"My Right to Try": The Dangers of Unregulated Stem Cell Clinics

David T. Harris

Professor of Immunology, Professor of Medicine (Division of Translational Medicine), Executive Director—Biorepository, QC Director—GMP Laboratory, and Scientific Director—Celebration Stem Cell Centre, University of Arizona, Tucson, AZ, USA.

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CORRESPONDENCE: davidh@email.arizona.edu

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Patients claim that they are unable to gain entrance into FDA regulated stem cell clinical trials in the United States either because there are no local trials available, or because it's too expensive to run such trials in the US. Some patient groups have even claimed that the medical community has conspired to keep novel life-saving therapies off the market. In response, patients have successfully lobbied their legislators to pass "right to try" laws in 24 states, in an attempt to bypass the FDA's oversight of these treatments.[1–5] These "right to try" laws were meant to be restricted to those patients seeking to use experimental drugs or therapies not yet approved, or those who could not qualify for either a clinical trial or compassionate use (it should be noted that the FDA granted 1,500 patient compassionate use requests alone in 2014 at an almost 95% success rate;).[6] It should be understood that "right to try" does not mean "free", however. Patients still have had to pay out-of-pocket costs for these treatments, which can reach tens of thousands of dollars. These "right to try" laws have stimulated both a rise in overseas medical tourism as well as a rise in US stem cell clinics with physicians claiming they have a right to treat patients under the practice of medicine, and to be legally protected by these laws in case of FDA investigation or patient lawsuit (often by asserting that the FDA has no prevue due to stem cells being used in same day procedures), as long as informed consent was obtained. If only it were this simple. Informed consent is based on the recognition of an individual's autonomy. The informed consent process insures the right to refuse treatment after being provided with information about the procedure. Thus, if one has the right to refuse participation then should one not have the right to actively participate?

Testing of new, unproven therapies is based on several basic assumptions. First, that there is sufficient pre-clinical (generally animal) data available to justify transition to people, that the clinical trials will be administered by experts who will look for and report any adverse effects, particularly if significant, and they will stop the trial if there is no proven benefit. Pre-clinical justification does not include second-hand and anecdotal claims. Second, those individuals who will participate in the trials will be well educated as to the potential benefits and harms, and will provide a true informed consent as to their participation.

Many individuals are not comfortable with the concept of dying; most will fight and struggle even with no hope of improvement, rather than striving to achieve a sense of peace and accept the inevitable that we all must eventually face. This observation raises the issue of whether there can ever be a truly informed consent if a subject is desperate or dying despite the use of all standard therapies. If not, then there is a real and great possibility of patients being exploited for fame and/or financial benefit. One might argue that such therapies would be OK even under these circumstances, as long as patients are not being put at unnecessary risk and if the costs are inconsequential. However, aside from the medical risks and costs, continued participation of uninformed patients in such "clinical trials" significantly hinders and undermines the ability to determine which therapies may be useful for which patients, and to do so in a timely fashion.

Patients claim that it is too expensive to offer these novel stem cell therapies in the US, and part of that claim is true. Clinical trials, especially at the end prior to licensing, can run into the hundreds of millions of dollars, and take a decade to finish.[7] The costs and the time involved can be daunting hurdles to bringing a new therapy to market. Thus, many patients truthfully find that it is faster and (but not necessarily) less expensive to leave the country to obtain these treatments. At the same time it is also easier for the stem cell clinic to make large profits overseas long before the medical utility of an approach is known or proven. Regulatory oversight, if it exists, is less burdensome and costly. Extensive doctor training and qualification is not always necessary or required (after all, a doctor is a doctor, correct?). I am sure that some combination of these two reasons is responsible for the rapid rise in medical tourism during the last decade. However, these stem cell clinics are not operating in foreign countries

because the FDA, doctors or the AMA want to keep therapies out of the clinic, but rather for reasons of oversight and profit. There are now more than 100 of these stem cell clinics in the US alone, even without consideration of offerings in the Caribbean (e.g., Bahamas, Dominican Republic), Central America (e.g., Costa Rica, Panama), and Asia (e.g., China).[8] There has also been a significant rise in Mexican stem cell clinics even closer to home.[9] Ineffective enforcement of national regulatory requirements has allowed the rapid spread of "pay-to-play" unproven stem cell therapies lacking adequate quality, safety and efficacy. As of 2012 there appears to be at least 396 medical establishments involved in cell therapy, from cell collections to operating clinical trials.[8]

It is said that no good deed goes unpunished. The US population is now getting old enough to have forgotten the role of the FDA in the thalidomide scandal of the 1950s.[10] At that time the drug had been approved to treat morning sickness in pregnant women in Europe although no teratology studies had been performed. Thus, the FDA did not allow the drug to be sold in the US. It turned out that use of thalidomide during the first trimester of pregnancy resulted in a generation of what was called "flipper babies" due the drug's stunting effect on limb development. At that time the FDA was hailed as a hero in protecting the US population from untested drugs and unscrupulous pharmaceutical companies; how quickly we forget. The FDA could play a similar function today in the stem cell arena. The FDA's role in these novel therapies could be to insure the right stem cells are given to the right patient, to assure stem cell potency prior to administration, to protect patients from problems of contamination and disease transmission, and to measure stem cell purity to prevent unwarranted side-effects.

Many stem cell clinics are unregulated and unlicensed, and their doctors are not trained in the practice (of collection, processing and use) of stem cell therapy. Further, there is no guarantee that the patient will not be harmed, as for the most part many patients must give up their right to sue in cases of negligence or malpractice, and for those that do not but are harmed anyway, there is little or no recourse. If one is considering frequenting a stem cell clinic in order to partake in an unapproved stem cell therapy, then the least one should do is ask about the training and qualifications of the practitioners. Ask at least as many questions as when one buys a car. Do clinic personnel have documented experience in sterile technique, in surgical techniques needed for the therapy, and in patient identification approaches needed to insure the correct stem cells are given to the correct patient? It should be noted that the FDA is considering its right to suspend the medical license of any physician that administers stem cell therapies in off-shore clinics with the intention of escaping federal oversight. This kind of threat could further and severely limit the number of qualified practitioners found at such clinics.

The increase in miracle stem cell cure claims and in numbers of stem cell clinics seems to have occurred at much the same time as what had been called a "rise in ignorance" of the general population when it comes to science. Whatever happened to the old adage, "if it seems too good to be true, it probably isn't"? One does not need to search very long or look very hard to find well-documented, investigative reports on such facilities and their services. For example, Celltex (the company that treated Texas governor Rick Perry) received warning letters from the FDA (2012 and 2013) for significant shortcomings which resulted in its shutdown in the US. However, it now operates in Mexico without any sort of oversight.[11] Prior to as well as during the same timeframe the Cell Surgical Network (operated by Drs. Lander and Berman) has advertised on its website an almost endless list of medical conditions that can be treated with its stem cell approach including various orthopedic, neurological and autoimmune conditions. Supposedly operating under their own IRB as the California Stem Cell Treatment Center, along with a franchise of clinics elsewhere in the US since 2010, it has seen increased scrutiny by the FDA. Although it has now cleverly worded its claims to avoid outright FDA censure, it seems very transparent in its reason for being.[12–13] In another high profile example, in 2014 Regenerative Sciences was also slapped by the FDA for culturing mesenchymal stem cells (MSC) for therapeutic uses (primarily orthopedic) in what it advertised as the Regenexx procedure (which I still see advertised locally on TV in my viewing region).[14] Finally, the Irvine Stem Cell Treatment Center, once part of the Cell Surgical Network, has been cited by the FDA (2015) for use of manipulated adipose-derived stromal vascular fraction (SVF) in non-homologous treatments (albeit under a so-called "pay-to-play" IRB protocol) without the required IND, in that such cell therapies are considered biological drugs.[15] Thus, the public seems to have been warned to some extent.

I have heard experts in the medical community claim that all of the positive results reported from these stem cell clinics are merely anecdotal, and that no one has ever really ever benefited from these types of clinical trials. However, I would argue that claim is not true and appears to be as partisan and misinformed as many arguments from the other side, in that I have seen dozens of patients benefit from these non-licensed stem cell treatments for cerebral palsy, traumatic brain injury, and other indications. And yes, in many cases the patients did need to pay out of pocket, and no, not all patients benefitted. Our job should be to determine who will most likely benefit and then figure out a way to have those patients undergoing those stem cell therapies qualify for insurance reimbursement, rather than be dismissive. At the most recent International Society for Cell Therapy conference (Singapore, May 2016) the stem cell clinic issue was again raised in a special session without much resolution. In fact, more than one physician in the audience admitted to either running such clinics and/or performing such procedures outside of a clinical trial and without an IND. Remarkably,

despite the previous disparagement of such activities during the same session not one of the panel members strongly objected. It really makes one wonder how anything will ever get done or if things will ever change. Or maybe, it's not really a problem as long as it's one of our members and not the general medical community?

This issue of unregulated stem cell clinics is even more significant because the field of regenerative medicine is just now starting to blossom. The worst thing that could happen would be something similar to the University of Pennsylvania incident where a subject was killed due to the negligence of the investigator. This incident set the gene therapy field back more than 10 years, almost killing off the endeavor entirely. It does indeed appear that stem cells of various sorts can provide significant benefits in a variety of clinical settings. However, if patients are injured or die due to the ineptitude of stem cell charlatans looking to make a quick profit, these promising therapies may never come to fruition or only after a much longer time period at much greater costs. I believe that now more than ever it really is "buyer beware" when it comes to stem cell therapies, and some regulatory oversight is required, but that oversight should not be onerous or overly expensive. But oversight in some form is needed, and soon.

Author Contributions

Conceived the concepts: DTH. Wrote the first draft of the manuscript: DTH. Developed the structure and arguments for the paper: DTH. Made critical revisions: DTH. The author reviewed and approved of the final manuscript.

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