

## *Dare to Dream*

Corporate Event, Helsinki, Finland

I used to be a metallurgist, trained in the science and art of metals. Metallurgy is an old profession, not the oldest one you understand, but old nevertheless. It is the personification of old age, for as we get older, we see silver in the hair, gold in the teeth, iron in the soul and lead in the feet.

Then I became a medical engineer and biomaterials scientist. There were many changes, especially adding to that list, with platinum in the nerves, titanium in the bones, Dacron in the arteries and silicones in the breasts.

But now I am a Tissue Engineer, one of the youngest of professions, which is the personification of youthfulness, although not of childishness. As we get younger, we return to the age of genes, now so fashionable and transferable, we revert to growth factors and hormones, and to progeny, and we even re-enter the womb, with embryos and their precious and precocious stem cells.

I am, of course, neither old or nor young. Certainly not too old or too young, just the right age, in fact, to dream, to dream of the

past and to dream of the future, which is why I am here this evening. To dare to dream is the theme. The theme of this evening and the theme of my address to you.

It was only when I was well into the preparation of this talk did I realise, however, that Dare to Dream is the right theme for the evening, but the wrong theme for me, It should not be Dare to Dream but Dream to Dare that I should discuss.

Let me explain. To dream is to imagine, to dare is to take a risk. I shouldn't be here telling you to dare to imagine, we can all do that with impunity since there are no consequences, but I should be enticing you to imagine taking a risk.

The assessment and management of risk sounds like a boring bureaucratic process, and indeed it can be, but handled right it can be exciting and exhilarating. Michael Schumacher, or perhaps I should use Kimi Raikkonen as the example here in Helsinki, undertakes risk assessment and management all the time. He imagines what he has to do, assesses the risk of the manoeuvre, and the executes it when his judgement tells him to go for it. He also assesses benefit, of course, not an inconsiderable point at €30 million per year. I am reminded of Dickens' Mr McCawber in this situation; duly paraphrasing and

bringing up to date - benefit 20 points, risk 19 points, go for it; benefit 20 points, risk 21 points, keep on dreaming.

So what has this got to do with orthopaedic surgeons and orthopaedic manufacturers. Quite a lot actually. No one can deny that, given a little contamination and osteolysis here and there, and allowing for a little surgical error here and there, we have a pretty successful patient-oriented industry and clinical service. But, as the famous British military general Lord Slim once said, All that doth not advance must retrograde – if you do not move forward then you will go backwards, or at least others will go forward faster than you.

Two of the most defining meetings in my professional life are relevant here, and it is probably significant that they both took place with men who are now dead. The first was with John Charnley, he then in the later years of his professional life, myself in my formative years. And did he get it wrong before he got it right. We all know that he used PTFE in his first patients, with monumentally disastrous results, but the responsibility for which he took fairly and squarely on his shoulders, and then used his own arms as the test site for the new polyethylene, subsequently to become one of the more successful of all biomaterials, but then bizarrely to become pilloried just as was PTFE. I regret that with polyethylene we

did not dream as well as we might and did not remember the lessons of previous dreams, but those are different stories. The point is that to encounter a visionary at an early stage in one's career is profound.

The second encounter, mostly appropriately on Giant's Causeway in County Antrim, Northern Ireland, was equally profound, as this was with Christian Barnard. And did he get in right before he got it wrong. I met him not long before he died last year and to listen to someone who had been a very successful dreamer was also profound. although of course his dreams were a little more expansive than his surgery.

Two clinical entrepreneurs, of quite different style and accent. They were both prepared to put their risks into practice and the world has been a better place since. Of course they had no regulators, accountants or lawyers peering over their shoulders, but lets put that on one side for the moment, since these are subjects of nightmares and not dreams.

So where to we go today, tomorrow or next year in our dreams.

Ladies and Gentlemen, you have a big challenge. Today, you, Mr Manufacturer, have a product. A product that follows all of the rules: with flow charts and design reviews, IP to protect and

metal surfaces to polish, boxes to sterilise, glossy brochures to market.

But how far can you go with this in the Reconstruction of the Body' You, Mr Surgeon, know all too well that the tissues you remove from your patient to make way for today's shining orthopaedic device doesn't even remotely look like or feel like metals, plastics and ceramics that constitute that device. Is it logical to take out that living ,viable, cellular, hydrated, anisotropic, heterogeneous, dynamically responsive, bloody tissue and replace it with the dead, anhydrous, acellular man made stuff, which can sustain mechanical forces but not life. It has been logical, of course, because we had no alternative, and Mr Manufacturer and Mr Surgeon collectively are to be congratulated by millions of patients who have had their pain relieved and mobility restored.

But know, because some people have been dreaming, we do have an alternative. We have a means to regenerate the materials of bone, cartilage, tendon and ligament, at least experimentally. Not yet the joints, the intervertebral discs, the whole anatomic bones, but that will happen, give or take a dream, or even a prayer.

Your problem, Mr Manufacturer, is that you can no longer have a product in the conventional sense. You will struggle with business models and pricing-reimbursement structures, and may struggle to make any money out of orthopaedic tissue engineering.

Because tissue engineering involves, by my definition the persuasion of the body to heal itself. Since as adults we do not innately have that ability, we have to re-acquire it, hence the reversion to the womb and the embryo and neonate, piled high with growth factors, switched on genes and appropriate receptors. Can you manufacture, as a saleable commodity, a piece of tissue. Can you sell to a patient a piece of his own tissue, even if you have taken part, at great expense, in the persuasion process. Can you protect the Intellectual Property of nerve tissue when that property is someone else's intellect. Can you take the risks of gene transfection now we know the fatal consequences of mistakes.

Of course you can, but this requires powerful dreams. The delivery of these dreams is what orthopaedics is about in the future. Many companies have recently failed catastrophically in this quest because of the lack of business models and regulatory pathways, the solutions to which need strong actions as well as dreams. There is only one way forward. Companies with

corporate strength and revenues derived from existing successful products have to work with the tissue engineers and entrepreneurial surgeons in adding regenerative medicine systems to the portfolio and watch them take over and expand the possibilities for the treatment of diseases and injuries of the musculoskeletal system.

There's a powerful dream. I wonder who dares.

You are aware that I work in Liverpool. You also probably know that one of Liverpool's most famous sons was John Lennon. Remember Imagine. You may say I'm a dreamer, but I'm not the only one, I hope some day you will join us, and the world will live as one.

Well certainly I'm not the only one dreaming in this area and there are already others dreaming of this regenerative medicine approach. Dream to dare is the only way forward.