2011 MD South Australia Research Report

It is once again a great pleasure to be able to write this year's Research Report for you albeit in a much briefer form than usual because it is necessary to write it in advance of the World Muscle Society (WMS) 2011 Congress that I will attend in Portugal towards the end of October.

Most of the present report will, therefore, be taken up with news from earlier clinical/scientific research conferences that I have attended in the last year and from medical/scientific journal articles that I have read.

Conferences: In early December last year the Australian Physiological Society held its annual conference in Adelaide. Australian research on muscle (in both the normal and diseased states) was, as usual, strongly represented at this meeting with lectures and other presentations from Professors David Allen from Sydney University and Angela Dulhunty from the Australian National University, among many others. The highlight for me, however, was the presence of Professor Robert Dirksen from the muscle research group at the University of Iowa, USA, which includes Professor Kevin Campbell, an internationally renowned muscle researcher, who has worked on gene therapy of muscle diseases as well as on basic muscle properties and function. Professor Dirksen had just published some important new research relating to chloride channels and the muscle stiffness condition, myotonia (my own research field) so we had lots to talk about. Interestingly, I had met his colleague, Professor Campbell, for the first time in a private afternoon-tea-time discussion on the same topics in Naples, Italy, in July last year at the 12th International Congress on Neuromuscular Diseases. For the 10th Annual Scientific Meeting of the Asian and Oceanian Myology Center that was held in conjunction with the Brendel Clinical Trust Neurology Meeting in Auckland, New Zealand, in February, this year, I was invited to give a lecture on muscle diseases involving chloride channels. Some 20 other researchers from Australia, New Zealand and several Asian countries also presented their research on topics ranging from mitochondrial myopathies through dystrophinopathies, myasthenias, limb girdle muscular dystrophies, respiratory failure and developments in diagnosis and potential treatments such as exon skipping for neuromuscular disorders. Although no stand-out treatment breakthroughs were announced at these meetings, it continues to astonish me how much we are learning about these diseases and how this knowledge will form the basis for future therapies.

Stem cells: Cell therapy is frequently in the news especially in regard to diseases and traumas that are currently incurable. These include the muscular dystrophies, Parkinson's disease and the spinal cord injuries that result in paraplegia and quadriplegia. Indeed, just in the last few days, Professor Alan Mackay-Sim of Griffith University in Brisbane has been given a People's Choice Award at the Australian Museum's Eureka Prizes for his work on stem cells derived from the inner lining of the nose (olfactory en-sheathing cells) that might prove useful in helping nerve cells to regrow in the spinal cord after it has been damaged. Unfortunately, similar research using stem cells (pericytes) from blood vessel walls has sounded a note of caution. Pericytes actually increase scarring (fibrosis) in the spinal cord and hinder nerve repair. Cell therapy holds a lot of promise for muscle wasting diseases, for heart weakness and for diseases and damage to the nervous system but, so far, in no case has this been converted into a treatment for which there is medical/scientific evidence of amelioration or cure. As I have written previously, if reports of a therapy of this kind sound too good to be true, then they probably are. Sometimes people imagine that there is a medical conspiracy that makes certain treatments available in Russia, China or India or in certain overseas medical clinics but which prevents them from being generally obtainable in Western countries. Common sense, on the other hand, tells us that when real credible medical breakthroughs occur, like growing sheets of skin cells for grafting in burns victims, the techniques are rapidly shared worldwide. And bone marrow transplants for numerous blood and immune system diseases quickly became common everywhere, as soon as reliable methods were worked out. For neuromuscular conditions, however, much research remains to be done in animals with equivalent disorders before cell therapy can be expected to be used successfully in humans.

Gene therapy using viral vectors: To date there is only one published clinical trial of this kind of gene therapy in a muscular dystrophy (LGMD type 2D) where three people were treated. This study from Professor Jerry Mendell's group at the Ohio State University, USA, was reported late last year. In one person the test was unsuccessful due to an immune reaction but, in two cases, the relevant alpha-sarcoglycan gene that was inserted continued to be functional for at least six months. No beneficial effect on muscle function was noted. As for cell therapy, much more analysis of tests in animals with relevant neuromuscular diseases will be necessary ahead of human treatments.

Drug therapy: Although the results of clinical trials of Ataluren (PTC124) in Duchenne muscular dystrophy (DMD) have been disappointing, other drugs for both DMD and other neuromuscular diseases hold considerable promise. The exon-skipping drugs, such as, PRO051 and AVI4658 have both been found to be effective in promoting the production of dystrophin in targeted muscles but not yet in sufficient quantity for a measurable therapeutic effect. Treatment of DMD is now a fertile area of research with many other drugs under development by both small and major pharmaceutical companies. It is interesting that although the pathological basis of myotonic dystrophy is very different from DMD, the strategies that are being applied to its possible drug treatment are the same. For people with spinal muscular atrophy (SMA) it is particularly exciting that the drug RG309 (Repligen Corporation) is in clinical trial having been fast tracked for development by the U.S. Food and Drug Administration. The science behind this drug is based on research in mice with SMA, and tissue cultured cells from SMA patients, initiated several years ago by Professor Arthur Burghes and colleagues of the Ohio State University, USA. It is in the area of drug therapy that translation from animal studies to clinical trials in humans is most advanced. We can expect many more clinical trials of promising drugs in the future.

Finally, I expect to be able to report on the latest research developments from the WMS 2011 Congress in Portugal some time towards the end of the year, after my return.

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