

‘Pioneer’ Paarl neuro sets alarm bells ringing



Dr Adriaan Liebenberg.

Photos courtesy of Die Burger.

A Paarl neurosurgeon claims to be on his way to a world first in repairing spinal cord injuries using therapeutic stem cell cloning, having removed 35 mm from the spinal cord of a quadriplegic man and injecting a ‘special’ matrix of the cells into the defect.

Dr Adriaan Liebenberg asserts that the stem cell work via his surgery is responsible for enhanced arm strength and the return of (delayed) sensation to the hands and feet of 32-year-old Tommie Prins, of Milnerton, paralysed in a sand-bar diving accident six years ago. However, two of the country’s top stem cell experts, regulatory authorities and university ethicists expressed deep alarm. Their concerns are that neither Liebenberg nor his partner, Dr Gert Jordaan (who has a PhD in Agriculture), have obtained ethical approval, subjected their work to peer review, published any of it, or secured Medicines Control Council (MCC) go-ahead. Jordaan earned a suspended jail sentence two years ago for doing spine-severing work on monkeys without the correct permit, though he did obtain Health Ministry approval for his research via the then incumbent, Barbara Hogan, thus bypassing other regulatory structures. The Health Professions Council of South Africa (HPCSA)’s Human Rights and Ethics Committee later over-rode Hogan’s decision, citing Jordaan’s connection with a medical doctor (Liebenberg), to justify its intervention. Dr Joey Gouws, Director of the

MCC’s Inspectorate and Law Enforcement, told *Izindaba* that no clinical trial using stem cell therapy has been approved by her body. An HPCSA spokesperson added that any unproven or ‘secret’ remedy was unacceptable for use in the treatment of a patient.

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Liebenberg showed newspaper journalists a 2008 HPCSA letter addressed to Jordaan and one of Liebenberg’s patients (one Mr Burger), purporting to give conditional approval for their work, plus the approval letter from Hogan. However, the HPCSA said it had followed up its own letter the following year, laying down specific conditions and asking several probing questions – to which it never received answers. Professor Ames Dhai, head of Bio-ethics at the University of the Witwatersrand, and member of the eponymous HPCSA committee at the time, confirmed vetting Liebenberg’s application and over-riding Hogan’s approval. ‘Our view was we could not support something like

that,’ she said, adding that ‘without robust research and full-phase clinical trials it was extremely difficult to say whether outcomes were harmful or beneficial’.

Absence of systematic, scientific scrutiny – Dhai

‘You cannot use un-researched interventions in the name of therapy. You can’t hide behind therapy. It must stand up to systematic, scientific scrutiny and we don’t have that yet.’ She believes if it can be shown that Jordaan and Liebenberg are using therapy without complying with legislation or approval from government structures, they are acting illegally. Professor Michael Pepper, Director of the Institute for Cellular and Molecular Medicine at the University of Pretoria and Professor Susan Kidson, Deputy Dean of Medicine at the University of Cape Town (and a widely acknowledged cell and developmental biologist), agreed that there had so far been no approval in South Africa (SA) for such stem cell research. Added Pepper: ‘I can almost guarantee that this is not an accepted form of therapy’. To his knowledge the procedure had never been done in SA before. He conceded that were its success proven, it would be a ‘major breakthrough’ globally, but stressed that nobody anywhere in the world had ‘even got close to repair yet’. He said it was ‘entirely possible’ that the spinal cord injury (between C4/C5) was partial and had begun recovering spontaneously, with the stem cell addition purely co-incidental.

Tommie Prins lost all feeling from about two fingers above his nipples to his toes in the accident. Nearly three years later, after some dedicated physiotherapy, he began to regain movement in his right arm. Pepper says this strongly suggests that the spinal cord laceration was incomplete. Liebenberg performed two surgical procedures, the first on 10 October last year in which he removed 35 mm of Prins’ spine between C3 and C5, injecting cells derived by somatic cell nuclear transfer (SCNT), also known as therapeutic cloning, into the defect. SCNT uses a donor egg and skin fibroblasts from the patient which are considered to be autologous embryonic stem cells. The second surgical procedure, on 24 October, was to augment the mix and fix a residual fluid leak from the spinal cord. Describing the first six-hour procedure, Liebenberg said scar tissue



Tommie Prins credits Liebenberg for the return of sensation and movement to his limbs.

that separated the two ends of the spinal cord was removed while electrophysiological monitoring by a neurophysiologist was done to limit damage to the functioning sections of the spinal cord. After the scar was completely removed, a special matrix containing autologous embryonic stem cells and growth factors were sealed in the defect. He said both procedures were carried out without any complications and the patient initially had no decrease in function. Since then there had been improvement in the function of both arms, in existing muscle function and strength, and new muscle movement in three muscle groups on the right and two muscle groups on the left. 'The patient has return of partial sensation throughout the body. This represents a staggering early response. The interim and final clinical results will be reported on by an independent clinician,' Liebenberg added.

He told an Afrikaans daily morning newspaper which confronted him with the experts' objections and their risk warnings: 'We're still going to do five to ten patients before we broadcast it in a scientific forum. Just now you get some clot in India copying us.'

Big gaps in legislation a major issue – Pepper

Pepper said the controversy highlighted the dangers related to both the procedure itself and the unpredictable behaviour of

the stem cells used at the site of the injury, warning that developmentally immature cells (embryonic or pluripotent) could go on to form tumours. The procedure risked infection, pain and further loss of sensation/function. If the patient's lesion was incomplete, 'one has to question the justification for complete removal of 35 mm of the spinal cord'. Another issue it raised was the fragmentary, conflicting and in some cases 'frankly incorrect' definitions governing such procedures in the existing legislation. This 'legislative vacuum' created opportunities for the development of unethical and unregulated practices in the SA stem cell field. While former Health Minister Barbara Hogan had authorised the initial research in October 2008, this in no way exempted the researchers from obtaining clearance from an ethics committee or from registering the procedure with the MCC, or obtaining peer review.

Pepper said he was not out to halt the progress of science or deny patients any potential benefits, but rather to protect patients against foreseeable problems and to protect the doctors involved against complications 'unforeseen under normal/reasonable circumstances in a society which is becoming increasingly litigious'. (Prins signed indemnity for the procedure and has undertaken to give Liebenberg exclusive media rights should the therapy work.) Professor Kidson said that to date there had been no successful stem cell derivations from embryos obtained by SCNT (therapeutic cloning) and 'most certainly no such cloned cells have been used for any therapeutic purpose'. Cell derivation not carefully quality-assured would create too great a risk of rogue cells (teratogenic, aberrant differentiation, for example into bone or muscle cells), she warned. The only stem cell line purportedly derived by human nuclear transfer had subsequently been shown to originate by parthenogenesis rather than by reprogramming from the somatic nucleus. She said that as far as she had been able to ascertain, nobody had ever tried to introduce such cells into humans before.

Mrs Marzelle Haskins, chief of PharmaEthics (one of only two bodies that can approve private clinical trials), said that while she had previously approved 'normal' neurological clinical trials of Liebenberg's ('Parkinson's and things like that'), she had never approved stem cell research. She declared herself 'very nervous' of stem cell research and recalled an e-mail several years

ago querying whether it was an approved therapeutic method, which she had forwarded to Professor Dhai. 'It might have been Liebenberg I cannot say for certain now,' she added.

Wits ethicist Professor Ames Dhai: 'You cannot use un-researched interventions in the name of therapy. You can't hide behind therapy. It must stand up to systematic, scientific scrutiny and we don't have that yet.'

Lab 'a tourist attraction waiting to happen' – Liebenberg

Asked for an interview, Liebenberg said he was 'not at the point of publishing anything in a medical journal' and referred *Izindaba* to the Melomed Hospital group for 'the news elements'. He told an Afrikaans daily morning newspaper which confronted him with the experts' objections and their risk warnings: 'We're still going to do five to ten patients before we broadcast it in a scientific forum. Just now you get some clot in India copying us.' He refused to disclose where the stem cell laboratory was, adding that 'in four months or so we'll surely be taking tour groups through it'. An e-mailed indemnity form sent to Tommie Prins reads: 'I understand that the procedure I am (*sic*) consenting to is an experimental procedure and that there is no clinical data to predict whether this procedure will be harmful or beneficial. I document that I will have no claim arising from this procedure or any complications thereof against Dr Liebenberg, members of his team, or Melomed Hospital Holdings'. A detailed informed-consent paragraph follows. Melomed Hospital Holdings said they accepted the documentation provided to them by Dr Liebenberg 'in good faith, deliberated the ethical considerations therein and on that basis allowed him to perform this ground-breaking stem cell transplant operation at our Melomed Bellville Private Hospital'. The hospital group said it also received various permissions from a 'wide range of authorities' – all of which had said there was no reason why the doctor could not proceed.

Both Kidson and Pepper warned that the experimental procedure could do SA's international scientific reputation great harm.

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