowed Jenny and Paul to effectively engage with the treating doctors to ensure the best outcomes for Hayden and Sarah. These connections were maintained and these experts regularly consulted by the family and their doctors back in NZ, though there were sometimes challenges regarding the acceptance of information found by them. Throughout the 1990s, both Sarah and Hayden had several major surgeries, and the work done to connect with relevant experts in different countries undoubtedly led to much better outcomes for both of them.

It was in these early times on the journey that Jenny committed to sharing the knowledge gained by networking with other families here and overseas, and throughout the 1990s, she worked closely with families, health professionals, and researchers in the disease and began building connections for related diseases too. This task was greatly assisted by the Internet which began spreading from the mid-1990s and by Paul's unwavering support. By the turn of the century, improving disease knowledge for health professionals and families, and ensuring best medical care and optimal social support systems, became her unpaid career.

Building the Networks. In 1999, my role as a parent of twins with a related disease, alpha-mannosidosis, led to my path crossing with Jenny, and we joined forces on the development of Lysosomal Diseases New Zealand (LDNZ), as an umbrella

support group for all lysosomal diseases, to give structure to efforts to support and inform affected families and to work to improve scientific research, medical care, and social support. We knew from our experience that research had to go beyond basics of the disease-causing mechanism. Research into best clinical care for our children was a vital need for ours and many other affected families. Families also need help to navigate the complexities of social support programs. Jenny took on the role of field officer for LDNZ, and after several years of operating without funds, we managed to scrape together the first grants to pay her modestly, for her significant contribution.

Within the next 2 years, Jenny played a pivotal support role in the development of the New Zealand Organisation for Rare Disorders, which I set up, and soon after she accepted a board role alongside me, with ISMRD, the International Advocate for Glycoprotein Storage Diseases, based in the USA. Through these roles, Jenny could make a contribution to information, research, and policy relating to rare diseases in NZ, as well as attend to the needs of the very rare subset of lysosomal diseases under the umbrella of ISMRD. Seventeen years later, she is still actively working in these roles.

Doing the Business. Since 2000, Jenny has participated in and often led significant efforts toward research on her children's disease and on related diseases. In addition, she has worked hard to influence policy for all rare diseases – all of this with no formal training in science or medicine. Starting as a secretary in the insurance company where she met Paul, she has worked hard to develop an extensive lay knowledge of the diseases and their needs, so she could advocate effectively for them and support research and clinical care for them.

Patient Advocacy Role. In 2000, she gave evidence to NZ's Royal Commission on Genetic Modification to describe her family's experience and to successfully advocate for the continuation of experiments that might lead to treatments for mucolipidosis and other rare diseases.

Scientific Conferences and Workshops. In 2002, she coauthored "The osteodystrophy of mucolipidosis type III and the effects of intravenous pamidronate treatment" (J Inherit Metab Dis 25 (2002) 681–693). She has since presented at family and scientific meetings on the results of this research from 2005 to 2015. She has been the central fundraiser and program organizer of four ISMRD conferences in the USA and is working on another later this year, 2017, in Europe. Each of these is designed to bring the scientists, health professionals, and families together to share experiences and learn from each other. Numerous research efforts had their genesis through connections made at these events.

In 2003 and again in 2008, she did the fundraising and central organizing role for a family and scientific conference in NZ for all lysosomal diseases. The 2008 meeting included a special workshop she organized for expert consideration of bone disease in mucolipidosis, and several research projects have sprung from this discussion.

In 2010, she repeated these fundraising and organizing roles for the International MPS Conference held in Adelaide, South Australia.

Support for Basic Research. Through fundraising efforts that Jenny has led, LDNZ has been able to support NZ researchers. We funded a study on treatment outcomes for patients with Gaucher disease and funded teams studying animal models of lysosomal diseases. Our small grants have provided important bridging to larger grants for work on Batten disease in sheep and Sanfilippo A disease in huntaway dogs. These research projects have made significant progress toward the

development of therapies for both diseases.

Research Partnerships. In 2013 and again in 2016, Jenny's central role in ISMRD's fundraising efforts led to a partnership with other advocacy groups and foundations to provide a grant of $40,000 in 2013 for research into heart issues in mucolipidosis, and a sum of $150,000 was raised in 2016 funding exploratory gene therapy for the disease in cell culture and animal models and a separate study into potential therapy for the bone problems in the disease.

Clinical Care. On several occasions over these years, Jenny has worked closely with me on problems with clinical care coordination for those with complex and chronic diseases, especially those who leave the relatively well-organized world of pediatric care and graduate into the "black hole" of adult services. Case studies have been used in conjunction with the Pediatric Society, health officials, district health boards, and the Health and Disability Commissioner (HDC), to identify failings and make improvements. Success in this work is frustrated by the tendency of adult specialists and their hospital managers to slip back into their traditional methods of "silo" delivery and to lose sight of the collaboration and coordination that is indicated by the patient needs and which is in fact their right under our HDC Code of Rights. These experiences highlight the related need for research into health service delivery, which this work has contributed towards.

Natural History Study. In 2005, Jenny provided leadership and fundraising support for the development of a natural history study into the nine glycoprotein diseases in partnership with a US medical center, from which mutation discoveries, genotype/phenotype correlations, nomenclature changes, transplant outcomes, and diagnostic techniques have been published. And she's not finished yet!!

The Broader Context of Rare Disease Research. Patient advocates can contribute to research in many ways, including as passive participants and donors, as partners with clinicians and researchers in specific studies, as planners of conferences to build interest in disease research, by influencing legislators and funding agencies about rare disease research, by raising funds to make research happen, by developing biobanks and registries, by funding natural history studies, by sitting "at the table" when plans and priorities are devised, by influencing clinical trial design and consenting processes and how research is evaluated by regulators, by debating research priorities, and by influencing screening and diagnosis policies and practices.

Individual advocates may be daunted by the tasks and the scale of work needed. But all can make a meaningful contribution in some way or another. It is not necessary to aim to be in the top echelon of movers and shakers. Start with what you know and what you can do. Every contribution is valuable. Build a network of like-minded people. Network with the scientists and clinicians at conferences. Ask questions and seek answers. Don't be scared to show the limits of your knowledge. If you have anxieties about this, remember that I personally have asked the most naïve question ever asked by any patient advocate at a scientific and medical conference. Remember that the experts are invariably helpful and considerate, and they will value your experience of dealing with the practical aspects of the disease on the day-to-day life of patients and families. Your experience is something they don't know enough about, and they are keen to learn from you.

Conclusion. Personal stories provide a compelling angle to this discussion, I believe, and I have used Jenny Noble's story because I see it as a very informative example of what can be achieved by an individual with commitment and determination for the cause and a willingness to be in it for the long haul. She has been

involved in many areas relevant to rare disease research, but not all of them. She played to her strengths and did what she could. She learned more when she needed to. But she did not aim to become a medical geneticist or research scientist. She did more at her level than she could likely have achieved if she had gone down that path. She deserves great recognition for her commitment for the cause, but perhaps the greatest accolade for her would be that her story has inspired patient advocacy readers to feel motivated to do more to support research and to feel comfortable that getting started at a level they feel confident with will be welcomed and valued. The power of one can be multiplied many times over, if we all do our bit.

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