

# Mario's Story

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## CHAPTER ONE

# The First Hours

That late Saturday afternoon in early May 1999 was gray and cold, and the emergency room at Children's Hospital in Boston was becoming hectic as it filled with the pediatric overflow of neighborhood health centers and private practice offices already closed for the day. Mothers lugging their sick children along with healthy siblings crammed into cubicles to talk to the triage nurse, the gatekeeper who would decide whether a child would languish in the reception area for most of the evening as a low-priority case or be deemed sick enough to come into the emergency area itself to wait in a cramped bed space for the first available physician. The mothers didn't complain. This was just one of the many nights some of them regularly spent in that well-worn reception space. Several were single mothers of a clutch of children. The whole family accompanied the sick one to spend the evening watching TV, guzzling soft drinks, and waiting for a doctor. This is the health care system for the uninsured. But overstressed urban teaching hospitals serve inconvenience with equal opportunity. The parents and children of the well-to-do languished as well, if they were deemed healthy enough to wait.

Mario, a nineteen-month-old, his mother, Flavia, and her mother-in-law had already spent most of a horrible afternoon in a pediatrician's office across the street. There, numbed with fear and shock, Flavia had been told to take Mario directly to the emergency room for immediate admission to the hospital.

She and her husband, Walter, were just barely keeping their heads above water. They were both immigrants, albeit from upper-middle-class Italian and Austrian families. Flavia's father was the regional manager of an express delivery company based in Milan. Walter's father was

a successful manufacturer in Vienna. Flavia and Walter had yearned to be educated in the United States. Flavia wanted to become a commercial artist and Walter a marketing manager. They met in a community college in New York and shortly thereafter began to live together in Boston, where they started their careers. They married, and Flavia became pregnant. Mario's birth was difficult and resulted in mild nerve injury to his right arm, but he slowly recovered. Flavia actually brought him as a neonate to Children's Hospital for an evaluation of his arm, never dreaming that she would soon be spending months living there with her son.

The first year and a half of their new parenthood went reasonably well. Flavia has a creative flair for her work, and her list of private clients was growing. Walter had a harder time finding what he wanted, but just two weeks before the fateful visit to the pediatrician, he had landed a job with benefits, including health insurance, in the marketing department of a local manufacturer.

Around the time that Walter had started his new job, Mario was showing signs of not feeling well. He had no appetite, and walking appeared to exhaust him. After an hour or so of his usual careening around the family's small condominium, he would tire and be forced to rest. He also had a runny nose and a cough that wouldn't go away. Flavia began to take his temperature frequently. Sometimes he had a low-grade fever and would sleep for hours during the day.

For a while, Flavia and Walter thought Mario just had a stubborn virus. But the lack of appetite bothered them. Flavia took Mario to the pediatrician's office, where the nurse practitioner examined him carefully. Mario appeared fine. He looked healthy. Confident in the nurse practitioner, the pediatrician spent only a few minutes with Mario. She suggested acetaminophen (Tylenol) for the intermittent fever.

A week or two later, Flavia and Walter noticed scattered red spots on Mario's legs. This time, the pediatrician examined Mario and saw the spots, which measured less than an eighth of an inch in diameter. The doctor concluded that they represented a rash that often accompanies a viral infection. Again, she advised Tylenol for the fever, and she told Flavia to bring Mario back if anything new turned up.

What turned up was Walter's mother. She took one look at her grandson and bundled him up for another trip to the pediatrician's office. While Mario slept in his mother's lap, the grandmother demanded a blood test. When the nurse objected, she insisted on the test immediately. The

nurse relented, did a finger stick on a howling Mario, and disappeared. A few minutes later, she reappeared looking haggard and disconcerted.

“We had trouble with the machine,” she lied. “We’ll have to repeat the test.”

Again the finger stick. Again Mario’s torrent of tears. Again the wait.

The pediatrician then appeared and said, “You have to go to Children’s Hospital and be admitted immediately. I will call the emergency room and tell them to make sure you see an emergency physician right away while you wait for a bed to become available.”

“But why?” Flavia asked.

“Keep your energy as much as you can, because you are going to need it,” Mario’s doctor responded. “The senior pediatrician in this practice is going to meet you in the emergency room as soon as he can and explain everything to you, but you must get over there immediately.” With that terrifying warning, the doctor returned to her other patients.

Somehow Flavia absorbed the instructions. She knew she had to hold Mario close and carry him across the street. She blocked out the implications of her pediatrician’s instructions so that she could make that short journey. Even her mother-in-law was silent. Grimly they made their way through the throng of sick and not-so-sick children in the reception area and were waved immediately into the emergency room to wait again. Walter was summoned from his new job as soon as the trio had settled in the cramped room. Flavia sat in a chair with Mario sleeping on her lap.

Flavia thought she was dreaming, but she remembers the details of the scene vividly. She recalls the pediatrician in charge of the practice entering the cramped space. “He was so tall and so skinny. He brought in a chair and turned it around so he could sit and lean forward on the back, and he didn’t beat around the bush. He just said, ‘Mario has leukemia.’” As she listened to the pediatrician, Flavia thought she had been struck down by fate.

The origin of the word *leukemia* is Greek. *Leukos* means “white” and *haima* means “blood.” *Leukemia* means “white blood.”

There are several classes of childhood leukemia based on the cell of origin. The most common class or type arises in lymphocytes, the small,

round white cells that circulate in the blood, lymphatic channels, and lymph nodes and are responsible in part for the control of infection by bacteria, viruses, parasites, and fungi.

In children, the most common subset of lymphocytic leukemia is acute lymphoblastic leukemia (ALL). It usually starts when a single, immature lymphoblast (the most immature precursor of lymphocytes) begins to grow uncontrollably in the bone marrow. Sometimes an enormous mass of cells derived from the original cell fills the marrow, the spleen, the lymph nodes, and the blood. In unusual ALL cases, so many leukemic cells accumulate in the blood that it actually turns white; hence the disease's name. But in most cases, the leukemic cells replace the marrow, where they prevent normal blood cell production and do not accumulate excessively in the circulation.

There are two major subsets of ALL based on the type of lymphocyte in which the leukemia arises. The most common is B-cell ALL. The B-lymphocyte is the producer of antibodies. Less common is T-cell ALL. T-lymphocytes directly kill viruses, fungi, and certain bacteria such as the tuberculosis bacillus.

When Walter heard the diagnosis, he began to laugh and couldn't stop. "You're kidding—what are you talking about?" It wasn't Walter's usual laugh, though. The laugh rose hysterically. Suddenly he turned very pale and fell totally silent for a few seconds. Then Walter collected himself and took charge. "Okay, what do we do now?"

When Walter asked that question, Flavia awakened from her dream-like state. Mario's life was not over today. She had to take action, come up with a plan. Through her desperation, she heard the pediatrician refer to two kinds of leukemia and mention that neither variety is great, but it is much better to learn you have one than the other—the "good" leukemia and the "bad" leukemia, she seemed to hear. She decided that Mario had to have the "good" leukemia. She clutched at that idea and repeated "good leukemia" like a mantra.

The hospital's prosaic boredom, discomforts, and a sense of some organized flow began to replace the terror in her heart. The academic medical center parade of doctors and their attendant medical students began. The intern, followed by the emergency medicine resident, followed by the resident in charge of the house staff on the oncology service; the attending (supervisory) emergency physician; the oncology attending and first-year oncology trainee (the fellow); the intensive care house staff;

the attending in intensive care; and all the nurses, medical students, and ward secretaries associated with them marched through Flavia's life over the next twenty-four hours. Keeping Mario either on her lap or next to her in a transportable bed, she tried to listen and kept repeating "good leukemia."

While Mario was still in the emergency room, several medical staff attempted to draw blood and start an intravenous drip of fluid, but Mario's veins were recalcitrant. Then an expert IV nurse came in with a basket of what looked like Roman candles: needles encased in tubes of plastic. Mario screamed when he saw her, but she eventually succeeded in starting the IV, although leaving bruises. Next came the long trip through X-ray and on to the oncology service, where Mario was put to bed in a room opposite the nurses' station, a site of constant noisy activity but the safest place on the ward because of its proximity to the nurses. Sometime near a restless dawn, Mario was transferred to the intensive care unit. A bed had finally become available. Flavia remembers one particularly kind nurse who saw she was exhausted and asked her if she wanted to lie on the bed with Mario while they were both rolled through the corridors and down the elevator to the unit. She might have fallen asleep for a moment on that voyage.

By this time, Walter had gone home to do an Internet search and read everything he could about leukemia. He prepared himself to call Flavia's client list of commercial art firms and let them know that her presentations would be indefinitely delayed. Walter's mother went with him.

Flavia stayed with Mario and the medical entourage. Out of the crowd of doctors stepped Scott Armstrong, a first-year fellow in oncology. She remembers their first meeting in precise detail. Flavia felt as though she had been drifting in a turbulent sea, drowning in the unexpected wreck of her life. Suddenly a life ring was flung to her from the fog. Holding the rope was Scott. In his inexperience, Scott had no idea of the importance of that moment, but he saved Flavia from profound depression.

Scott Armstrong is an Oklahoma boy. He is not physically big, but he is determined and has a fine mind to boot. Early on, he knew he was destined for science. Chemistry and math fascinated him in high school, and he had good teachers who encouraged him. At the University of Oklahoma, he had a chance to work in relating the latest aspect of

molecular biology to the blood-clotting system. The experience convinced Scott to become a physician scientist committed to a career involving blood-related cancers. That way, he could explore his passion for science and help people at the same time. He entered the M.D./Ph.D. program at University of Texas Southwestern Medical School. Scott worked in the lab of two of the best biomedical research trainers in the business, Michael Brown and Joseph Goldstein, physicians who had won a Nobel Prize for their work on cholesterol metabolism. Scott wasn't particularly interested in cholesterol, but he knew he would learn to be a scientist in that laboratory. Hematological (blood-related) oncology could wait until he completed his residency training.

During his schooling, Scott realized that he wanted to work with sick children. He related to them as friends, wanted to help them, and found his soothing, confident manner was a comfort to agonized parents whose children faced death. He applied for postgraduate pediatric training at Children's Hospital, where I was chief of pediatrics. I received a brief letter about him from Joe Goldstein. The last sentence was, "Just take him, you won't regret it."

My residency program did not regret it. Scott was an excellent addition to the house staff. Cheerful on little sleep and enormously competent, he set a fine record on every rotation. The combined Children's Hospital and Dana-Farber Cancer Institute's program is prestigious, and competition for slots in its hematology oncology fellowship is intense. Scott made the cut in the first round of decisions. He started his first year of fellowship in the July prior to Mario's May admission.

His first patient as a fellow was an eight-month-old infant (by medical definition, infants are children younger than one year old) with leukemia. Scott was particularly challenged by the very rare mixed-lineage leukemias he saw in infants. He learned that older children with the usual ("good") form of acute childhood leukemia (acute lymphoblastic leukemia, or ALL) do very well today. Eighty to eighty-five percent of them are cured of the disease. Scott mastered the art of differentiating that kind from the less common one, acute myeloblastic leukemia (AML), which arises in larger white cells designed to attack and ingest bacteria. This is the "bad" leukemia; its response to treatment, though reasonable, is not as good as the response of children with ALL. Until twenty-five years ago, every such child died; today, about half of children with AML remain disease-free.

Scott introduced himself to Mario's exhausted and frightened mother, speaking warmly and carefully to her. He had already examined Mario, who did not have remarkable physical findings other than the red spots on his legs, and he knew that Mario had a low platelet count. Platelets are responsible for initiating the clotting of blood; hence the small hemorrhagic red spots on Mario's legs. Mario was somewhat anemic as well, but it was the white blood cell count of nearly one million per cubic millimeter of blood (normal is about five thousand) that had prompted the emergency admission and transfer to the intensive care unit. It was difficult to decide whether the swarm of malignant white cells were ALL or AML cells. They formed the classic picture of mixed-lineage leukemia (MLL) seen in infants. Flavia, who was praying for "good" rather than "bad" leukemia, was going to have to face that her son might have a third kind: "terrible" leukemia.

Scott knew he had to be careful in his initial conversations with Flavia. She was alone, exhausted, and extremely vulnerable. Whatever he told her would have to be backed with solid evidence and not conjecture. She immediately pressed him: "Is this the good leukemia?" His answer was that he could not be certain until other laboratory tests were concluded, but in any case, the immediate risk was not the type of leukemia but the very high white blood cell count. The level of leukemia cells in Mario's blood would have to be reduced immediately, for several reasons. The most pressing was that leukemic cells tend to clump. Sticky, sugary proteins on their surfaces, a general characteristic of cancer cells, make them adhere to blood vessel walls and to one another. The result is a plug that can block a major blood vessel and cause a stroke. Mario might not recover from such a crisis. The leukemic cells might also die more rapidly than normal cells. When they die, they burst and release their contents—huge amounts of potassium and phosphorus—into the circulation. The sudden release of that load might stop Mario's heart.

Scott's first action was to perform an exchange transfusion, a procedure in which Mario's blood, with its swarming leukemic cells, would be removed and replaced with normal blood. That would lower his leukemic cell count and avert a crisis. As soon as that exchange occurred, Scott promised to deal with the exact type of leukemia and propose a treatment.

Flavia listened and signed the consent forms after reading them cursorily, but her mind was almost blank. (So much for informed

consent under stress.) She had only three thoughts: Would Mario survive all this? Would he finally become well? Would she have him back again? She couldn't say she really understood Scott's approach, but she trusted him on sight.

Scott mobilized the specialized staff, and the exchange procedure started at once. Leaving Mario in the competent hands of the intensive care people, Scott called Lewis Silverman, a staff physician at Children's Hospital and the Dana-Farber Cancer Institute and an assistant professor at Harvard Medical School, to go over the next steps in what would turn out to be a two-year effort to save Mario.