Active Parents, Parental Activism: The Adipose Stem Cell In Vitro Lab Study

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In June 2005, my wife and son and I were preparing for our first trip to the United Kingdom, and everything was in order: tickets, visas, foreign exchange. Ten days before our trip, my wife and 4-year-old son travelled to Chandigarh, where both of our parents live, to say goodbye to her parents as well as do some last-minute shopping. I stayed in Delhi to work and save up leave for our trip. Excitement was high.

However, while my wife and son were in Chandigarh, my father-in-law called. My father-in-law is a paediatric doctor, and my mother-in-law is a general practitioner. My son had been diagnosed with some sort of muscle-wasting disease. 'Something doesn't look right', he said. 'It's his calves. They look much bigger than those of a normal child. It's called hypertrophy'.

At that exact moment, I knew our trip abroad would go for a six. After the initial disappointment of cancelling our holiday and the tumult of emotions when I realized my son had a serious 'condition', I began to try

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to put the pieces together. The 'condition', as it turned out, was something I'd never heard of, Duchenne muscular dystrophy (DMD). This rare disease is an X-linked chromosome and is autosomal recessive, thus affecting boys at least 99 per cent of the time. For some the life span is 17 years, others 20, and others about 25. One can't be sure. Thus began my initial foray and subsequent deep immersion into a new world of medicine and treatments that I continue to this day. In that initial 4 months, I studied DMD until I understood it as thoroughly as a layman could and found it is a rare, genetic muscle-wasting condition that affects only boys and can lead to early death.

So here I was, a conventional man with a regular middle-class life faced with a cataclysmic challenge concerning my own son. No one in my family had really had a medical problem, certainly not one this big. I was a sensitive, emotionally vulnerable person at the time and was going under with all the tension and strain as well as the painful reality my son may not live that long. I was all but a nervous wreck. The blow turned all my thoughts, ideologies, and presuppositions 180 degrees.

While researching DMD, I still had to work and get on with my life. Every spare minute I was at my computer, deep into the internet, researching, exploring, and networking. It was then that I chanced upon the science of stem cells, which I hadn't heard about until then. It was the first time in my life I had had to make a very serious decision. I had been reading everything possible on stem cells, but I still needed to know they worked. Should I subject my son, a mere child, to a relatively less understood line of treatment? All I knew was that conventional biomedical avenues had nothing to offer. I started talking extensively with other DMD parents, but none had chosen the stem cell option. And then there was a big consideration—the expenses. It was not a decision we could make with a snap of our fingers, especially while we were groping in the dark about DMD and its response to stem cell therapy.

The internet was my life jacket. I am not very technically savvy, but I spent most of my non-office hours scouring the net and connecting with people all over the world who had anything to do with stem cells: researchers, doctors, clinicians, and parents. But when I asked parents if they were doing research on stem cells, they would say they thought the cure for

DMD was still decades away or maybe another 5 years. However, I began to get a hang of stem cell science and to talk to many DMD parents. Almost every city has a DMD support group: Delhi had one and so did Mumbai. I joined the Delhi group and attended a few meetings, but apart from drinking tea and chatting, there was not much action. During these meetings, people would share their children's experiences. If someone said, 'My son fell down and broke his arm', I would become alarmed and depressed. I began to pray regularly, a certain kind of prayer I did every day without fail. I felt this would see me through; after all, the doctors were shutting the doors in our faces. Doctors are not gods, something will happen, a miracle, I would tell myself. These were doctors who were waiting for research journals to land on their tables. Their daily practices kept them busy and padded their wallets. So I stopped going to doctors. But I needed to blame someone for this calamity. So I began to blame God, and believe it or not, that helped me. I would chat with God regularly and spent a lot of time praying.

Four years went by. By now I'd come to the conclusion that I could not wait for things to happen by themselves. I had to gather myself and *do* something. My son's condition was deteriorating; I didn't have the luxury of time. Until he was 8, he was like a normal kid, running around and playing with friends. In DMD, there is what you call a threshold level. I thought he would walk until he was about 13 or 14, but in 2010, when he was 9 and a half, he suddenly announced he couldn't walk. That day I was badly hit, yet again.

I said to myself that praying alone wouldn't solve the issue. I had to take very practical steps. I would buy time if that's was what I needed to do. I got in touch with a researcher who had recently moved to Hyderabad, South India, from Canada, where she had been doing stem cell research. I chatted with her for nearly an hour, and it was a wonderful conversation, just like you would want a researcher or doctor to react towards you. I had by now become a sort of lay expert in DMD and stem cells. I shared a lot of my information with her and she was happy to be informed about what was happening globally regarding stem cells, in particular, for DMD. Around this time, I connected with the Mumbai DMD group, which agreed with my ideas on stem cells, and I had become the 'action man' willing to go the extra mile.

I decided that I would put my son through an experimental clinical trial. It was risky and something that the insurance companies wouldn't touch because it is a genetic disorder with unproven therapies. Unlike other trials, we would need to pay the high cost. I connected four or five fathers from the DMD group with the researcher in Hyderabad, and we told her we would like to be partners in the trial. I couldn't have done it alone. We had also found a paper written by a Brazilian researcher on positive results from adipose stem cell research, and we began to communicate with her, receiving positive feedback on her research. Our goal was to use this research and get an in-vitro cell culture done in the lab. However, even if one lab completes a successful in-vitro study, this does not mean the same can be done successfully elsewhere. The same has to be achieved by another lab, which tries to replicate the study and take it further. Just because it has been done successfully in *some* lab doesn't mean one can start injecting people with it. The same study has to be replicated in *one's own* lab as well.

Although the researcher in Hyderabad was concerned about the cost and the experiment's uncertainties, she agreed to do it with adipose (fat tissue) from a donor who had had liposuction. No animal models were used, because the researcher in Brazil had already done so and to good effect. We spoke to several institutes in India already doing adipose infusions and becoming convinced about their safety. We DMD fathers funded the study, which took 9–12 months, showing good results. The studies showed traces of dystrophin, the protein missing in DMD. We made the brave decision to use adipose-derived mesenchymal stem cell infusions for 14 of our children.

Based on our consultations with the Brazilian researcher, we initially wanted to inject 200 million cells. However, people worldwide were giving 50 million. Then there was a line of treatment that, depending upon the patient's weight per kg, you could give 2 million per kg. So if the child is 40 kg, then you multiply that weight by 2, meaning you would give him 80 million cells. So this was a thought, a scientific thought maybe, but it had no basis as far as I was concerned. Because of our research and discussions with doctors, we felt more cells needed to be given within a specific period of time. Thus, keeping safety in mind, the first infusion was 200 million per child, but we divided those 200 million

over 4 infusions or 50 million per week for 4 weeks. Then we came across parents with children who had different conditions, and they were giving 80 million in one shot, and we deduced that if 80 million didn't have adverse reactions, then we could split the 200 million into 100 and 100. Thus, the second infusion was after seven to 8 months with 250 million cells, 125 each. These two infusions went very well, so we stuck to that. About 20–30 per cent of cells are flushed from the body, so cells need to be replenished and infused on a regular basis.

We parents did most of the research and determined the protocols, such as how many cells we wanted and the number of infusions. From our research, we also understood that the blood circulating inside the body at the time the veins are infused is circulating at a temperature of around four degrees centigrade. That inside temperature is what is known, technically, as the hypoxic effect. We asked the researcher in Hyderabad to culture the cells in what is known as a hypoxic chamber so that the cells would be cultured in the same atmosphere found inside the body. When the cells are taken from one atmosphere and injected into a similar one, the cells will have fewer adjustments and the genes won't be shocked.

Of the 14 children who went through the same process, the younger ones showed marked improvement. My son had two rounds of infusions over a 7- to 8-month period, and since he was in a wheelchair, it was difficult to gauge the level of improvement. Until about the age of 9, he seemed like a regular kid. But if one observed him carefully, one could see that he walked on his toes, had an uneven walking pace, and had to put in major efforts to climb stairs. After the treatments, his progress was slow but stable. In other words, whatever was going in was fighting the disease. What I was doing, in effect, was buying time until something better came along.

Meanwhile, our support systems were our wives, who were and are extremely supportive while we did the research and treatment procedures. My wife is a rock star: she handles things much better than I do. Being a daughter of doctors, she was constantly pushing me to do medical things. I don't know where she gets her energy. In all those gruelling years, she never went under, and the last 12 years wouldn't have been possible without her. She was a mountain of strength to me when I was emotionally wrung out. My son is a super star: he is also very positive, has adjusted to

his situation, attends school in his wheelchair, and behaves like any normal child. For our part, we have never made him feel that he lacks anything. For us he is perfect.

The usual line from doctors is, 'We have nothing on it right now, we'll see when it happens'. For them it's business as usual. No one tells you anything. I had to educate myself from scratch. If I go to a doctor and say to him, 'Doctor, we want to try stem cell treatment for DMD, he will say, No, don't do it. There is no cure. There is no breakthrough data as of now'. Maybe they were right from their own perspective, but I was looking for hope, involvement, and empathy. But just because he says it, why should I not try it? Does it mean we should pooh pooh the experiments that are happening now? I don't want to go to doctors anymore. More than anything else, I face so much apathy and opposition.

Because the All India Institute of Medical Science (AIIMS) is a government hospital and not looking for profits, they are not as concerned with being leaders in research and wanting to achieve new objectives in this science. They are bogged down with bureaucracy and the typical workings of an Indian government agency; it takes forever to take any decisions. The main advantage of working with them is the possibility of a clinical trial, which could be an effective treatment. I got in touch with AIIMS in 2006, and the head of the stem cell department and the head of paediatrics know me by name. I told my DMD group I was talking to AIIMS about the adipose method, but I was very frustrated by the lack of progress. Initially the group was excited because it was free of cost and AIIMS has the best technology in India. But after 2 years of not making any progress, I am not depending on them anymore. One of the dads in the group is now actively in communication with them, but if they agreed to take this forward, I would rather go with them than anyone else.

For the longest time, I have been interacting with the Indian Council of Medical Research. When I was first trying to understand stem cell science, they were the only ones who could provide information about bona fide stem cell researchers. But when I started asking how they were expediting progress in stem cell research, it was a dead end. They are just sitting on their official seats to give permission for this and that; for example, if someone wanted to put up a stem cell lab, they would okay it. When I was in contact with them, all they would do was criticise people doing

stem cell therapies, as if it is their job; for instance, they simply dismiss it, saying stem cells are just placebos. If I asked them to address the problem, they would say they were not the regulators. Who were the regulators? Nobody seemed to have an idea!

I may be harsh when it comes to dealing with the doctors and the government agencies. I do understand their helplessness, as they too are dependent upon our system, which is very frustrating on all levels.

These treatments are expensive. The cells, which now come from Hyderabad, are expensive, and then, of course, there are the hospital charges and the preparations before the infusion therapy, such as blood tests and so forth. Each infusion costs me Rs. 3.5 lakhs once every 6 months, which is a lot of money. Since it's still in an experimental stage, we are getting the treatment at cost, but costs may go up dramatically once stem cells become an accepted line of treatment in a hospital or clinic. Even now, the hospitals in Delhi are making money out of me because they are aware of the situation and helplessness of people like me who are desperate and will try an unproven therapy.

People have been asking me, jocularly, why adipose should be so expensive. Aren't people dying to lose their fat? But we wanted it to be from a woman between the ages of 16 and 21, and many at that age are not fat—at least, they aren't coming for liposuction, and if they don't, it's also because it's expensive. The Hyderabad researcher does manage to find donors. Although those donors don't really mind what use it's put to, we inform them for ethical reasons. In fact, I would say that it's ethical for the plastic surgeon to donate this, especially, since we are not making any profit out of it and are using it on our own kids, but then we are not in a position to bargain.

In Delhi, where I live, the response towards this line of treatment is lukewarm. Many of the DMD parents in this city have a block against trying something new, and when I tell them about the money involved, they think I'm making a sales pitch. Thus, I've stopped trying to discuss or debate it with them, and I just give them the information if they need it. Initially, my in-laws, who are in their 70s and pretty traditional, had no clue about stem cells even though both of them are doctors. But now the entire family—including my parents and my brother, who have supported me emotionally and financially—is proud of me. I am blessed to

have their unstinting support and never could have done this without their help. I thank each and every one of them.

I'm regularly asked how all this has affected me. I am much calmer and more patient, and I pick my battles, focussing only on things that matter. People say I've become more balanced. If I feel down or low, I now have a built-in mechanism to come out of it. I get up, dust myself off, and walk on. When my son could no longer walk, one of the most difficult things for us was his social isolation. Being unable to run and play with his friends meant he lost some of them. We thought of moving from where we lived, but he would have lost the few friends he had. And we too were getting socially isolated because our son was so dependent on us. Many of our old friends had stopped visiting us because we were caught up in our new life. But all in all, this experience has made me a better person.

People sometimes see me as an 'expert' or a social activist since I have informed myself so thoroughly about stem cell research and practice, even more than normal bio-medical doctors. The fact is that I can offer my son more than what all these so-called researchers can. I began doing this only for the love of my son, and if others benefitted, then so be it. I don't even want to go to any conference or academic gathering. In India, the reality is that nobody cares about a disabled child, and even if I were to narrate my story, nobody cares. It is ironic that India is a spiritual country but it has so much apathy. For instance, in Geneva or the UAE, some of the countries we have visited, people stop and help you in malls, in lifts. They push the chair and wait for you and only enter if there is enough space. Here everybody rushes in. I repeat—nobody cares, not the system nor the politicians. Living with a disabled member of a family is just one big obstacle in this country.

But for us parents, the life of our child is precious and it's a matter of life and death. We cannot afford to wait and do nothing. Our son had the fourth infusion of stem cells with hypoxic temperature cells, in Gurgaon. Although we don't see any improvements in my son, he is stable. Again, we are trying to delay the degeneration process. No one wants to see their son die. They say that what you resist persists. So my philosophy is to go with the flow and do what I have to do. Perhaps this is my own special spiritual journey, a trial by fire as it were. But we are living our lives and

living them happily so far in spite of the roller coaster of emotions constantly being experienced.

We continue our endeavour with a hope in our hearts that at least we have done the best we can do. I wish parents like us could turn their grief into action by whatever little we all can contribute. I am sure we all can look towards a better and a healthier life and future. I am continuing with the therapy with a hope of delaying as much as we can and hoping for that eureka moment that brings a wave of health for all little angels to live as healthfully and normally as possible. The science of stem cells is very interesting; when we get hold of the specifics and learn to control this science, it will be a magic bullet for almost all medical treatments. The whole of the human body is made up of stem cells; hence, one can imagine the huge outcome of this science, which will be revolutionary in nature.

Ripudaman Singh has been working in the banking and financial field for more than 22 years. He holds a bachelor's degree in Commerce and a master's degree in Personnel Management from Pune University, India. He has had a very successful professional work experience in various leadership roles. He became involved with stem cells when his son, presently 16 years old, was diagnosed with Duchenne Muscular Dystrophy in 2005. He has been following stem cell research very closely for more than nine years and participates in various other research activities. Over the years, he has become an advocate for stem cell research and its huge potential, if practiced in the right way. He is passionately committed to finding stem cell–based therapeutic solutions for incurable conditions in children of all ages.