

Guest Editorial

Twenty-one years later: Twenty-first century rehabilitation

Welcome to Volume 1 issue 3 of the *Journal of Pediatric Rehabilitation Medicine*. A focus for this issue is the rehabilitation of Duchenne Muscular Dystrophy (DMD). Our authors have put together a series of article on the history and care of boys with DMD. Dr. Michael Nigro, my neighbor to the east, a long time leader in southeast Michigan and the United States in the care of neuromuscular disease, provides a historical context to our management. Articles on seating and mobility, cognitive and behavioral involvement, and cardiovascular management provide excellent reviews of our current understanding of their place in the care in DMD, and will be valuable assets to clinicians. A few nonrelated MD articles complete the issue.

As we look ahead to the role of rehabilitation in the future care of DMD, just a brief look backwards. Hoffman et al made tremendous strides in our knowledge of the pathophysiology of DMD with the identification of the dystrophin gene and protein in 1987 [2,3]. Since then, it has been hoped that this new knowledge would soon lead effective treatments. Over the past 21 years, our care of DMD has changed little. Corticosteroids have been shown to extend duration of ambulation, but we do not know (yet) if this changes overall outcome. Questions I had as a resident have still not been definitively answered (e.g. how much strength training is safe in DMD?). Boys born in 1987, are now 21. I have not had much new hope to offer.

This is not unusual for pediatric rehabilitation specialists, to not have cures for disorders-cerebral palsy, myelodysplasia and spinal cord injury-but to maximize function and quality of life. In the early twenty-first century, we are on the verge of changing this for DMD. Fall, 2007 at the American Academy of PM&R Annual Assembly, Dr. Hoffman presented preliminary data on the use of exon skipping with “morpholinos”. Videos of dogs with the canine equivalent of DMD

comparing treated and untreated dogs were astounding (I do not say they were miraculous, as these were the result of hard work and good science). More information on this treatment strategy is available from Yokota [5]. In addition, a phase 2b trial is beginning for PTC-124, a “readthrough” agent, which allows transcription through stop codon mutations (see Aurino and Nigro for a much more thorough discussion [1]). For more information on the clinical trial, please visit www.clinicaltrials.gov, using identifier number NCT00592553.

Effective treatments will not end the need for rehabilitation, but change our patients’ needs. These treatments, when available, will likely not reverse the pathological changes that have already occurred. This will be a bit of a Pandora’s box – to get at the hope, we will have a new set of “evils” to deal with. Boys who are at the mid- and late stages may stabilize their course. This will change DMD into a chronic condition, not just a disorder of child- and young adulthood, but hopefully into old age. Specialists in adult rehabilitation (and all medical specialties) will now need to be involved in their care. We see obesity and the metabolic syndrome as an increasing problem in our patients with disabilities [4]. What role will this play in a population that has been exposed to chronic steroid treatment, with small muscle mass and limited physical capacity? What will the exercise response, a major therapeutic strategy for metabolic syndrome, be in these men?

Argento and Kaufmann discuss the cognitive aspects of DMD in this issue. How will these new treatments affect the cognitive and behavioral outcomes? Because of the devastating physical affects, the CNS role of dystrophin has been less well studied. Will there be more long term cognitive consequences that we were previously unaware of because of the shortened lifespan? Will any of these new treatment strategies affect the central nervous system?

Many of the patients we care for will require a wheelchair at some point during the progression of their disease. Pangilinan and Mannlein provide a framework for one to consider. With improved technology and manufacturing, the options for patients has significantly improved compared to generations before. The proper seating and chair provides mobility which is a must for all patients requiring a chair. Providing all our patients with the appropriate equipment will be the challenge.

Russell et al. review the cardiac complications related to BMD/DMD. With a significant number of patients now dying from cardiac related issues, therapeutic treatment at a young age should be considered for all patients. What impact will these treatments have on these patients? Will some benefit more from afterload reduction and or beta blockers? Will patients live long enough to consider heart transplantation as "routine?"

As we progress through the twenty-first century, perhaps the first age of genetic medicine, we as rehabilitation specialists (most of us quite removed from the basic science of genetics) will need to be closely involved in the research of these treatments, studying ways to maximize the functional outcomes and ultimately improve the quality of life of our patients. Each of these treatments will raise new challenges for us to address.

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References

- [1] S. Aurino and V. Nigro, Readthrough strategies for stop codons in Duchenne muscular dystrophy, *Acta Myologica* **25**(1) (2006), 5–12.
- [2] E.P. Hoffman, R.H. Brown, Jr. et al., Dystrophin: the protein product of the Duchenne muscular dystrophy locus, *Cell* **51**(6) (1987), 919–928.
- [3] E.P. Hoffman, C.M. Knudson et al., Subcellular fractionation of dystrophin to the triads of skeletal muscle, *Nature* **330**(6150) (1987), 754–758.
- [4] E.A. Hurvitz, L.B. Green et al., Body mass index measures in children with cerebral palsy related to gross motor function classification: a clinic-based study, *Am J Phys Med Rehabil* **87**(5) (2008), 395–403.
- [5] T. Yokota, E. Pistilli et al., Potential of oligonucleotide-mediated exon-skipping therapy for Duchenne muscular dystrophy, *Expert Opinion on Biological Therapy* **7** (2007), 831–842.