

Illegal, Immoral, and Deplorable

As HeLa grew like crabgrass in laboratories around the world, a virologist named Chester Southam had a frightening thought: What if Henrietta's cancer cells could infect the scientists working on them? Gey and several others had already shown that some rats grew tumors when injected with live HeLa. Why not humans?

Researchers were breathing in the air around HeLa cells, touching them and transferring them from vial to vial, even eating lunch at lab tables beside them. One had used them to grow a vaccine for a common cold-like virus, which he'd injected—along with bits of HeLa—into more than four hundred people. Yet no one knew whether a person could actually catch cancer from HeLa or other cancer cells.

"There is the possible danger," Southam wrote, "of initiating neoplastic disease by accidental inoculation during laboratory investigation, or by injection with such cells or cell products if they should be used for production of virus vaccine."

Southam was a well-respected cancer researcher and chief of virology at Sloan-Kettering Institute for Cancer Research. He and many

other scientists believed that cancer was caused by either a virus or an immune system deficiency, so Southam decided to use HeLa to test those theories.

In February 1954, Southam loaded a syringe with saline solution mixed with HeLa. He slid the needle into the forearm of a woman who'd recently been hospitalized for leukemia, then pushed the plunger, injecting about five million of Henrietta's cells into her arm. Using a second needle, Southam tattooed a tiny speck of India ink next to the small bump that formed at the HeLa injection site. That way, he'd know where to look when he reexamined the woman days, weeks, and months later, to see if Henrietta's cancer was growing on her arm. He repeated this process with about a dozen other cancer patients. He told them he was testing their immune systems; he said nothing about injecting them with someone else's malignant cells.

Within hours, the patients' forearms grew red and swollen. Five to ten days later, hard nodules began growing at the injection sites. Southam removed some of the nodules to verify that they were cancerous, but he left several to see if the patients' immune systems would reject them or the cancer would spread. Within two weeks, some of the nodules had grown to two centimeters—about the size of Henrietta's tumor when she went in for her radium treatments.

Southam eventually removed most of the HeLa tumors, and those he didn't remove vanished on their own in a few months. But in four patients, the nodules grew back. He removed them, but they returned again and again. In one patient, Henrietta's cancer cells metastasized to her lymph nodes.

Since those patients had all had cancer to begin with, Southam wanted to see how healthy people reacted to the injections, for comparison's sake. So, in May 1956, he placed an ad in the Ohio State Penitentiary newsletter: *Physician seeks 25 volunteers for cancer research*. A few days later he had ninety-six volunteers, which quickly increased to 150.

He chose the Ohio prison because its inmates had cooperated in several other studies without resistance, including one in which they'd

been infected with a potentially deadly disease called tularemia. Research on inmates would come under scrutiny and start being heavily regulated about fifteen years later, because they'd be considered a vulnerable population unable to give informed consent. But at the time, prisoners nationwide were being used for research of all kinds—from testing chemical warfare agents to determining how X-raying testicles affected sperm count.

Southam began injecting prisoners in June 1956 using HeLa cells that his colleague, Alice Moore, carried from New York to Ohio in a handbag. Sixty-five prisoners—murderers, embezzlers, robbers, and forgers—lined up on wooden benches for their injections. Some wore white hospital garb; others came off work gangs wearing blue dungarees.

Soon tumors grew on the prisoners' arms just as they'd grown in the cancer patients. The press ran story after story about the brave men at the Ohio Penitentiary, praising them as "the first healthy human beings ever to agree to such rigorous cancer experiments." They quoted one man saying, "I'd be lying if I said I wasn't worried. You lie there on your bunk knowing you've got cancer in your arm. . . . Boy, what you think about!"

Again and again reporters asked, "Why did you volunteer for this test?"

The prisoners' replies were like a refrain: "I done a girl a great injustice, and I think it'll pay back a little bit what I did to her."

"I believe the wrong that I have done, in the eyes of society, this might make a right on it."

Southam gave multiple cancer cell injections to each prisoner, and unlike the terminally ill patients, those men fought off the cancer completely. And with each new injection, their bodies responded faster, which seemed to indicate that the cells were increasing the inmates' immunity to cancer. When Southam reported his results, the press hailed them as a tremendous breakthrough that could someday lead to a cancer vaccine.

In the coming years, Southam injected HeLa and other living cancer cells into more than six hundred people for his research, about half

of them cancer patients. He also began injecting them into every gynecologic surgery patient who came to Sloan-Kettering's Memorial Hospital or its James Ewing Hospital. If he explained anything, he simply said he was testing them for cancer. And he believed he was: Since people with cancer seemed to reject the cells more slowly than healthy people did, Southam thought that by timing the rejection rate, he might be able to find undiagnosed cases of cancer.

In a statement he'd later repeat again and again during hearings about his research, Southam wrote, "It is, of course, inconsequential whether these are cancer cells or not, since they are foreign to the recipient and hence are rejected. The only drawback to the use of cancer cells is the phobia and ignorance that surrounds the word *cancer*."

Because of that "phobia and ignorance," Southam wrote, he didn't tell patients the cells were cancerous because he didn't want to cause any unnecessary fear. As he would say, "To use the dreaded word 'cancer' in connection with any clinical procedure on an ill person is potentially deleterious to that patient's well-being, because it may suggest to him (rightly or wrongly) that his diagnosis is cancer or that his prognosis is poor. . . . To withhold such emotionally disturbing but medically nonpertinent details . . . is in the best tradition of responsible clinical practice."

But Southam wasn't their doctor, and he wasn't withholding up-setting health information. The deception was for his benefit—he was withholding information because patients might have refused to participate in his study if they'd known what he was injecting. And Southam probably would have continued doing this for years had he not made an arrangement on July 5, 1963, with Emanuel Mandel, director of medicine at the Jewish Chronic Disease Hospital in Brooklyn, to use the hospital's patients for his research.

The plan was that Mandel would have doctors on his staff inject twenty-two JCDH patients with cancer cells for Southam. But when he instructed his staff to give the injections without telling patients they contained cancer cells, three young Jewish doctors refused, saying they wouldn't conduct research on patients without their consent.

All three knew about the research Nazis had done on Jewish prisoners. They also knew about the famous Nuremberg Trials.

Sixteen years earlier, on August 20, 1947, a U.S.-led war tribunal in Nuremberg, Germany, had sentenced seven Nazi doctors to death by hanging. Their crime was conducting unthinkable research on Jews without consent—sewing siblings together to create Siamese twins, dissecting people alive to study organ function.

The tribunal set forth a ten-point code of ethics now known as the Nuremberg Code, which was to govern all human experimentation worldwide. The first line in that code says, "The voluntary consent of the human subject is absolutely essential." The idea was revolutionary. The Hippocratic Oath, written in the fourth century BC, didn't require patient consent. And though the American Medical Association had issued rules protecting laboratory animals in 1910, no such rules existed for humans until Nuremberg.

But the Nuremberg Code—like other codes that would come after it—wasn't law. It was, essentially, a list of recommendations. It wasn't routinely taught in medical schools, and many American researchers—including Southam—claimed not to know it existed. Those who did know about it often thought of it as "the Nazi code," something that applied to barbarians and dictators, not to American doctors.

When Southam began injecting people with HeLa cells in 1954, there was no formal research oversight in the United States. Since the turn of the century, politicians had been introducing state and federal laws with hopes of regulating human experimentation, but physicians and researchers always protested. The bills were repeatedly voted down for fear of interfering with the progress of science, even though other countries—including, ironically, Prussia—had enacted regulations governing human research as early as 1891.

In the United States, the only way to enforce research ethics was in the civil courts. There, lawyers could use the Nuremberg Code to

establish whether a scientist was acting within the ethical boundaries of the profession. But taking a researcher to court required money, know-how, and the knowledge that you were being used for research in the first place.

The term *informed consent* first appeared in court documents in 1977, in a civil court ruling on the case of a patient named Martin Salgo. He went under anesthesia for what he thought was a routine procedure and woke up permanently paralyzed from the waist down. The doctor hadn't told him the procedure carried any risks at all. The judge ruled against the doctor, saying, "A physician violates his duty to his patient and subjects himself to liability if he withholds any facts which are necessary to form the basis of an intelligent consent by the patient to the proposed treatment." He wrote that there needed to be "full disclosure of facts necessary to an informed consent."

Informed consent focused on what doctors were required to tell their patients; there was little mention of how it might apply to research like Southam's, in which subjects weren't the researcher's patients. And it would be decades before anyone thought to ask whether informed consent should apply in cases like Henrietta's, where scientists conduct research on tissues no longer attached to a person's body.

But to the three doctors who refused to help with Southam's research, injecting cancer cells into a person without consent was a clear violation of basic human rights and the Nuremberg Code. Mandel didn't see it that way. He had a resident give the injections in their place, and on August 27, 1963, the three doctors wrote a resignation letter citing unethical research practices. They sent it to Mandel and at least one reporter. When Mandel got the letter, he called a meeting with one of the doctors, and accused them of being overly sensitive because of their Jewish ancestry.

One member of the hospital's board of directors, a lawyer named William Hyman, didn't think they were being overly sensitive. When he heard about the doctors' resignation, he asked to see the records of patients in the study. But his request was denied. Meanwhile, just days

after the doctors resigned, the *New York Times* ran a tiny news item deep in the paper under the headline SWEDEN PENALIZES CANCER SPECIALIST, about a cancer researcher named Bertil Björklund. He'd been giving himself and patients intravenous injections of vaccines made from HeLa cells, which he'd gotten from George Gey's lab in such enormous quantities, they joked that instead of injecting them, Björklund could just fill a pool with HeLa—or maybe even a lake—and swim around in it for immunity. Björklund's HeLa injections got him expelled from his laboratory, and Hyman hoped for similar results with Southam. So, in December 1963 he sued the hospital for access to medical records related to the study.

Hyman compared Southam's study to Nazi research and got affidavits from the three doctors who'd resigned—they described Southam's research using words like *illegal*, *immoral*, and *deplorable*. Hyman also got an affidavit from a fourth doctor explaining that the patients in the study wouldn't have been capable of giving informed consent even if Southam had asked: one had advanced Parkinson's disease and couldn't talk, others spoke only Yiddish, one had multiple sclerosis and "depressive psychosis." Regardless, Hyman wrote, "I was informed that consent was not necessary . . . that it was unlikely that Jewish patients would agree to live cancer cell injections."

That caught the media's attention. The hospital called the suit "misleading and fallacious." But newspapers and magazines ran headlines saying:

**PATIENTS INJECTED WITH CELLS NOT TOLD THEY
WERE CANCER . . . SCIENTIFIC EXPERTS CONDEMN
ETHICS OF CANCER INJECTION**

They said the Nuremberg Code didn't seem to apply in the United States, and that there were no laws protecting research subjects. *Science* magazine called it "the hottest public debate on medical ethics since the Nuremberg trials," and said, "The situation at present appears rather perilous for everyone." A reporter from *Science* asked

Southam why, if the injections were as safe as he swore they were, he didn't inject himself.

"Let's face it," Southam responded, "there are relatively few skilled cancer researchers, and it seemed stupid to take even the little risk."

Patients who'd unknowingly been injected with cancer cells by Southam read the articles and began contacting reporters. New York State Attorney General Louis Lefkowitz learned about Southam's research through the media as well, and immediately launched his own investigation. In a scathing five-page document filled with exclamation points, he accused Southam and Mandel of fraud and unprofessional conduct, and demanded that the Board of Regents of the University of the State of New York revoke their medical licenses. Lefkowitz wrote, "Every human being has an inalienable right to determine what shall be done with his own body. These patients then had a right to know . . . the contents of the syringe: and if this knowledge was to cause fear and anxiety or make them frightened, they had a right to be fearful and frightened and thus say NO to the experiment."

Many doctors testified before the Board of Regents and in the media on Southam's behalf, saying they'd been conducting similar research for decades. They argued that it was unnecessary to disclose all information to research subjects or get consent in all cases, and that Southam's behavior was considered ethical in the field. Southam's lawyers argued, "If the whole profession is doing it, how can you call it 'unprofessional conduct'?"

This rattled the Board of Regents. On June 10, 1965, its Medical Grievance Committee found Southam and Mandel guilty of "fraud or deceit and unprofessional conduct in the practice of medicine" and recommended that their medical licenses be suspended for one year. The Board wrote, "There is evidenced in the record in this proceeding an attitude on the part of some physicians that they can go ahead and do anything . . . and that the patient's consent is an empty formality. With this we cannot agree."

Their decision called for more specific guidelines in clinical re-

search, saying, "We trust that this measure of discipline will serve as a stern warning that zeal for research must not be carried to the point where it violates the basic rights and immunities of a human person."

The suspensions of Southam's and Mandel's licenses were stayed, leaving them both on one-year probation instead. And the case seemed to have little impact on Southam's professional standing: soon after the end of his probationary period, Southam was elected president of the American Association for Cancer Research. But his case brought about one of the largest research oversight changes in the history of experimentation on humans.

Before the Board of Regents announced its decision, the negative press about Southam's work had gotten the attention of the NIH, which funded his research and required its investigators to get consent for all studies involving humans. In response to the Southam situation, the NIH investigated all their grantee institutions and found that only nine out of fifty-two had any policy in place to protect the rights of research subjects. Only sixteen used consent forms. The NIH concluded: "In the setting in which the patient is involved in an experimental effort, the judgment of the investigator is not sufficient as a basis for reaching a conclusion concerning the ethical and moral set of questions in that relationship."

As a result of its investigation, the NIH said that to qualify for funding, all proposals for research on human subjects had to be approved by review boards—independent bodies made up of professionals and laypeople of diverse races, classes, and backgrounds—to ensure that they met the NIH's ethics requirements, including detailed informed consent.

Scientists said medical research was doomed. In a letter to the editor of *Science*, one of them warned, "When we are prevented from attempting seemingly innocuous studies of cancer behavior in humans . . . we may mark 1966 as the year in which all medical progress ceased."

Later that year, a Harvard anesthesiologist named Henry Beecher

published a study in the *New England Journal of Medicine* showing that Southam's research was only one of hundreds of similarly unethical studies. Beecher published a detailed list of the twenty-two worst offenders, including researchers who'd injected children with hepatitis and others who'd poisoned patients under anesthesia using carbon dioxide. Southam's study was included as example number 17.

Despite scientists' fears, the ethical crackdown didn't slow scientific progress. In fact, research flourished. And much of it involved HeLa.