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A Paradigm for Spinal Cord Injury Recovery

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Good morning. It's my privilege, on behalf of, really, all people, I think, who live with spinal cord injury and related conditions to have the opportunity to sincerely thank the New South Wales Government, and in particular the Minister, Frank Sartor, and his team. I know the Minister has had to leave. And especially Kerry Doyle and Dani Redmond at the Office of Science and Medical Research, for their commitment to this day and for the Re:Connections Forum, and, of course, the extremely vital research program being undertaken as a result of the work of Rowena Tucker and the New South Wales Government's Spinal Cord Injury and Conditions Fund. Hearing the Minister's commitment to the long-term future of that program is really heartening and I think we all ought to put our hands together and show our appreciation for it. It really is vital and really heartwarming to have a government continue to show its commitment to something to go the long road with us.

I'd also like to acknowledge and pay tribute to all those here today, and I know there are very many of you. I don't really know if there is anyone left working in the spinal injury units today in New South Wales. But thank you for all coming today, and to all of those who work tirelessly in support of people with spinal cord injury and related conditions. This field is, as you know, demanding and mostly thankless. It's certainly rarely lucrative, and in dealing with us, you're dealing with often difficult circumstances and solutions do not come easily. For committing your lives to improving our lives and our prospects, sincerely we are in your debt.

The issues we'll address today are part of a global pandemic: More than 2 million living with spinal cord injury around this planet. Fortunately we aren't alone in our quest for cures. Ted, Edelle, James, I can't see you all, but thank you very much for coming here, spending your time to share your knowledge and expertise with us. We have followed your careers and been enlightened by your work over a number of years. So thank you very much.

Before we take a look at where we are and how we might move forward with spinal cord injury recovery, I think we also ought recognise the vision and determination of people who are, in large part, responsible for the concept of bringing our notion together in this way. I'm speaking of Bob Carr, Kerry Doyle, Jo Knott, Nick Rowley, Alison Alderton, who is not with us today, and all the people who made *Making Connections* happen in 2003.

The photo on this slide was taken in 2003 and it's 50 years after Sherpa Tensing, Hilary and co, first scaled Everest. I think the 100 or so campers at the base here, illustrate how once what was impossible becomes possible, and then it becomes so much like a walk in the park. I mean, even people who don't have legs are scaling Everest these days. I think where we are today is somewhere back with Hilary and Tensing. We're on the verge of conquering that which was forever unconquerable, but it will be conquered because we possess the collective will to do so. Since 2003, we've made progress, but really nothing can more starkly highlight the urgency and dedication that we must apply to our task than the tragic and premature loss of Reeve. Christopher was a man who, more than anyone, articulated to the world the feelings of people with spinal cord injury, who live every day wishing for a path to recovery. Reeve did capture our attention with his courage and dedication to fighting the war on paralysis, in what, I am sure you'll recognise, was the most difficult of circumstances.

As people with spinal cord injury who cheered him when he fought our battle, we must now honour him by continuing to fight with the same urgency and energy and resilience and determination. The loss of Reeve must not allow us to retreat into old habits, to treat spinal cord injury as incurable malady where, really, tools for

survival are the only prescription. As people with spinal cord injury, we must do much more and take it on, own our responsibility for recovery. We must educate ourselves, we must organise our advocacy and we must be partners with those who seek to help us. We really can't sit back and complain if we don't seek to own the problems and the solutions. We must be advocates of change, moving the mountain of scientific expertise and clinical practice. I know that Reeve, whilst he was here, was engaged in a debate with advocates for the improved care of people with spinal cord injury. Like Reeve, I would acknowledge that we need to commit to the highest possible standards of care, but in my view care and cure are two players on the same team. As I see it, resources and funding must be applied in a balanced way to ensure the very highest levels of recovery are achieved. Improving recovery improves the independence and daily quality of life for which we all strive. It's only improving recovery that reduces the need for care by reducing dependants. In short, care and cures are allied, they are not our enemies.

My focus today, for obvious reasons, is spinal cord injury, and I want to apologise to those of you who are here today dealing with other neurological conditions. I hope you'll find that my thoughts are in some way relevant to your own battle.

But let's now consider how we might improve recovery. Let's, first of all, look at what the collective dedication of neuroscientists has taught us thus far. I'll just summarise it, I can't go through the whole raft of knowledge that we have now and that we've collected in the last 10 or 20 years. But it's clear, significant number of fibres can be regenerated in the damaged cord. It appears that growth and other factors enhance the regenerative effect. We do know, now, some, some would say most, of the tools to mask or block the inhibitory environment that regenerating fibres encounter. We know that certain types of cells, when transplanted into the damaged cord, appear to assist in the capacity of existing fibres to function normally. And we know that we know not enough. We know that there is still much to learn. But the last 10 years has seen animal studies begin, really for the first time in history, to translate into clinical trials. These discoveries are of absolutely enormous credit to many people today here in this room, to the neuroscience field, to neuroscientists and of course to the clinical teams who seek to emulate their studies.

But neuroscientists alone, of course, won't cure paralysis. In exercise rehabilitation, the physios and physiologists have shown us that, just like able-bodied people, you've got to use it or you'll lose it. But using it can be achieved by spinal cord injured people in a number of ways. Inactive muscles, atrophy and the wasting of the muscle not only affect its capacity to function normally, but it impacts the surrounding skin and bone and circulation. Utilising functional electrical stimulation, FES leg cycles and the like, has a range of beneficial impacts. I don't want the scientists to shoot me for using a single case study, but to emphasise my point and from my own experience, I know that regular use of an FES leg cycle reduces and, in fact in my own case, has eliminated my need to take anti-spasmodic drugs like Baclofen. Leg cycling increases my fluid output, which I believe reduces my encounters with UTIs. The leg cycle reduces the swelling in my feet and the movement provides me with some pressure relief and improves my own digestion. These are things I know. Whilst I'm cycling, I can strap my arms into an arm cycle and exercise my aerobic capacity. I credit this exercise with increasing my max oxygen consumption by around 30 per cent, and keeping my lungs and breathing as strong as possible. There is a range of studies that also show other things, like cycling, arresting and reversing the loss of bone density that we all experience. Exercise restores neurotrophin levels and in fact is essential to neuronal health. Muscle loss can be reversed even when exercise is taken up years after injury. The passive ranging of limbs, invoking muscle activity

through eccentric and concentric muscle movements, Pilates, floor-based exercising done regularly and repetitively act in much the same way as they do for everyone else. They improve muscle tone, flexibility, joint range of movement, it stimulates our circulation and our cardiovascular system. But at the end of all that, exercise just makes us feel better and reduces pain. I think we shouldn't forget that there is enormous value in feeling better. It's easy to think that a spinal injury is not life-threatening, but if you realise that the incidents of suicide in spinal cord injury is around five times the average in the population, I think you've got cause to consider it again.

But it's really interesting to me that this exercise research isn't new. As far back as I could find — 1980 — studies were reporting the benefits of exercise in the spinal cord injury population. Yet, really, with a few notable but isolated exceptions, what have we done to instigate ongoing structured exercise programs as a standard of care for people living with paralysis? So, really, exercise is great, but spinal cord injury clinicians and physios working in isolation, they won't cure paralysis.

I'd like to talk about the success of exercise rehabilitation in the United States, in terms of the fact that it's led to the establishment of dedicated SCI recovery regimes. Last time I looked, around a dozen, mostly private, centres had sprung up. I'd like to tell you about one of those centres. As I said, there is a few now, but I've had first-hand experience of this one. It's called Project Walk and it's in San Diego in California. Project Walk presently has more than 60 clients in various phases of their program. It's an extremely labour-intensive program. About 90 per cent of the time you're on the chair, out of your chair, on the floor or in a machine being worked by one or two of their trainers. People with spinal cord injury are going there three times a week, sometimes more, for three hour sessions to learn how to improve their functional recovery. For a lucky few, that recovery has meant rolling in one day and, maybe two or three years later, walking out. For everyone there, though, recovery is regarded as a life-long process. The key difference the recovery strategy you'll be offered by Project Walk, and I think this is the real point of difference to my knowledge of traditional SCI rehabilitation, is that their approach is all about progressive relearning. They call the five phases of recovery and you don't advance to the next phase unless you pass go.

Pretty briefly, those phases are what they call reactivation, as in, kind of, knock knock, who's there. They're trying to activate dormant muscles. In phase 2 they work on development and stabilisation, and that's about gaining core trunk control. Progress there to stage 3, and it's about strength, and of course that's pretty self-explanatory. Stage 4 moves to function and coordination, and this is where the program really starts to heat up and you start to see progress. If it gets past stage 4, you're into stage 5, they call that the "Gate Phase", and pretty much past stage 5 and you're walking again. What I want to highlight here is that their approach is structured, that it recognises that recovery takes years. It's not about jumping on a body weight support at treadmill training, effectively phase 5 of the program, and expecting improvement in overground walking speed in a matter of months if your body hasn't had the capacity, through achieving all the goals of phase 1 and 2 and so on. Edelle, I'm not trying to knock treadmill training, it's a vital component, particularly for people with incomplete injuries. That's been shown: It's profoundly beneficial. Besides, in the last 11 years, frankly, treadmill training is about the most fun I've had with my clothes on.

But before the sceptics start to jump on me, I want to point out that Project Walk is promoting recovery, it's not promising a cure. These guys admit that the longer you're injured, the tougher recovery is, and they have the greatest success treating injuries as soon as possible. But the point here is that they're ensuring recovery is

optimised, and that's something I think we're simply not doing. They'll take on pretty much any determined, appropriately healthy individual. They're not just picking the cherries, as some have suggested. I think it's really in the results, but this where the shift is beginning. I want to point out that, to their credit, Project Walk is undertaking a collaborative study with the Reeve Urban Institute to scientifically evaluate their methods and outcomes. Along with Reeve Urban, these guys are working the Geren. They're a California-based biotech [company] who are planning stem cell therapy for acute spinal cord injuries. So I'll let you join the dots, but I think this is immensely positive progress.

I think program design is really vital. We'll talk about it a little bit later, but we must think about our recovery expectations in trial designs. One of my real concerns is that even with all this evidence, we're still bagging exercise as a means to maximising recovery. Isolated studies have been held, on occasion by some, to prove that treadmill training has no benefit. I think the facts are that treadmill training, in isolation, as with all recovery strategies conducted in isolation, has less beneficial effect than if they're conducted as part of a strategic recovery program. But guess what? Exercise recovery centres in isolation, they won't cure paralysis.

Let's now consider what we've learnt with human trials and experimental therapies that have been reported so far. First, there is absolutely no shortage of willing participants. Approximately 1,000 people around the world now, maybe more, have undergone the knife in the quest for recovery. The ground-breaking safety trial in Brisbane dealt with 600 inquiries for six eventual places. Most trials and therapies have a long waiting list and there is a very good reason for that. I want to ask all research and clinical people to understand that people with spinal cord injury have had their body disconnected from their brain, but not their brain disconnected from reality. We understand that for the most part there are risks in these trials and that there is a limited likelihood of success even. But it's paternalistic to save us from ourselves by opting to do nothing, when the evidence demands otherwise. We who have spinal cord injury back the courage and the dedication and the compassion of those who seek to drive our recovery. We back this by showing our willingness to participate in trials, in the hope that we move science forward. But to paraphrase Christopher Reeve, we must urgently go forward.

Animal studies, of course, must continue, but they must break new ground and advance the sum knowledge. We must also have the mechanism to test successes in the lab in well-designed human trials. So much promising basic research seems to disappear into a black hole. There is a disconnect there somewhere that we must overcome. Secondly, trials have shown us so far that we can transplant cells into the damaged cord safely, if we do it to world's best practice standards. Amongst the 1,000 patients reported, mortality and complications are low. As recently reported by the Brisbane group, after one year there were no adverse reactions. Third, from more than a dozen different experimental therapies and trials, what do we generally see? We're seeing a fairly limited improvement in ASIA motor score, but a generally much greater improvement in sensory score. Why? I suppose there are a number of hypotheses. One is clearly that what is being done doesn't sufficiently regenerate lost fibres or provide sufficient support for the remaining fibres. On one view, the lack of that more significant improvement could, in part, be due to the failure or the attempts to re-innovate long-dormant muscle groups. But despite these successes, the trialling of cellular therapies remains controversial. The dictum "Do no harm" can be a convenient doorman in the face of progress. As I've highlighted, though, the evidence suggests that the trials to date have met the "do no harm" criteria. We therefore need to move, as Chris Reeve would say and as Frank Sartor would say, beyond the shallow end of

the pool and swim in the ocean. These first generation therapies ought to give us confidence to start introducing new trials and new approaches that have been successful in animal models.

But, really, what have the first generation of trials meant for what we're doing clinically? I don't know if it's a lack of resources or a lack of belief, or overloaded health campuses, or simply inertia associated with being taught there is no recovery in spinal cord injury. We're still telling 15 and 20-year-old kids, "You'll never walk again." We're sending them off into what I'd call the wheelchair wilderness. In my view, if we want to meet our duty of care and implement the knowledge we have today and commit ourselves to doing the very best we can, we can develop and implement a prescription for a much greater recovery. I think what we've got today is a jigsaw puzzle, and although we don't have all the pieces of the puzzle, we have a great many of them. What we must do is begin to bring these pieces together, and in so doing make an imperfect picture, but a picture that will become clearer as every piece is added. It will be a far superior guide in future successes and trying to find the missing pieces. We must follow the example of leaders and find the time and energy to develop mechanisms to collaborate across disciplines and truly harness the sum total of our knowledge.

But how can we do this and where do we start? Right up at the top is a change of attitude and mind-set in the clinical environment. Why is it that we consign young people to 40 years or more locked up with paralysis and we hardly bat an eyelid! How does this compare with other ailments? If I had kidney disease the prescription would be, "First we're going to keep you as healthy as possible with regular dialysis, so this will become a big part of your life. You'll be here three times week for at least four hours, and you'll be doing this until we have a cure for you. Right now that's a compatible kidney donor, which we don't have. So get used to seeing us for the next few years because your health depends on it. Yes, we recognise that it will cost around 60 grand a year, but that's what we're going to spend because we live in a civil society." Some of you will tell me, "But kidney disease is life-threatening and spinal cord injury isn't," and in one sense that's true. But I think the strange thing is that because we've worked out how to survive life in a wheelchair, it's become kind of acceptable, like wheelchairs are the cure for spinal cord injury. It's like we're on permanent dialysis. The urgency for cures, in a clinical sense, has been lost. In 2006 that's just not acceptable.

If I compare the treatment of kidney disease with spinal cord injury, we ought to be providing an intensive exercise recovery facility for every person that firstly allows them to maintain best possible health. Secondly, it maximises the recovery of function with a long-term, structured, intensive program. Thirdly, it prepares us physically to respond to our donor kidney, to respond to a cure. But I don't want you telling me there isn't enough funding because we're talking about fundamental treatment, and funding is a function of making a case based on the available evidence, and the available evidence abounds. Nine years ago we were told that funding neurotrauma research in Australia through speeding camera fines was impossible. Today, because of good advocacy and governments that listen and seek to solve real problems, we have funds in three states investing more than \$5 million per annum in neurotrauma research. Recovery centres for spinal cord injury are a matter of advocacy; they're making the case based on the evidence. So top of the list is belief. Second, we must provide the environment for recovery. As I've talked about, that's recovery centres where the mantra is about working hard and maximising functional return. Third is something I call recovery by design. What do I mean by recovery by design? Well sometimes I think, in designing clinical trials, we're expecting too much and not ensuring all the elements are there to succeed. For example, not implementing recovery training as part of a trial. I

think the way we think about trials is generally to answer a single scientific question by eliminating all the variables and focussing on one or two wholly outcome measures. This is all very well for the scientific credibility in the conduct of the trial, but the design places patient recovery as secondary. It's just possible, as much as I love and respect neuroscientists, that good science is standing in the way of best recovery. I think we can address this problem, in part, by implementing long-term exercise recovery as part of a standard of care.

So here is the challenge: All of this effort has brought us towards cures, and it's brought us to this point, and in so many ways we can be thankful for the progress and dedication of all of you here. But we must now provide opportunity and belief for people with spinal cord injury to commit themselves to the hard work and retraining of health and recovery. That's by taking a whole-of-life approach to spinal cord injury, and that starts the first day somebody is injured. We must address all the pieces of the puzzle every time we think about recovery. We must all educate ourselves about all the pieces of the puzzle, but we also take our piece of the puzzle and fit it to the rest. We must provide trial participants with the capacity to recover, and provide all the elements in trial design to facilitate recovery. We must believe that if we apply ourselves and address the puzzle strategically together, as a whole, instead of in isolation, that the puzzle can be solved.

We can all be thankful for Chris and Dana. They changed the way we think about spinal cord injury. When I remember them, I do like to think they made it. Thanks for listening. I wish us all a day of enlightenment and discovery.