The Mind of a Disease

By JONATHAN WEINER

THE EMPEROR OF ALL MALADIES

A Biography of Cancer

By Siddhartha Mukherjee

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All patients begin as storytellers, the oncologist Siddhartha Mukherjee observes near the start of this powerful and ambitious first book. Long before they see a doctor, they become narrators of suffering, as Mukherjee puts it — travelers who have visited the "kingdom of the ill."

Many doctors become storytellers too, and Mukherjee has undertaken one of the most extraordinary stories in medicine: a history of cancer, which will kill about 600,000 Americans by the end of this year, and more than seven million people around the planet. He frames it as a biography, "an attempt to enter the *mind* of this immortal illness, to understand its personality, to demystify its behavior." It is an epic story that he seems compelled to tell, the way a passionate young priest might attempt a biography of Satan.

Mukherjee started on the road to this book when he began advanced training in cancer medicine at the Dana-Farber Cancer Institute in Boston in the summer of 2003. During his first week, a colleague who'd just completed the program took him aside. "It's called an immersive training program. But by immersive, they really mean drowning," he said, lowering his voice the way many of us do when we speak of cancer itself. "Have a life outside the hospital," the doctor warned him. "You'll need it, or you'll get swallowed."

"But it was impossible not to be swallowed," Mukherjee writes. At the end of every evening he found himself stunned and speechless in the neon floodlights of the hospital parking lot, compulsively trying to reconstruct the day's decisions and prescriptions, almost as consumed as his patients by the dreadful rounds of chemotherapy and the tongue-twisting names of the drugs, "Cyclophosphamide, cytarabine, prednisone, asparaginase. . . ."

Eventually he started this book so as not to drown.

The oldest surviving description of cancer is written on a papyrus from about 1600 B.C. The hieroglyphics record a probable case of breast cancer: “a bulging tumor . . . like touching a ball of wrappings.” Under “treatment,” the scribe concludes: “none.”

For more than 2,000 years afterward, there is virtually nothing about cancer in the medical literature (“or in any other literature,” Mukherjee adds.) The modern understanding of the disease originated with the recognition, in the first half of the 19th century, that all plants and animals are made of cells, and that all cells arise from other cells. The German researcher Rudolph Virchow put that in Latin: *omnis cellula e cellula*.

Cancer is a disease that begins when a single cell, among all the trillions in a human body, begins to grow out of control. Lymphomas, leukemias, malignant melanomas, sarcomas all begin with that microscopic accident, a mutation in one cell: *omnis cellula e cellula e cellula*. Cell growth is the secret of living, the source of our ability to build, adapt, repair ourselves; and cancer cells are rebels among our own cells that outrace the rest. “If we seek immortality,” Mukherjee writes, “then so, too, in a rather perverse sense, does the cancer cell.”

Mukherjee opens his book with the story of one of the founders of the hospital where he trained — Sidney Farber, a specialist in children’s diseases who began as a pathologist. In 1947, Farber worked in a tiny, dank laboratory in Boston, dissecting specimens and performing autopsies. He was fascinated by a sharklike species of cancer called acute lymphoblastic leukemia, which can move so fast that it kills an apparently healthy child within only a few days. A patient would be “brought to the hospital in a flurry of excitement, discussed on medical rounds with professorial grandiosity” and then sent home to die.

In the summer of 1947, a 2-year-old boy, the child of a Boston shipyard worker, fell sick. Examining a drop of the baby’s blood through the microscope, Farber saw the telltale signs of acute lymphoblastic leukemia, billions of malignant white cells “dividing in frenzy, their chromosomes condensing and uncondensing, like tiny clenched and unclenched fists.” By December, the boy was near death. In the last days of the year, Farber injected his patient with an experimental drug, aminopterin, and within two weeks he was walking, talking and eating again. It wasn’t a cure, only a remission; but for Farber it was the beginning of a dream of cures, of what one researcher called “a penicillin for cancer.”

The next year, Farber helped start a research fund drive around a boy who suffered from a lymphoma in his intestines, a disease that killed 90 percent of its victims. The boy was

cherubic and blond, an enormous fan of the Boston Braves, and his name was Einar Gustafson. For the sake of publicity, Farber rechristened him Jimmy. That May, the host of the radio show "Truth or Consequences" interrupted his usual broadcast to bring his listeners into Jimmy's hospital room to listen in as players on the Braves marched into Jimmy's room and sang "Take Me Out to the Ball Game."

By the summer of 1952, Farber had built an imposing new hospital, Jimmy's Clinic. Soon, he was working on an even grander scale, with the help of an extraordinary socialite and medical philanthropist, Mary Lasker. ("I am opposed to heart attacks and cancer," she once told a reporter, "the way one is opposed to sin.") Mary and her husband, Albert, an advertising executive, joined forces with Farber. They wanted, as Mukherjee writes, "a Manhattan Project for cancer." Together, through masterly advertising, fund-raising and passion for their common cause ("The iron is hot and this is the time to pound without cessation," Farber wrote to Mary Lasker), they maneuvered the United States into what would become known as the war on cancer. Richard Nixon signed it into law with the National Cancer Act in 1971, authorizing the spending of $1.5 billion of research funds over the next three years.

In political terms, the war was well timed, coming at a time when America's collective nightmares were no longer "It Came From Outer Space" or "The Man From Planet X," but "The Exorcist" and "They Came from Within." Mary Lasker called the war on cancer the country's next moon shot, the conquest of inner space.

In scientific terms, however, the war was disastrously premature. The moon race had been based on rocket science. But in the early 1970s, there really wasn't a science of cancer. Researchers still did not understand what makes cells turn malignant. Now that they were so much in the spotlight, and in the money, they fell into bickering, demoralized, warring factions. The "iconic battleground" of the time was the chemotherapy ward, Mukherjee writes, "a sanitized vision of hell." Typically it was a kind of limbo, almost a jail, in which absolutely no one spoke the word "cancer," the inmates' faces had an orange tinge from the drugs they were given, and windows were covered with heavy wire mesh to keep them from committing suicide. "The artifice of manufactured cheer (a requirement for soldiers in battle) made the wards even more poignantly desolate," Mukherjee writes.

"The Emperor of All Maladies" is a history of eureka moments and decades of despair. Mukherjee describes vividly the horrors of the radical mastectomy, which got more and more radical, until it arrived at "an extraordinarily morbid, disfiguring procedure in which

surgeons removed the breast, the pectoral muscles, the axillary nodes, the chest wall and occasionally the ribs, parts of the sternum, the clavicle and the lymph nodes inside the chest." Cancer surgeons thought, mistakenly, that each radicalization of the procedure was progress. "Pumped up with self-confidence, bristling with conceit and hypnotized by the potency of medicine, oncologists pushed their patients — and their discipline — to the brink of disaster," Mukherjee writes. In this army, "lumpectomy" was originally a term of abuse.

Meanwhile, more Americans were dying of cancer than ever, mainly because of smoking. Back in 1953, the average adult American smoked 3,500 cigarettes a year, or about 10 a day. Almost half of all Americans smoked. By the early 1940s, as one epidemiologist wrote, "asking about a connection between tobacco and cancer was like asking about an association between sitting and cancer." In the decade and a half after Nixon declared his war on cancer, lung cancer deaths among older women increased by 400 percent. That epidemic is still playing itself out.

Mukherjee is good on the propaganda campaign waged by the tobacco companies, "the proverbial combination of smoke and mirrors." As one internal industry report noted in 1969, "Doubt is our product, since it is the best means of competing with the 'body of fact.' " This episode makes particularly interesting reading to anyone following the current propaganda campaigns against the science of climate change.

Meanwhile, those who studied the causes of cancer in the laboratories and those who treated it in the clinics were not always talking to each other. As Mukherjee puts it, "The two conversations seemed to be occurring in sealed and separate universes." The disease was hard to understand either intellectually, in the lab, or emotionally, in the clinic. In the lab, because it is so heterogeneous in its genetics and its migrations in the body. In the hospital, because its course is horrible and so often slow, drawn out. When it comes to cancer, Mukherjee writes, "*dying*, even more than death, defines the illness."

Mukherjee stitches stories of his own patients into this history, not always smoothly. But they are very strong, well-written and unsparing of himself: "Walking across the hospital in the morning to draw yet another bone-marrow biopsy, with the wintry light crosshatching the rooms, I felt a certain dread descend on me, a heaviness that bordered on sympathy but never quite achieved it."

The heroes of the last few decades of this epic history are Robert Weinberg, Harold Varmus, Bert Vogelstein and the other extraordinary laboratory scientists who have finally worked

out the genetics of cancer, and traced the molecular sequence of jammed accelerators and missing brakes that release those first rebel cells. As James Watson wrote not long ago, “Beating cancer now is a realistic ambition because, at long last, we largely know its true genetic and chemical characteristics.” We may finally be ready for war.

As a clinician, Mukherjee is only guardedly optimistic. One of the constants in oncology, as he says, is “the queasy pivoting between defeatism and hope.” Cancer is and may always be part of the burden we carry with us — the Greek word *onkos* means “mass” or “burden.” As Mukherjee writes, “Cancer is indeed the load built into *our* genome, the leaden counterweight to our aspirations for immortality.” But *onkos* comes from the ancient Indo-European *nek,* meaning to carry the burden: the spirit “so inextricably human, to outwit, to outlive and survive.” Mukherjee has now seen many patients voyage into the night. “But surely,” he writes, “it was the most sublime moment of my clinical life to have watched that voyage in reverse, to encounter men and women *returning* from that strange country— to see them so very close, clambering back.”

Jonathan Weiner is the Maxwell M. Geffen professor of medical and scientific journalism at Columbia University. His latest book is “Long for This World: The Strange Science of Immortality.”