The Cutting-Edge Medical Breakthroughs That Are Transforming Our Health

CELLS ARE THE NEW CURE

ROBIN L. SMITH, MD + MAX GOMEZ, PhD

Foreword by Sanjay Gupta, MD

FOREWORD

One of the first stories I covered as a television reporter was the restriction on US federal funding for research on stem cells. It was August 2001, and for the next eight years, many scientists would spend more time trying to find new sources of funding than actually doing research. When the restrictions were relaxed in March 2009, there was a sense of optimism in the stem cell community but also a feeling the United States was nearly a decade behind other countries and now had to make up a lot of lost ground.

To be fair, supporters of the restrictions felt they were acting in defense of human life in protecting embryos. Furthermore, during this time several lessons were learned in the world of stem cell research that might not otherwise have been learned. First, the early data from embryonic stem cell pioneers did not prove particularly promising. Additionally, induced pluripotent stem cells (iPSCs)—adult cells induced to exhibit the same properties as embryonic stem cells—were discovered. Finally, adult stem cells, thought for sixty years to reside only in bone marrow, were found in many more tissues. As we now know, this greatly opened up the range of therapeutic possibilities.

And yet, in the United States we still feel the hangover of that eight-year drought in stem cell research. Patients are understandably dubious of their true value, as too many charlatans have made

laughable claims unsupported by scientific data. While the number of clinical trials has increased, the US medical system doesn't yet offer formal clinical training programs to teach stem cell therapies. My colleagues in medical journalism write with greatly tempered optimism that borders on cynicism whenever we do stories on the promise of stem cells. And at this writing, the US Food and Drug Administration has approved only one stem cell therapy product, Hemacord, to restore low blood cell counts. In fact, the FDA is sometimes stymied at how to regulate adult stem cells at all, especially when they are extracted from and then injected back into the same human body. It seems that adult stem cells don't fall neatly into the definition of device or drug, the two categories on which the FDA focuses.

As things stand now, if you have heard of Americans getting stem cell treatments, they are usually wealthy individuals who have run out of options and are willing to try anything, even if it is untested and unproven. That doesn't inspire a lot of confidence, but it is the story I have often heard in the mainstream and scientific media almost since I started my careers in journalism and neurosurgery.

That was the backdrop when I first received a call from the authors of this book, Robin L. Smith, MD, and Max Gomez, PhD. They wanted me to participate in Cellular Horizons, a conference in Vatican City focused on cell-based therapies. That's right, Vatican City. After fifteen years of bearing witness to the constant collisions of science and theology, the impact on federal funding, and several-year cycles of optimism and pessimism, things were coming full circle. I would hear from scientists, ethicists, and Pope Francis himself about their faith in stem cells.

Make no mistake, the Catholic Church continues to oppose research or therapies that involve the destruction of embryos. It does, however, support adult stem cell research and asked scientists from all over the world to present their data. These were reputable scientists and regulators from Germany, China, Japan, India, and Australia. The United States was also well represented with researchers from major hospitals and universities presenting compelling data on a variety of ailments.

Sabrina Strickland, MD, of the Hospital for Special Surgery in New York City is using stem cells as a viable alternative for painful osteoarthritis. Eduardo Marban, MD, PhD, at Cedars-Sinai Heart Institute in Los Angeles used them to reduce scar tissue size in the muscle after a heart attack. One of the more provocative trials I heard described is taking place at Duke, where Joanne Kurtzberg, MD, is looking into the use of stem cells for children with autism. While not all stem cell researchers agree this is a rational application of stem cell therapy, there is an increasing number of children going to profit-driven clinics that offer up no data. The Duke trial will at least produce some answers about the impact of cellular therapy on neurons in the brain at various stages of development.

As a journalist, I was particularly interested in meeting the patients behind all the data. Having seen the enormous challenges of autoimmune disease in my own family, I agreed to moderate a panel with Richard Burt, MD, from Northwestern University and his beautiful young patients Grace Meihaus and Elizabeth Cougentakis. At age seventeen, Grace developed rapidly progressive systemic scleroderma that not only hardened her skin but caused multiple internal organs to become scarred and inflamed. Out of options, she found Dr. Burt and underwent an autologous hematopoietic stem cell transplant. Her symptoms improved within months, and she was able to return to college and her way of life. Elizabeth's myasthenia gravis, another autoimmune disease, first affected the small muscles of her eyes, then progressed to a point where she could no longer feed herself or walk. Within six months, she was on a breathing machine and being fed with a tube. If I hadn't heard her describe it as vividly as she did, I would not have believed that Elizabeth started to feel better immediately after treatment as she regained control of her eyes and other motor functions. Eight years later, she is completely healthy and requires no medications. As a father of three daughters, I was buoyed and encouraged by what the future could hold for them and other children around the world if they ever became ill.

We are a long way from seeing these therapies become widely applied. There are still appropriate scientific, regulatory, and cultural hurdles to overcome. And yet, it has become increasingly clear that someday soon even the most ardent critics will come to support the belief that our greatest healing tools may lie within the human body itself. As this field is still very much in its infancy, it is hard to gather all the knowledge in one place. Books like this should be seen as part of a living, breathing body of knowledge that will grow, evolve, and be reborn. What will never change, however, is the measured yet relentless optimism these pages bring.

—SANJAY GUPTA, MD

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DR. RICHARD BURT'S SEARCH FOR A STEM CELL MIRACLE

Richard Burt, MD, is working on an effective reset button for MS. His procedure is called an autologous nonmyeloablative hematopoietic stem cell transplantation. That mouthful of jargon means that he begins by harvesting immune stem cells from a patient's own blood. Then the patient undergoes low-dose chemotherapy to kill the majority of his or her white blood cells—the ones that are responsible for myelin attack. And finally, the previously extracted blood stem cells are reinfused into the patient, where they restore an immune system newly tolerant of the myelin it used to attack.

"These cells are easy to retrieve from the body," Burt says. "I can use hundreds of millions of the cells to make a new immune system for people with autoimmune diseases. The answer is stem cells, the primitive cells that give rise to all other cells in the body."

Dr. Richard Burt (right), Elizabeth Cougentakis (middle), and Grace Meihaus (left) at the Third International Conference on the Progress of Regenerative Medicine and Its Cultural Impact.

Between 2003 and 2014, 151 patients with relapsing-remitting MS were treated with this procedure at Northwestern University's Feinberg School of Medicine, where Burt is chief of medicine-immunotherapy and autoimmune diseases. Over the next few years after treatment, the volunteers were given multiple tests to measure their disability. The Expanded Disability Status Scale was used to measure cognition, coordination, and walking. Patients also underwent MRI scans and filled out extensive questionnaires to assess overall quality of life before and after treatment. In 2015 Burt reported the results in *JAMA*.

"In MS, the immune system is attacking your brain," Burt said. "After the procedure, it doesn't do that anymore."

The data agree. After chemotherapy and infusion of their own (i.e., autologous) blood stem cells, more than 80 percent of the patients in Burt's clinical trial did not relapse for the remainder of the trial (which seems much like a cure to people outside the medical field). More than half showed improvements in their disabilities, meaning that the

procedure had not only slowed or stopped the progression of the disease but many patients were even able to recover function that had been lost.

Roxane Beygi was enrolled in this trial in September 2010. "I saw a miracle happen right before my eyes," says her mother, Evita. "Dr. Burt gave Roxane a second chance."

"Before, I had major fatigue where I couldn't even get out of bed," Roxane says. "Now, I get up at six to get ready for school. During the day, I'm busy with my studies, and I exercise regularly. Life is definitely much better. I have a lot of hope. I have a future now. Dr. Burt will always remain my hero."

"Current drug therapies for MS do not reverse disability or improve quality of life, and leave patients dependent on lifelong drug usage," says Burt. "However, if the results of stem cell transplants hold up in an ongoing randomized trial, it will fundamentally change the lives of patients suffering from MS."

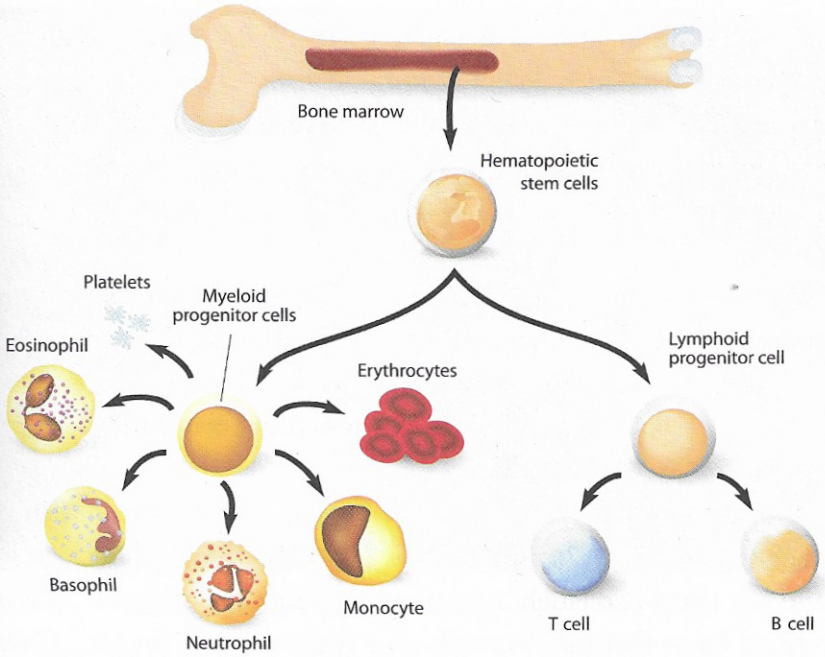
REBOOTING THE IMMUNE SYSTEM WITH HEMATOPOIETIC STEM CELLS

Because Burt's technique essentially resets the immune system, it may be useful in treating autoimmune conditions far beyond multiple sclerosis. And Burt is indeed pushing the technique forward in a range of other conditions.

One condition for which autologous stem cell transplant is showing definite promise is systemic scleroderma.

When she was seventeen and a senior in high school, Grace Meihaus noticed that patches of her skin had suddenly become tight. Also, her fingers and toes swelled up and turned blue whenever it was cold outside. "That was really scary when it first happened," said Grace. "I didn't know what was going on with me. I felt different, and I didn't know why."

An active California teenager, Grace soon found herself tired all the time, struggling through exercise workouts that had once been



Hematopoietic stem cells can give rise to a variety of blood cells, including red blood cells and disease-fighting white blood cells of the immune system.

easy. A year later, her condition worsening, she made her way to a rheumatologist who quickly diagnosed her with systemic scleroderma. The ailment's name comes from the Ancient Greek *skleros,* meaning "hard," and *derma*, meaning "skin." Hardening of the skin is the most visible symptom, but when the condition is systemic, this hardening goes more than skin-deep, affecting other major organs of the body including the heart and lungs.

Grace was given a medication to ease her symptoms, but it didn't help. People with severe scleroderma often die within five years of diagnosis. "That really had me scared," she says. "I didn't know what to expect. My life now had a possible expiration date."

By 2015, as Grace's symptoms worsened, she became depressed and anxious, and her illness forced her to leave college. Through a scleroderma support group, she learned about Dr. Richard Burt at Northwestern and an experimental scleroderma study he was directing.

By the time Grace and her parents met with Burt, the disease had already started to harden her lungs, causing shortness of breath. "Knowing that I desperately wanted to go back to living a normal life, I agreed to join his study," Grace says. "I was extremely optimistic that everything was going to work out for me. My motto was 'hope dies last.'"

Several months later, Grace underwent Burt's stem cell "mini-transplant" procedure. After first harvesting stem cells from her blood, then administering chemotherapy for five days to wipe out most of her white blood cells and bone marrow, Burt then infused Grace's stem cells back into her body.

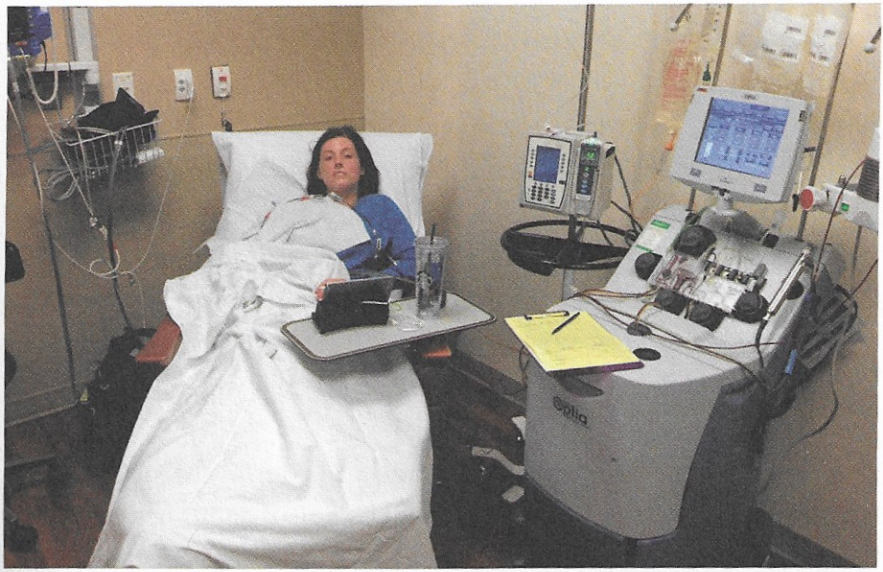
Within just a few days, Grace found that her skin had loosened, first on her hands and later on her face. "One day, I looked in the mirror and saw that I had laugh lines around my mouth," she said. "It was then that I knew that the stem cells were really working for me." Over the next few weeks, her energy returned, and her shortness of breath vanished. She could enjoy exercising again.

"I am very happy the way things have worked out for me," says Grace. "I feel normal, one year after the procedure. Five years after my first diagnosis, knowing that I am finally feeling better and the scleroderma is now under control, my life is back to normal, and I have a brighter future now. Even though the stem cell procedure was tough and difficult, it has all been worth it. It's remarkable when you think about it: my life was transformed by a little bag of my own stem cells, and I am grateful to be in good health once again."

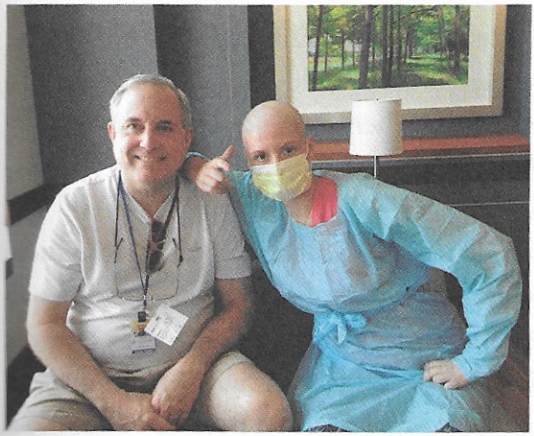
MYASTHENIA GRAVIS: A LIFESAVING STEM CELL THERAPY

Grace Meihaus' stem cell story is amazing, but it isn't unique.

Elizabeth Cougentakis was healthy, athletic, and an outstanding student—until she turned thirteen. In that year, 2004, she was diagnosed



Grace Meihaus before treatment at Northwestern Memorial Hospital in Chicago, Illinois (July 2015).



Left: Grace during treatment with her father.
Right: Grace six months later, in January 2016.
(Photos courtesy of Grace Meihaus)

with myasthenia gravis, a serious neuromuscular autoimmune disorder that leads to muscle weakness and fatigue. In order to contract, human muscle cells need the stimulation of the neurotransmitter chemical

acetylcholine. These cells have receptors on their surfaces that are a bit like the tentacles of sea anemones, waving in order to catch acetylcholine molecules. In myasthenia gravis, the immune system attacks and destroys these receptors, leaving muscle tissue unable to contract.

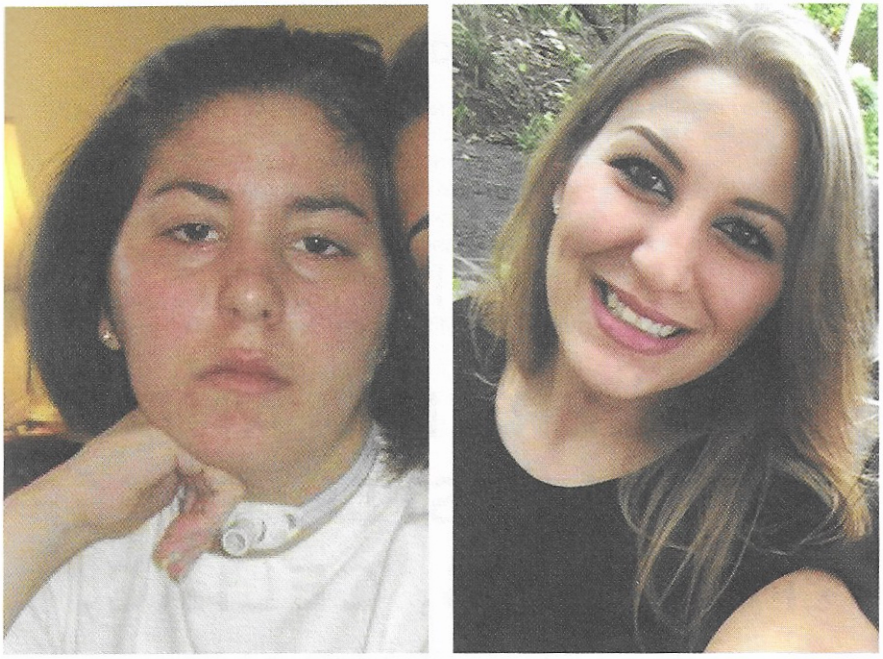
"The first thing I noticed was that when I smiled, my cheeks would droop and not go up. It looked like I was either upset or in pain," says Elizabeth. "Later, my eyes would droop and my vision started to blur. I started seeing double. Within a month, it had progressed to my arms and legs, and I lost all strength. I had trouble swallowing food . . . [and] I was choking on saliva and other liquids."

For most patients, daily medications can control the symptoms of myasthenia gravis. Elizabeth, however, was one of an unlucky few. Her condition continued to progress, and she quickly became completely disabled. Her breathing became difficult and labored, and two years after being diagnosed she needed a ventilator to breathe. Her parents began to feed her through a tube. Still, she continued to slip away.

After spending three months in an ICU, Elizabeth was finally sent home. Her doctors were perplexed. They told her parents they had never seen such a severe case of myasthenia gravis. They felt that she would be more comfortable with around-the-clock in-home professional care.

Over the next year or two, Elizabeth and her parents pursued several avenues, including having her thymus removed and traveling to Venezuela to explore experimental treatments, all to little effect. Then, in 2006 Elizabeth joined Dr. Burt's stem cell study at Northwestern. As in his treatment of other autoimmune diseases, Burt harvested stem cells from Elizabeth's blood, administered a short course of chemotherapy, then reinfused her stem cells.

Elizabeth had been on a feeding tube for two years, but after this treatment, her symptoms gradually lessened and finally disappeared. Within a year after Burt's procedure, she had recovered completely. For the last ten years, she has been completely healthy and requires no medication.



Elizabeth Cougentakis pictured before and after her treatment at Northwestern Memorial Hospital. Elizabeth was not able to control her facial muscles before treatment and, as seen in her later photo, regained facial expression after treatment. She has been healthy since her stem cell treatment in 2006. (Photos courtesy of Elizabeth Cougentakis)

Not everyone in Burt's trials makes a full recovery. Sometimes the immune system is able to reset itself, and sometimes it goes back to the same destructive behavior as before cellular treatment. This variability is one of the reasons the US Food and Drug Administration is progressing very deliberately toward approval of cell-based treatments for autoimmune conditions. But for Roxane Beygi, Grace Meihaus, and Elizabeth Cougentakis, autologous stem cell transplant is as close as medicine comes to a miracle cure. For more and more autoimmune diseases, in which the body's cells are the cause of a condition, they can also be the cure.