Stem Cell Treatments Raise Thorny Questions for Researchers, Clinicians

By Karyn Hede

Scientists and clinicians in La Jolla, Calif., at the end of last November, celebrated the grand opening of the 150,000-square-foot Sanford Consortium for Regenerative Medicine (SCRM), a modern, four-story glass-and-metal symbol of the hope for the healing properties of stem cell treatments. Funded in part with a $43 million grant from public funds that created the California Institute for Regenerative Medicine, the SCRM is charged with bringing stem cell research to the clinic. But developing in parallel with places such as the SCRM is a shadow industry of stem cell treatment centers that already purport to use stem cell therapy to treat a spectrum of diseases.

Clinics such as the California Stem Cell Treatment Center, in Beverly Hills, which according to its website offers “care for people suffering from diseases that may be alleviated by access to adult stem cell–based regenerative treatment,” are using stem cells derived from a patient’s own fatty, or adipose, tissue for cosmetic and experimental treatments for degenerative diseases. The U.S. Food and Drug Administration’s Center for Biologics Evaluation and Research, which regulates use of biological cells and tissues, permits such treatments—provided that those cells are intended for use in that same person (autologous) and are “no more than minimally manipulated,” according to an FDA spokesperson. The California Stem Cell Treatment Center states on its website that it “does not claim that any applications, or potential applications, using these autologous stem cell treatments are approved by the FDA, or are even effective.”

But the possibility of a regulatory crackdown hasn’t stopped dozens of stem cell clinics from collecting tens of thousands of dollars from patients willing to travel to countries such as South Korea, Mexico, and China to receive stem cell treatment. The practice, dubbed “stem cell tourism,” has proliferated in recent years and is gaining in popularity as high-profile professional athletes and prominent public figures have opted for stem cell treatments.

Now some professional organizations and individual scientists are arguing that it’s time for stem cell researchers to speak out against unproven medical practices involving stem cells—or risk losing the public’s trust.

“There’s this gray area of medical innovation,” said Lawrence Goldstein, Ph.D., director of the University of California, San Diego, Stem Cell Research Program and chair of SCRM’s scientific research steering committee. Goldstein, who helped write Proposition 71, in which California funded $3 billion in human stem cell research, noted that squashing medical innovation by restricting physicians’ ability to innovate within their profession benefits no one. However, “if it becomes systematic, then it starts to look a lot like research versus innovation, and that’s regulated. The question is, what do you do in that gray area?”

That’s where state medical boards come in. Without federal regulation on stem cell treatments, some state medical boards are stepping in to regulate stem cells’ medical use. The Texas Medical Board is debating new rules that would require a state-appointed panel to review safety procedures for any proposed new stem cell therapy. The review was prompted by a report that Gov. Rick Perry had stem cells isolated from his own fat injected into his back during a spinal fusion procedure in Texas.

Injecting fat derived from one part of the body into another has been standard practice in aesthetic and reconstructive surgery for years. But what’s medically fine in one part of the body is not necessarily fine in another, said Goldstein. “While the experience with adipose stem cells in some sites suggests that it is safe, in some ways, it doesn’t mean that it’s safe anywhere . . . . We don’t just assume because adipose stem cells were safe in subdermal application that that means it’s safe to put them in the brain or put them in the bloodstream or the heart.” Perry’s procedure and others like it would not be allowed with the new safety review in Texas. The board’s proposed rules were tentatively approved February 10, with final approval expected at an April 13 meeting.

Stem Cell Promise and Risk

The use of hematopoietic stem cells, which can generate blood cells and regenerate damaged bone marrow, has been a potent therapeutic tool in cancer treatment since the first bone marrow transplants in the 1960s. The ability to identify, isolate, and characterize these stem cells from other locations in the body, apart from the bone marrow, has led to the current proliferation of therapeutic uses. Some stem cell pioneers are enthusiastic about the therapeutic potential of other types of stem cells, such as mesenchymal stem cells (MSCs) found not only in bone marrow but also in fat, muscle, and the pulp of baby teeth, among other locations.

Hillard Lazarus, M.D., director of novel cell therapies at University Hospitals at Case Western Reserve University in Cleveland, performed some of the first experimental studies with MSCs to speed recovery after bone marrow transplantation and to treat graft-versus-host disease, in which the immune system attacks tissues or organs transplanted from a donor. Lazarus’ research showed that transplanting donor MSCs along with donor bone marrow reduces graft-versus-host reactions. He holds a patent for using MSCs to enhance bone marrow engraftment.
“These mesenchymal cells have a number of interesting properties,” said Lazarus. “They live in association with bone marrow cells and secrete factors that nurture bone marrow.” But they do other things, he added. They inhibit local immune responses, making the cells candidates for combating autoimmune diseases. Lazarus and principal investigator Jeff Cohen, M.D., are leading an open-label phase I safety study of autologous MSC transplantation in patients with relapsing forms of multiple sclerosis involving vision loss at the Cleveland Clinic Hospital.

Lazarus and his colleagues have several other open FDA-approved trials testing the safety of MSCs in patients, and Lazarus is also working with a company, Athersys, a commercial partner of Case Western’s Center for Stem Cell and Regenerative Medicine.

But Lazarus says that the line separating legitimate medical research from experimentation on desperate people seeking pain relief or healing for currently incurable diseases has been breached.

“A lot of these fee-for-service places will do anything; they’ll fly [patients] to Singapore for the day to squirt the cells in,” Lazarus said. Meanwhile, he added, “we are trying to painstakingly carry this field forward.”

**Long-Term Effects**

Researchers know little about the long-term risks of autologous stem cell treatments.
One of the few areas in which the risk has been studied involves the practice of using fat tissue containing MSCs to help reconstruct the breast after surgery for breast cancer. A recent review by Robert Pearl, M.D., from Royal Free Hospital in London, and colleagues at the Queen Victoria Hospital and Oxford University in Oxford, UK, published in the July 20, 2011, issue of the *Journal of Plastic, Reconstructive, and Aesthetic Surgery*, concluded that transferring fat-derived stem cells to an environment of previous malignancy could, in theory, pose a risk of recurrence. However, short-term studies of cancer recurrence have found no increased risk in breast cancer patients who opted for fat-transfer procedures. Pearl and his coauthors call for registries of patients to allow long-term tracking of trends.

In an e-mail exchange, Pearl, who studies cell adhesion molecules in cancer progression and metastasis, pointed out that “some researchers are concerned that stem cells taken out of their niche and away from their normal homeostatic constraints may be less stable and thus more prone to malignant transformation. In the absence of long-term outcome data, quantifying such a risk is difficult.”

The International Society for Stem Cell Research, a nonprofit membership organization established to promote stem cell research and public education about stem cell therapies, has become concerned enough about the proliferation of unproven stem cell treatments that it developed an educational website, http://www.closerlookatstemcells.org, to educate the public about the potential dangers of stem cell tourism. It also sponsored a public forum titled “A Dose of Reality on Alternative Stem Cell Treatments: What You Don’t Know Can Hurt You” during its 2010 meeting in California. The society points out that some patients have had serious injury and others have died after receiving treatments, and that patients should not let testimonials sway them.

Efforts to educate the public are commendable, according to David B. Resnik, J.D., Ph.D., bioethicist and institutional review board chair at the National Institute for Environmental Health Sciences, but stem cell scientists and clinicians must ensure that patients are kept from harm by refusing to share cell lines and other resources with physicians who may be operating outside accepted medical practices, he said.

Resnik and coauthor Zubin Master, Ph.D., of the University of Alberta’s Health Law and Science Policy Group, argue in a position paper published in the July 2011 *EMBO Reports* that scientists and physicians should request to see research protocols and other documentation ensuring the responsible use of stem cells. They should also insist on a material transfer agreement that governs how the materials will be used and spells out whether the materials would be used in humans and under what conditions.

“It may not fix the problem, but it’s better than doing nothing,” said Resnik. “You want the public to trust the field of stem cell research. You don’t want to be tainted with the scandals and the corrupt clinics.”