



Has Carl June Found a Key to Fighting Cancer? - - Philadelphia Magazine (PA) - August 1, 2013

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What's your full name?

Where are you?

What month is it?

What day of the week is it?

Walter Keller tried to speak, but no words came out, only a dry rasp. The man asking the questions had dark, close-cropped gray hair and a kind, level gaze.

Eventually the man left the room. Walt wriggled up in his bed. Someone put a hand on his shoulder and pressed him gently back into the mattress.

Walt—tall and rawboned, with marbly green eyes and muscles hardened by a lifetime of physical labor—tried to elevate himself. An earsplitting noise went off. A nurse came running in and told him to get back down. When she left, Walt found that the nurses had clipped an alarm to his bed that would alert them whenever he tried to get up. He ripped it off and threw it to the ground.

The man was back:

What's your full name?

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Walt had to get out of this room. He had a baseball game to coach, over at the ball field in Upland, California. The Upland Pony Giants were waiting for him. Michael was waiting, the skinny kid with the cannon arm, and Cody, the kid who could steal two bases on one pitch. The game was starting in five minutes—didn't anyone understand that?

Walt glanced to his side and saw his 19-year-old son, Dustin. Dustin was here, thank God. Dustin would listen.

“Dustin, get my shoes,” Walt croaked. “Dustin, I have to get out of here. I’ll give you a ride on the boat.”

Walt knew his boat was right outside the door of the room—the wakeboard boat he drove every year up and down Lake Mohave in Nevada, giving water-ski rides to his grandkids. His boat was right here at the hospital. If he could only make it out of the bed, to the door, he could climb into the boat and drive it back to his house.

Dustin shook his head: broad shoulders, soft voice, cherubic face, dark brown hair.

“Dustin,” Walt said, eyes soaked with confusion, “you are infuriating me.”

Walt wasn’t in California, as he thought. He was 2,700 miles east, in **Philadelphia**, where he’d come to be a guinea pig in a test of a new kind of cancer treatment. Leukemia had invaded his bone marrow and spread like a stain through his lymph nodes; the traditional options, including chemo and radiation, had failed. He was 58, and his body groaned with tumors potentially weighing as much as seven pounds. Walt needed something radically different if he was going to live. And the treatment he’d been given a few days ago was certainly that.

Over the past several years, a couple of hundred mice had received it, but Walt was only the seventh adult human. (Six men had preceded him, as well as a six-year-old girl.) The treatment wasn’t a chemo drug, and it wasn’t a vaccine. Instead, doctors at the University of Pennsylvania had tried to make Walt’s own body the drug. In an approach known as gene therapy, they’d taken his own immune cells, modified them to give them new powers, and injected them back into his blood.

Gene therapy represents a break from the medical past. Like open-heart surgery, antibiotics and low-cost medical imaging, it’s a “disruptive” technology capable of changing the way doctors do business. It could transform how we treat many types of cancers in people of all ages—if it can be made to work. But that’s the problem. Before this trial at Penn—a Phase 1 trial, the earliest possible human test of a new treatment—gene therapy had scarcely worked in cancer, anywhere in the world. A typical gene-therapy experiment in cancer was as exciting as a sip of warm tea. Nothing happened, good or bad. In other kinds of gene-therapy trials, there had been tragedies: At Penn in 1999, in a trial run by doctors unrelated to the team treating Walt, a teenager with an inherited liver disease had died after a gene-therapy infusion sparked a runaway reaction.

But Walt’s doctors had done things differently than past scientists. Their approach was original and

new. And, incredibly, they'd already succeeded in making tumors vanish in a few of the patients who'd come before Walt. Using their custom technology, the Penn physicians had jolted two cancer-riddled men into sudden apparent remission—an outcome dramatic enough to earn mentions on TV news and a write-up in the New York Times. In September 2011, the paper described Penn's work as "a turning point in the long struggle to develop effective gene therapies against cancer."

But now, eight months later, at the Hospital of the University of Pennsylvania, something dramatic was happening inside Walter Keller's body—a riot of cells and signals. His blood pressure had crashed, so doctors had pumped him full of fluid to raise it, and the fluid had blown up his neck like a balloon. Socks were wrapped around his bloated legs to help with blood circulation. His kidneys were failing. He shook at times with "the rigors," excruciating full-body shivers that made his whole body feel the way his heart would if he had just run up a huge hill.

Scientists don't talk about "curing" cancer. A cure is the hope so great, so seemingly out of reach, that it must never be invoked. They've built a wall around the word. Still, the Penn researchers—as careful as they were, as professionally sober and skeptical—couldn't help but wonder: Was their small experiment the start of something that could one day affect thousands, tens of thousands, more? Was it revealing a secret about the human body that could point the way to treatments for other cancers, not just leukemia? There was no way to know until they gathered more data. They needed to show that the therapy was safe. And they needed to prove that the early patients—the men whose tumors they'd blasted away—weren't flukes.

Which is why so much now depended on Walter Keller. If Walt's condition improved and his tumors diminished, the trial would move forward, and the potential of the Penn therapy—the result of a decades-long quest of scientific passion and discovery—would continue to grow. But if he suffered harm, Penn would have to pause the trial and maybe stop it altogether. Then everything would spiral down. Other scientists would argue that gene therapy was a dead end. Funding would dry up; research would wither. The Penn doctors might never get another chance to prove the merits of their idea, and we might all lose out. It had taken 20 years to get to this point, and it could all be over in the space of a few moments.

1996, Bethesda, Maryland

Captain Carl June had a way of making science seem almost mischievous—something in the curl of his lip, the folding of his hands in his lap. He was an intense character even by the standards of the U.S. Navy medical community, which tended to attract driven personalities. He'd played football as a younger man. He was 42 now and ran ultra-marathons; his calves were like titanium rods.

He directed a research lab on a Navy medical campus. The main goal of his lab was to make the

human immune system do things it hadn't evolved to do. Improve it. "Put it on steroids," he liked to say.

June had a tinkerer's temperament, a fascination with inventing tools to make new kinds of inventions possible. Some of this he had absorbed from his father, a chemical engineer in the San Francisco Bay area. As a kid, June planned to go into science, but then the Vietnam War came, he enlisted in 1971 and received a congressional appointment to Annapolis. He trained for a time as a sailor on a nuclear sub. "Very cool technology," June would later recall. "And then the war was over, so they said, 'You don't have to do this stuff. You can go to medical school.' So I did that, and it was cool." After med school, the Navy sent June to Seattle to learn how to perform bone-marrow transplants. If there ever was a radiation leak on a sub, the Navy would need doctors to give the sailors new immune systems, which is essentially what a bone-marrow transplant does. The procedure saves lives, but at considerable risk; it's estimated to kill one in five. June saw heroic transformations as well as tragic deaths.

Now, in his Bethesda lab, June mostly studied HIV, the virus that causes AIDS. It was another lens for looking at the immune system, its powers and limitations. HIV is so insidious because it infects the very immune cells, called "T cells," that would normally kill it. June wanted to know everything about T cells. But it was hard to study them, because it was hard to grow them in the lab. So June created a better way. Working with a quiet, meticulous researcher named Bruce Levine, June discovered that he could coat artificial beads with proteins that mimicked the natural cells that normally coax T cells to divide. The beads, round and about half the size of a cell, were made partly of iron; when you wanted to use the T cells that had grown, you just passed the cells and beads over a magnet. The beads got stuck on the magnet, and the cells flowed through.

June enjoyed his work at the Navy, and peers across the country respected his creativity—"a real genius," Laurence Cooper, an immunologist at the University of Texas MD Anderson Cancer Center, calls him—but by 1996, he'd begun to feel restless. The Navy only funded research into infectious diseases like HIV, and he wanted to study cancer. His wife, Cynthia, had recently been diagnosed with ovarian cancer. They had three kids in high school and college. June wanted to use what he'd learned about the immune system to tackle the disease. And more than that, he wanted to find a way to get his ideas out of the lab and into the wider world of suffering and need.

June retired from the Navy in 1996. For the next three years, he continued working in the same lab as a civilian, employed by a foundation, while caring for his wife as she endured chemo. "I learned a lot about being on the other side of a bed," June says, "and what it's like going through the ups and downs of cancer therapy. I had no idea of the impact."

In 1999, Penn offered June a prestigious appointment at its medical school. It was the chance he'd

been waiting for. He moved to Philly, bringing Levine with him, and launched a new lab to translate basic science into drugs that could be commercialized, including cancer drugs. Meanwhile, Levine began to build a pilot facility that could produce drugs and vaccines in small batches: the Clinical Cell and Vaccine Production Facility. It was like a biotech company in miniature. In 2005, Levine scaled it up, moving into a warren of renovated lab space in a hospital building off Spruce Street.

Some of its first creations were custom cancer vaccines for the benefit of June's wife. "She wanted to go for the home run," June recalls. She wanted to see her kids grow up. He was sympathetic, of course; in her place, he'd have wanted the same. But in talking to some of his colleagues about risk, June came to realize that not everyone would. "Some people are not risk-takers at all," he says. For the first time in his career, June was forced to think about what it really meant, on a human level, to become a guinea pig in a cutting-edge medical trial—or to turn down that chance. What's more rational? To fight, or to accept your fate with grace?

The vaccines didn't work well enough to save Cynthia June. After five years of treatment, including two bone-marrow transplants, she died in 2001.

1996, Upland, California

Robin was on the phone. She was down at nearby Ralphs supermarket, where she worked checkout. The union had brought one of those mobile health vans to the store. Walt should come get a physical exam, she said. Why not? It was free.

To humor his wife, Walt drove to Ralphs and climbed into the van. He gave a sample of his blood. A few days later, he picked up the phone. "There's something wrong with your blood," a voice said. "We're praying for you."

Leukemia. Walt, it turned out, had the most common type: chronic lymphocytic leukemia, or CLL. Walt had always worried he might get cancer one day—his father had died of non-Hodgkin's lymphoma, and Walt had spent decades sucking down wood-stain fumes in his job as a cabinet refinisher—but still, the diagnosis felt like an ambush. At 43, he was scared of losing everything he'd built. He'd come so far from the little house in neighboring Montclair, where he'd grown up poor and afraid.

One day when Walt was 14, his stepfather burst through the door, carrying a gun. He told Walt not to move. He grabbed Walt's mother around the waist and pushed her out into the side yard. Walt heard a gunshot, then two more. He went into the yard. His stepfather and mother were both splayed out on the ground. The man had shot her, then shot himself. Walt stood there in shock. His mother was bleeding from her nose and ears. He went back into the house, got a pillow from his room, and put it

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