

Stem cell researchers face down stem cell tourism

Bryn Nelson

A variety of international efforts hope to warn patients off unregulated treatments

In April, a paralysed man returning to Colorado from experimental stem cell therapy in India said he could feel the waistband of his pants for the first time in years. Like others before him, he couldn't say how many cells he had received or how his treatments had worked. Nor had his doctor published any details.

In the end, members of [CareCure](#), an online forum for patients, caregivers and their advocates were left to parse through a tantalizing yet frustratingly incomplete anecdote once again.

"Not another one of 'those' stories," one longtime forum member wrote.

"I want to keep on reading about 'those' stories. KEEP posting," another responded.

Eventually, Wise Young, the CareCure forum administrator, weighed in with an all-too-common appraisal. "The sad thing is that the people who are doing this treatment don't seem to be assessing the patients in a rigorous way, documenting what they are doing and seeing in the patients, and [they are] keeping the procedure and the treatment secret," writes Young, a neuroscientist at Rutgers University in New Brunswick, New Jersey, who has visited such practitioners to persuade them to be more open. "If they are serious about wanting to help people, they would be doing it correctly."

Such 'stem cell tourism', where people travel thousands of miles and pay thousands of dollars to receive unregulated care, is nothing new, and for years Young has been one of the few scientists on an educational campaign. Now, with more stem cell applications being pushed toward clinical trials, the international research community is stepping up.

Stem cell research society plans to set guidelines

Like many other organizations, the International Society for Stem Cell Research (ISSCR) gets peppered with e-mails from patients desperate for reliable advice. Clarity is in short supply when it comes to separating medical hucksters or 'stem cell tourist traps' from clinicians searching out legitimate interventions for patients with no other options, says Insoo Hyun, cochair of the society's Task Force on the Clinical Translation of Stem Cells, which was formed just [last year](#).

Hyun, a bioethicist at Case Western Reserve University in Cleveland, Ohio, expects his task force to deliver a draft of new clinical guidelines this June. He hopes the nonbinding document will both lay out much-needed definitions for what constitutes an above-board clinical centre and provide consensus on stem cell procurement and therapeutic standards. After soliciting feedback on the draft, the task force aims to have final guidelines by the year's end.

And if clinics refuse to abide by them? "All we can do, as a society, is issue a set of general guidelines and principles," Hyun says.

The hope is that governments could use the guidelines to establish enforceable regulations. "In many locales, they're waiting to see what we do and then go off that," says Hyun. Along with a solid framework for regulatory bodies to chew on, he wants to provide specific advice on what the public should look out for. For example, have clinics done any preclinical studies or adverse-event reporting? Do they follow up with patients? Have they disclosed all financial conflicts of interest? Who's ultimately responsible for treatment-related injuries? "It's one thing to say 'You don't want to go to country X', but another to say why," Hyun says.

Shaky motivations

Jeannie Fontana, executive director of patient services at the Burnham Institute for Medical Research in La Jolla, California, learned that distinction firsthand when she began seeking out stem cell clinics in 2000, three years after her mother's diagnosis with amyotrophic lateral sclerosis (ALS). "I travelled the world to try to find something that would be potentially beneficial," she says. "I did not see any therapy out there worth taking the risk." Eight years later, she still hasn't.

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Insoo Hyun

International Society for Stem Cell Research

One clinician in the Dominican Republic requested US\$25,000 for a stem cell treatment he said would cure ALS patients. Fontana, who has an MD and a PhD, offered to run a clinical trial for him just to verify the data. The doctor agreed, but only if she would promise not to publish. She declined. "The fact that the clinic wouldn't want to do that makes me a little more suspicious of what the motivations are."

With clinics commanding up to US\$70,000 for treatments, the status quo of unverified claims may be hard to change, especially when anecdotal success stories foster hope among prospective clients. Fontana has heard directly from some patients who say they've benefited from overseas procedures, but she's also heard from those reporting no effect or outright harm. "Most of the people fall into the second or third category," she says.

Fontana believes most people are getting the message that such treatments are unproven. "They clearly understand that there's risk here, but they're willing to try something because the risk from doing nothing is unacceptable." With few or no spots available in trials run by researchers who are committed to thoroughly documenting procedures and outcomes, patients will continue to seek out others promising help.

Although some nonprofit groups have yet to take a position on stem cell clinics, others, including individual researchers and medical organizations, have come out swinging. In response to an inquiry for this article, Kieran Breen, director of research and development at the Parkinson's Disease Society in the United Kingdom, sent back a sharply worded statement singling out reports of stem cell treatments offered in the Netherlands, Germany and China. "There is no evidence whatsoever that these work, and indeed they may be particularly harmful for people, with the potential for irreversible side effects," he said. "The Society does not recommend people to undergo these treatments as they are untested and may, in the worst case, be fatal."

The last sentiment has become a common refrain among researchers. "I think it's almost a matter of time before there's an adverse event, and how do we prepare for that?" Hyun says. "We don't want to follow the path of gene therapy and fall into a lot of the pitfalls there." When the time comes, the stem cell community needs to have some guidelines in place so it can point to what was or was not done when the therapy goes bad, he says. "Now, you don't even really have a basis for criticism."

Stabilizing runaway stem cell practices

Richard Boyd, director of the Monash Immunology and Stem Cell Laboratories at Monash University in Melbourne, Australia, sees the spate of unproven stem cell therapies as a "runaway economy" in dire need of a stabilizing force. If murky practices lead to tumours or deaths, the resulting scandal would help lend credence to the naysayers. "The whole momentum of stem cell research runs the risk of faltering, of stumbling to a halt," he says.

Until some quality control is implemented, Boyd says, standards are likely to remain all over the place. In some instances, clinics aren't even injecting human-derived cells. Bio-Cellular Research Organization, a Newark, Delaware-based company with a manufacturing plant in Slovakia and offices in Malaysia, Taiwan, India and Switzerland, has boasted of its ability to treat hundreds of patients with a stem cell xenotransplantation procedure based on injecting stem cells from fetal and newborn rabbits.

"That's pretty scary," Boyd says.

And with only word-of-mouth to go on, who can say whether a patient who spent a small fortune on a stem cell therapy for a neurological condition and can now feel his toes or waistband really owes his improvement to stem cells instead of, say, to physical therapy or a placebo effect? "I think you have to weigh those one or two seeming successes versus the large number of failures that you don't hear about," Boyd says. On the other hand, he worries, researchers might also be discounting therapies that could prove valuable. "It makes you think, 'Crikey! Maybe we are being oversensitive to this'."

Clinics and stem cell scientists in Melbourne will soon announce arrangements with government regulators that might bring more balance to questions of therapeutic legitimacy. The private sector can provide funding that governments rarely can, Boyd says, whereas government backing could help disseminate timely information, provide oversight and maintain public stem cell banks. He hopes the scheme being developed in Melbourne could be an exportable model once its own protocols are in place. Beyond Australia, discussions so far have involved China, Singapore, Dubai, and Switzerland, among other countries.

One eventual goal is to establish the kind of monitoring and clinical information collection that could help verify or reject claims and establish more rigorous safety benchmarks. "That would be the absolute dream, if you could get to the people who are doing these treatments [and have them provide information]" Boyd says. But such negotiations will probably prove delicate. "If you start challenging them, they shut up and that's it; you won't get anything."

Despite a few "renegade" clinics, Boyd says that most therapeutic centres he's approached have been open to more scientific oversight. He's also "very optimistic" about the prospect of the new ISSCR guidelines bringing more order to the field.

Last November's debut of the Australia-China Centre for Excellence in Stem Cell Research established another framework in the form of a federally funded partnership between Monash University and Peking University, in Beijing, China. The agreement, involving researchers, hospitals and local regulatory authorities, funds visiting scientists and workshops to promote clinical translation and commercialization of stem cell research. Boyd, who serves as project director, says the centre is expanding to include an outpost in the Chinese city of Harbin, and potentially in Chengdu as well.

Monitoring the claims

More progress could come through an effort to quantify the claims of questionable centres. Ubaka Ogbogu, a research associate at the Health Law Institute at the University of Alberta in Edmonton, Canada, has teamed up with institute research director Timothy Caulfield and colleagues to analyse the content of 25 websites offering stem cell therapies around the world. The aim is to advise the ISSCR task force and other international agencies with timely input. "We're trying as much as possible to provide evidence to help guide policy development in this area," Ogbogu says.

Although the analysis is still preliminary, it has already uncovered several recurring themes, including a consistent underplaying of risks and a broad range of alleged benefits ranging from diabetes and heart disease treatments to increased libido and enhanced male climaxes. "None of the websites noted that the therapies they were offering were still experimental by Western regulatory standards," Ogbogu says. Instead, many invoked familiarity with other forms of transplantation medicine to justify their claims. Of the few sites listing relevant studies, none appeared in prominent peer-reviewed journals. One website, in fact, listed false citations for the journals where its studies allegedly appeared.

Most evidence instead relied on case reports and brief anecdotes that Ogbogu compares to the commentary section of websites such as YouTube. His group hopes eventually to assemble a panel of scientists to examine the claims, although he concedes the analysis may prove difficult precisely because of the lack of accessible evidence.

Despite the challenge, he says, the matter of public trust is paramount. And because some aspects of stem cell research are already controversial, one "really bad story" could throw the whole field into a tailspin. "It's really difficult to deal with this from a policy standpoint," Ogbogu says, "but that doesn't mean we're not going to try."

Campaigns for expensive stem cell therapies can now be found on many crowdfunding websites. But are the patients and the donors being misled about the benefits and the risks? The excitement around stem cell therapy revolves around the ability to grow more of these cells in the laboratory so they can be used to produce new tissue, replace damaged cells, and unravel disease mechanisms. You might also enjoy Disappointingly, the researchers found no change in the trial's primary endpoint: motor function one year after baseline infusion. They did report better outcomes at higher doses (highlighted in some media coverage) but Paul Knoefler at the UC Davis School of Medicine isn't persuaded. Clearly, "stem cell tourist" clinics, which intentionally operate in countries where the regulatory environment is "shall we say" less than rigorous are nowhere near as cautious, as they charge tens of thousands of dollars a pop for stem cell treatments that might or might not actually have real stem cells in them. You'd think that such a thing couldn't possibly be going on in the US. You'd be wrong. Last week, Paul Knoefler, a stem cell scientist who has previously contributed to Science-Based Medicine, teamed up with Leigh Turner to publish a paper in Cell Stem Cell estimating the number of stem cell clinics in the US. The number they came up with astonished me. Stem cell clinics: A large and growing industry. Stem cell research is used for investigation of basic cells which develop organisms. The cells are grown in laboratories where tests are carried out to investigate fundamental properties of the cells. Aborted fetuses are not the only source of stem cells. There are stem cells in the both placenta and blood contained in the placenta. Also the primary source of stem cells is from blastocysts. The controversy regarding the method involved was much tenser when researchers used Embryonic Stem Cells as their main method for stem cell research. **DISCLAIMER:** These points are based on the old debate about the methods of stem cells research, from before 2007. Since then, scientists have moved on to use more ethical methods for stem cell research, such as iPS.