Stem cell talk

Stem cell-based therapy is at last moving into mainstream medicine, after many years of hype and hope. But there's also fear that this therapy has been exaggerated by the numerous clinics that promise startling improvement to patients who pay large sums for treatment. What kinds of stem cell therapy are really legitimate and which are dubious? And how can people know the difference? Bradley Fikes, the San Diego Union-Tribune's biotech reporter, gives his perspectives on this important industry.

Preamble

A little about myself. I've long been a biomedical geek. When I was a kid, I wanted to be a doctor. When I was 9, I got this enormous medical dictionary, and read it obsessively. I carried that tome around with me until it fell apart.

However, I eventually realized that being a doctor involved too much responsibility for me. If I made a mistake, I could kill someone. That's something I couldn't live with. So instead I got into journalism, where errors are less dangerous.

I first fell in love with journalism at my college newspaper, the Daily Aztec at San Diego State University. The Daily Aztec has produced a plethora of extremely talented reporters and photographers I'm glad to have worked with. Once I held three positions, reporter, assistant editorial editor

and entertainment writer. These were paid, not lavishly, but I was actually able to live on the income. I also went to classes in between jobs at the paper.

And now I'm a biotech reporter, involved in medicine and medical research as an explainer to the public. So while universities like UCSD may make the breakthroughs, the public often hears about them from SDSU alumni like myself.

My first experience with biotech was at San Diego State, where I learned of antibody manufacturing through cells. I quickly got lost when the professor described what a hybridoma was, and I never wrote the story. It was just too much.

Eventually, I just accepted that biotech and life itself is a Rube Goldberg machine, where A hits B, which rolls over to C ... and we eventually end up with Z. That's the system life got through evolution, and that it can be amenable to being tamed for human uses is remarkable.

I began reporting on biotech in 1990 at the San Diego Business Journal, where I also covered health care. Since the two subjects are closely related, it was a good match. And there I met people who are still influential in biomedicine today. These include Ivor Royston and Howard Birndorf, co-founders of Hybritech, San Diego's first biotech company.

I met Stanley Crooke, CEO of Isis Pharmaceuticals, recently renamed Ionis for obvious reasons. And I got a sense of how the San Diego biotech community worked together.

Part of my coverage extended to water and drought issues,

and in that capacity I saw the local biotech community unite for the first time. In 1990 or early 1991, I'm not exactly sure when, I saw biotech executives talk at a San Diego City Council meeting about the absolute necessity of having a reliable water supply for their companies. The council acted.

After a couple of short job changes, in 1997 I went to the North County Times, where biotech was just one of many beats I had to cover as a business reporter. For long periods, I was the only business reporter, so I had to wear many hats. Real estate, tourism and hospitality, military, telecommuncations.

I also ran into a guy named Irwin Jacobs, who ran a small, upstart company called Qualcomm. Have you heard of it? One of the things I did around that time, in 1998 I think, was to jury-rig an old Qualcommn Thin Phone and an analog PC Card modem to connect to CompuServe on a handheld computer called a Sharp Zaurus, which just happened to have a PC card slot. I showed the combination to Jacobs, and a person with me said his face lit up. I was too busy demonstrating the contraption to notice.

Around 2000 to 2001, I made a brief detour to working for a biotech company, DoubleTwist. It was based in Oakland and I telecommuted from Oceanside. I wrote articles and chose stories and press releases for a portal page. It worked really well, but the company ran short of cash after its IPO failed. The North County Times accepted me back.

But after more than a decade of diversifying my attention among several beats, I wound up at the San Diego Union-

Tribune, when the paper purchased the North County Times. The Union-Tribune had no biotech writer at the time, and I applied and was accepted for the position.

And now I'm going to segue over to the advertised topic of this talk, stem cells!

Stem cells are many things. In embryos, they are the ancestral cells that give rise to the various tissues and organs in the body. But some kinds of stem cells stick around even after birth. These cells are the body's repair kit. They heal wounds, regenerate liver, the intestinal lining, red and white blood cells, and even produce new brain cells.

That power has attracted the attention of physicians and researchers over the decades. The first stem cell therapy was bone marrow transplantation. Doctors didn't even know what kind of cells they were transplanting, but knew that something in the bone marrow was capable of regenerating blood, including the immune system.

Over the years, researchers came to identifiy the various hematopoieitic stem cells, and their capabilities. And they found other types of stem cells. In 1998, researchers at the University of Wisconsin identified certain cells in human embryos that we know today as embryonic stem cells.

The discovery of embryonic stem cells in humans -- they had earlier been found in animals -- touched off a ginormous ethical and political debate I'm sure you are familiar with. In California, that debate caused the passage of Proposition 71, which appropriated $3 billion in bond money for a new agency, the California Institute for Regenerative Medicine.

CIRM supports all kind of stem cell research, not just embryonic.

Here, I'm going to outline the newer, legitimate uses of stem cell therapy. Later, I will discuss the gray areas, where treatments aren't specifically authorized, and the clinics may not be on the up-and-up. Distinguishing between legitimate and illegitimate uses is difficult, and there are valid differences of opinion between some patient activists, scientists, and regulators.

In the last few years, embryonic stem cell therapy has begun moving into the clinic.

San Diego-based ViaCyte right now is conducting a human clinical trial of a therapy for type 1 diabetes derived from embryonic stem cells. These cells are matured into progenitor cells destined to become islet cells, making insulin and perhaps other hormones. They are encapsulated in a semi-permeable barrier to keep out the immune system, but allow insulin and nutrients to pass through.

As I have said, non-embryonic stem cell therapy has been around for years, first with hematopoieitic stem cells, and later with others that are still in the research or clinical testing stage. There are adipose stem cells, mesenchymal or stromal stem cells, a whole zoo of stem cells. Mesenchymal or stromal cells exert an anti-inflammatory influence, which may help with autominnune diseases, for example.

In San Diego, a group of doctors, scientists and Parkinson's patients are raising funds for another cell replacement therapy. Using skin cells from the patients themselves,

researchers have produced artificial embryonic stem cells called induced pluripotent stem cells, or IPS cells. These cells are matured into neurons that make dopamine, the kind destroyed in Parkinson's, impairing movement. The goal is to place these cells into the brain just before the maturation is final. That way, the cells "grow up" in their new home, where they can make the needed introductions to their new neighbors, growing connections, etc.

Because these cells are virtually identical genetically to the neurons in the patients' brains, it's expected that immune rejection shouldn't be a serious issue, although that is part of what the trial is designed to test.

And in Australia, Carlsbad's International Stem Cell Corp. has just started a trial of a therapy for Parkinson's working on a similar principle. The stem cells will be matured into dopamine-producing neurons. They will be implanted directly into the brain. These stem cells are not derived from embryos, but unfertilized, or parthenogenetic, human egg cells. They are partially immune-matched to the patients to minimize the chance of rejection.

The clinical trials I have described all have the following characteristics: They were approved by government agencies that regulate the trials, they are approved by institutional review boards at the hospitals they are conducted at, and they don't cost the patient money.

Stem cell researcher Paul Knoepfler has written about his concerns with unauthorized and possibly illegal stem cell clinics at his blog - ipscell.com

One reason for concern is that stem cells are living, not inanimate like a hip replacement -- and those can also be troublesome. Because they are living, stem cells can multiply and get into unwanted places. They can also do unexpected things.

http://www.scientificamerican.com/article/stem-cell-cosmetics/

In one troubling case, a women who got a transfer of her own adult stem cells at a Beverly Hills clinic -- bone fragments in her right eyelid. Scientific American described the predicament in a December, 2012 story. I will quote from its description as to how this happened:

"When cosmetic surgeon Allan Wu first heard the woman's complaint, he wondered if she was imagining things or making it up. A resident of Los Angeles in her late sixties, she explained that she could not open her right eye without considerable pain and that every time she forced it open, she heard a strange click—a sharp sound, like a tiny castanet snapping shut.

"After examining her in person at The Morrow Institute in Rancho Mirage, Calif., Wu could see that something was wrong: Her eyelid drooped stubbornly, and the area around her eye was somewhat swollen.

"Six and a half hours of surgery later, he and his colleagues had dug out small chunks of bone from the woman's eyelid and tissue surrounding her eye, which was scratched but largely intact. The clicks she heard were the bone fragments grinding against one another."

Here is the description of how the original procedure was performed:

"First, cosmetic surgeons had removed some the woman's abdominal fat with liposuction and isolated the adult stem cells within—a family of cells that can make many copies of themselves in an immature state and can develop into several different kinds of mature tissue.

"In this case the doctors extracted mesenchymal stem cells —which can turn into bone, cartilage or fat, among other tissues—and injected those cells back into her face, especially around her eyes. The procedure cost her more than $20,000, Wu recollects.

"Such face-lifts supposedly rejuvenate the skin because stem cells turn into brand-new tissue and release chemicals that help heal aging cells and stimulate nearby cells to proliferate.

"During the face-lift her clinicians had also injected some dermal filler, which plastic surgeons have safely used for more than 20 years to reduce the appearance of wrinkles. The principal component of such fillers is calcium hydroxylapatite, a mineral with which cell biologists encourage mesenchymal stem cells to turn into bone—a fact that escaped the woman's clinicians. "

End of quotes. The woman was successfully treated, but some stem cells may linger in her -- possibly to cause more trouble later.

That was a clear case of the danger of freelance stem cell therapy without adequate supervision.

A grayer area is found with the San Diego company Stemedica. They do regulated clinical trials in the United States. But they also sell their stem cells to a company in Tijuana, Novastem, for procedures. While Novastem says it's working under the Mexican clinical trial process, critics say the standards may not be adequate.

In late 2014, Stemedica and Novastem joined forces to treat hockey great Gordie Howe, who according to contemporary accounts was getting close to death. Howe has dementia and had endured brain damage from strokes. One of his sons, Murry Howe, is a radiologist, and told me he had personally vetted Stemedica's science.

Stemedica was still criticized for its role, such as supplying the treatment for free -- patients of Novastem normally pay for their treatment. But unlike the woman with bones in her right eyelid, nothing bad happened to Gordie Howe. Indeed, his condition improved significantly.

I'm going to pause here to read from articles I wrote about his treatment, and updates from other newspapers.

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If you're looking for any decisive conclusion, you'll be disappointed. It really does look like Gordie Howe improved after his stem cell therapy, and that the therapy helped him. Before the treatment, Howe was reported as being close to death. After treatment, he was able to travel and appear in public.

Of course, good results in one person doesn't prove the treatment is responsible, which is why we have clinical trials. But that cold logic doesn't impress patients who are in mortal

danger, or their families. If the treatment is otherwise considered safe, why not let people get it as soon as possible, without the artificially imposed delay?

In other words, the clinical trial process Stemedica has to go through means that people who could potentially benefit must wait, even if they might not live long enough to receive treatment.

Moreover, although Howe's physical condition is significantly better, he still has dementia. That's a tradeoff his family is willing to make.

Now there are other cases of more controversial conduct, such as with the Texas stem cell clinic Celltex, which treated former Gov. Rick Perry for back problems. Celltex ran afoul of the FDA and received a warning letter. After its FDA problems, Celltex moved to Mexico, beyond the FDA's reach.

This contrasts with Stemedica, which remains in San Diego and, along with subsidiaries, conducts clinical trials in the U.S.

And the scary thing is, there is no easy way to tell reputable from questionable stem cell therapists. One would think that the U.S. government's own registry, at clinicaltrials.gov, would be a mark of quality. It isn't. While it's hosted by the National Institutes of Health, clinicaltrials.gov doesn't review the clinical trials it lists - which can be anywhere in the world -- for validity.

Caveat emptor. Read and ask questions. Find qualified medical professionals you can trust. Read blogs like

ipscell.com that are written by experts in the field.

Good luck.