

Since 1989, more than 10,000 patients with **multiple myeloma** and related disorders have made their way to Little Rock. They've come from near and far, from at home and abroad, because they believe in the revolutionary techniques pioneered by **Dr. Bart Barlogie** in the ongoing fight against the cancer that destroys the **marrow** in their bones. But while there may be some overlap in terms of the **treatment** used and their diagnoses, each person who arrives comes with a different story. They are mothers, fathers, daughters and sons. ¶ This is the story of Annie Mae Nix.

By Paul McDonnold

FAMILIES ARE ABOUT RELATIONSHIPS, and this story is about a family— an exceptional one— the kind you would like to know. Their beginnings trace to a small town, Montevallo, set in a valley in the heart of Alabama during a time of momentous change. Legal racial segregation had ended, presenting a generation of African-Americans with opportunities their forebears hadn't known. Echol Lee Nix was a hardworking young man with his sights set on a better life. Annie Mae Moore was a friendly girl with a warm smile. The two grew up going to the same schools and the same Baptist church. They married young in 1971.

Echol attended college on a football scholarship, graduated with honors, became an officer in the Air Force and went on to a career at the chalkboard and later behind the pulpit. Annie Mae's focus centered on the four children she and Echol had together across a span of some 16 years. She wanted to see them grow into men and women who would carry on values of faith, courage and service to others.

But in Sept. 1994, the entire family's focus shifted dramatically to Annie Mae, when she sat in a Montgomery doctor's office and heard the kind of news that makes your life fall down around you. Cancer was growing in her marrow—the spongy core of her bones.

It was called myeloma, a cancer of the plasma cells found in the marrow, cells whose job is the production of antibodies to fight infections. It was a rare cancer, incurable. And the prognosis was discouraging, to say the least: six months to a year to live. Her doctor admitted he was not an expert on the disease. But he had heard of a place. It was in Arkansas.

First, however, the kids needed to be told. Echol and Annie Mae's oldest child, Pam, was out of school and would soon join the Air Force. Son Echol Jr. was

a burgeoning scholar at Morehouse College. Earnest, "Lil' Bruh" to his siblings, was in the eighth grade. They understood what was now at stake. It was only 6-year-old Keturah who was too young to grasp the import of the word "cancer."

"Is it contagious?" she asked.

At the University of Arkansas for Medical Sciences' Myeloma Institute for Research and Therapy, all the stories begin something like this.



BART BARLOGIE, THE PHYSICIAN-scientist who founded the Myeloma Institute, has been its director for the past 25 years, building it patient by patient into one of the world's leading myeloma centers. Walk into the Institute on any given day, and you'd see some 300 patients there seeking treatment. In 2013, more than 1,100 participated in the Institute's various clinical trials. All told, patients have come from all 50 U.S. states and 58 foreign countries.

Barlogie's office is on the eighth floor of UAMS's Pat Walker Tower. His desk faces a large picture window and balcony. The State Capitol, about two miles east, is plainly visible even on this overcast day. On a bookcase behind the desk, along with weighty medical tomes, sits a black motorcycle helmet, a fitting complement to the red scarf and leather jacket he is wearing.

There is more to Barlogie than meets the eye. His calm manner and friendly smile belie an intense intellect and

drive to succeed. Words flow from him at a tranquil river's pace, propelled by careful thought. They take us back to a time before the Institute existed, some 10,000 patients ago. In 1974, Barlogie was finishing his medical residency in his native Germany, focusing on acute leukemia (cancer of the blood), when he attended a lecture by a physician visiting from M.D. Anderson Cancer Center in Houston, Texas.

The visitor's name was Emil Freireich. Listening to the lecture, Barlogie was hearing one of the major figures in cancer research, who had made his reputation working with childhood leukemia. As detailed in the book *The Emperor of All Maladies*, Freireich had a theory that no single drug could kill all of a patient's cancer; some malignant cells would survive and relapse into a stronger cancer than before. The best approach, then, was to hit the disease with everything you had at the beginning, before malignant cells could develop resistance.

Unfortunately, clinical trials showed this approach

to have a high level of toxicity. Patients sickened and sometimes died from the treatment itself. For patients who survived it, however, the approach also produced deep remissions that stood the test of time. Later researchers would name the protocol Total Therapy and refine it to the point that, today, some forms of childhood leukemia have cure rates of more than 80 percent.

The young, ambitious Barlogie and the older, established Freireich impressed each other, enough that Barlogie agreed to move to America and take a position at M.D. Anderson. It was there that Barlogie would discover his own research niche in the area of myeloma.

"I wanted to know why people wouldn't treat myeloma as a normal [treatable] cancer," he says. At the time, most treatment was palliative—comforting the patient

as they waited to die. But Barlogie didn't want just to comfort patients, he wanted to cure them.

One of the patients who showed up looking for a cure was Walmart founder Sam Walton, who had first come to M.D. Anderson with leukemia. Treatment had put that into remission until he was diagnosed with myeloma in 1989. Barlogie treated Walton, and later that year he accepted a position directing myeloma research for UAMS and moved to Little Rock. In addition to Walton, about 100 of Barlogie's other patients followed him. Compared to those at M.D. Anderson, the new facilities were limited. For one thing, there were not enough private rooms, but that would change over time. The main thing was that Barlogie now had the freedom to pursue his own research agenda: working toward a cure for myeloma.

The first step was already underway. Across the U.S., new combinations of chemo drugs were showing promise against myeloma in clinical trials. The paradigm of "palliative care" was shifting. Barlogie pushed it further by pioneering the technique of bone-marrow transplant for myeloma. Though Sam Walton passed away in 1992, by that time Barlogie had performed the world's first double-marrow and outpatient marrow transplants for myeloma. His research group at UAMS then received the first myeloma project grant ever awarded by the National Cancer Institute.

It was an exciting time in Little Rock. The city enjoyed the national spotlight that came with having a former governor in the White House. The day after New Year's 1995, the Clinton family touched down in Air Force One at the airport that would later bear their name. That same month, Annie Mae Nix arrived with Pilots for Christ, an organization of pilots who provide free transportation for people with medical or other special needs. As Annie Mae Nix walked into UAMS with her eldest son, Echol Jr., they faced a wall inscribed with a large quote by the American poet Edwin Markham:

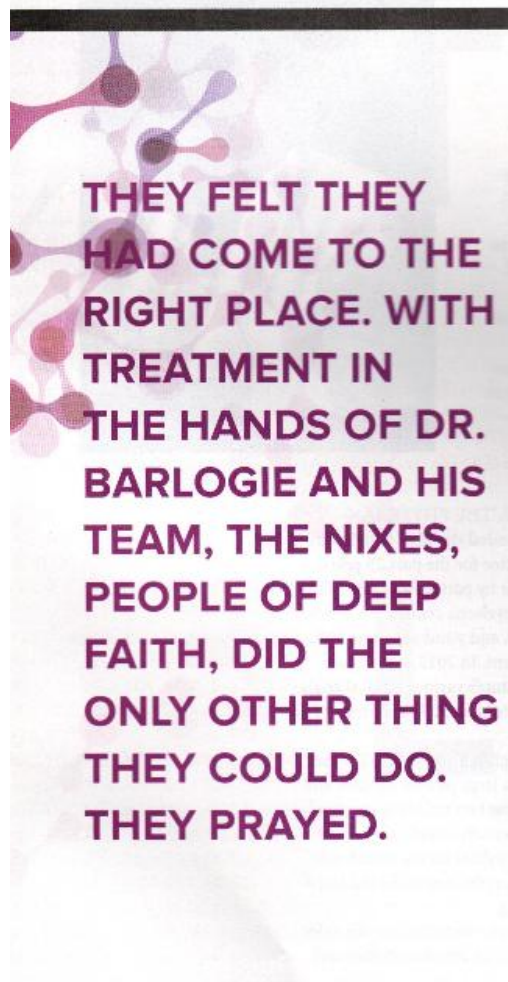
"There is a destiny that makes us brothers; none goes his way alone. All that we send into the lives of others comes back into our own."

They felt they had come to the right place. With treatment in the hands of Dr. Barlogie and his team, the Nixes, people of deep faith, did the only other thing they could do.

They prayed.

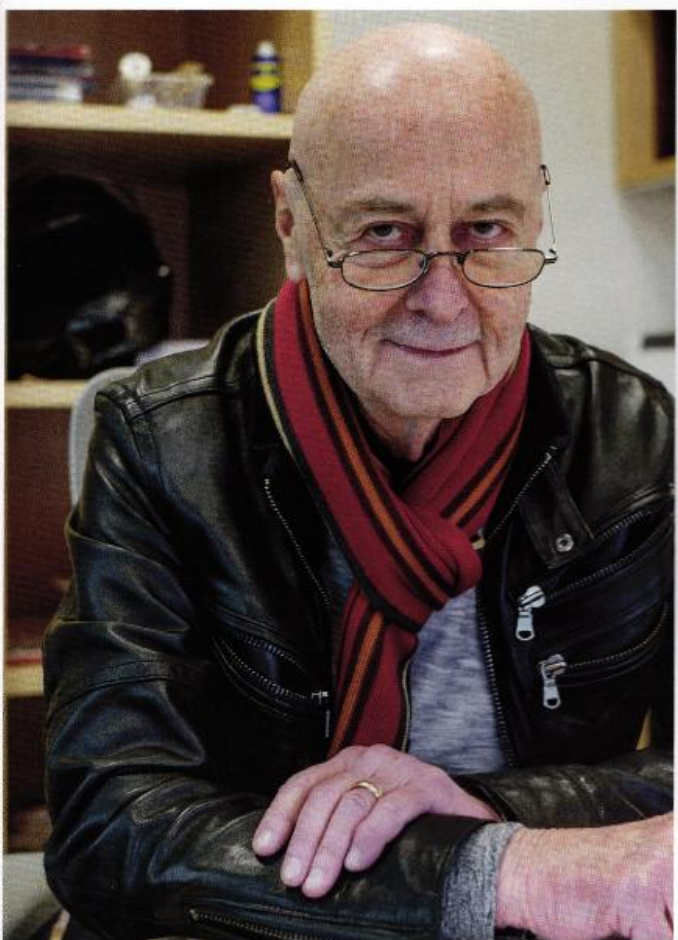
“I N THE BEGINNING WAS THE WORD," the Gospel of John says. In Annie Mae Nix's beginning, there were many words, a story of life recorded in each of the trillions of cells in her body. You can imagine it unwinding from the cell nucleus like a scroll—an invisibly thin spiral of DNA some three feet long, a language in four chemicals that scientists denote by the letters A, C, T and G.

The letters form a long story, enough to fill hundreds of books. Each "word" is three letters long—ATG, AAG, CAG, etc. Collectively they function as an instruction manual for the cell, telling it to produce, for example, the proteins that will make a heart cell or an eye cell, a



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PHOTOGRAPH BY JEFFREY B. HARRIS



In the 25 years that Dr. Bart Barlogie has helmed the Myeloma Institute, patients have flocked to Little Rock from all 50 U.S. states and 58 foreign countries for the treatment he and his team have pioneered.



muscle or a bone. DNA also tells the cell when to divide (reproduce itself), as well as when to die and make room for other cells.

A healthy cell becomes cancerous when changes occur in its DNA. It can happen in many ways, such as a copying error when the cell divides, or coming into contact with radiation. When that occurs, the sections of DNA that control when the cell divides or dies are struck by typographical errors. The cell begins to divide uncontrollably, spreading throughout the body.

In the case of Annie Mae, it was her plasma cells that had exploded out of control. In addition to crowding out normal blood cells, malignant plasma also has the effect of softening and dissolving bone. Annie Mae's X-ray showed holes the size of golf balls along her spine.

Barlogie initiated Annie Mae's treatment by harvesting and freezing her stem cells. He then prescribed an intense regimen of chemotherapy. Chemo is used against cancer because it decimates the cells of the body that divide rapidly, as cancer cells do. But chemo also wreaks collateral

damage on normal cells, making it painful to endure. Despite this, Annie Mae said a blessing over the cocktail of 14 pills she took daily even after returning home to Montgomery. When she came back to Little Rock in June 1995, the test results were as good as anyone could have hoped. Annie Mae's myeloma had gone into remission. The holes in her spine had mended.

IN THEIR OWN CELLS, THE NIX children carry shuffled versions of the DNA of each of their parents. You can see the evidence of Echol Sr. in Earnest's broad shoulders, and of Annie Mae in her daughter Keturah's warm smile. Back in Montgomery, with Annie Mae's cancer in remission, the family was able to return to a more normal life. She went back to work at Dozier Elementary as a teacher's aide for special-needs kids. Echol Jr. graduated from Morehouse and went on to Vanderbilt for graduate study. Pam married and had a son, Timothy, in 1997—the Nixes' first grandchild.



Thanks to the efforts of the Myeloma Institute—her family and her faith always by her side—Annie Mae Nix lived a life that far exceeded her initial prognosis.



This was near Thanksgiving, and Echol Sr. and Annie Mae shared a happy Thanksgiving dinner with Pam in the hospital at Eglin Air Force Base in Florida.

Unfortunately, life did not continue so happily. With myeloma, relapse is common, and by July 1999, Annie Mae's had returned, sending her back to Little Rock for more treatment. Since her last visit, the Institute's star had continued to rise. It had become the first in the world to use gene-expression profiling (analyzing the DNA of a patient's cells) to inform myeloma treatment. And Barlogie had successfully demonstrated that thalidomide, once prescribed as a sleeping pill, was an effective treatment for myeloma. He co-authored a paper on the topic for the *New England Journal of Medicine*.

This time, Annie Mae's treatment would revolve around transplantation of stem cells. Stem cells are a special kind of cell that can transform into virtually any other kind of cell. After the new round of chemo decimated Annie Mae's marrow of both cancerous and healthy cells, her stem cells that had been frozen back in 1995 would be injected to form new, clean marrow.

For Annie Mae, the treatment was worse than before.

There were times she cried from the pain. But she didn't lose faith. Instead, she talked openly with people she met about the illness. She counseled and encouraged them in their own struggles. When Annie Mae's hair fell out from the chemo, instead of wearing a wig she created a new look with makeup and large earrings. At the airport in Chicago a stranger came up to her and remarked on this, saying she had been thinking about such a look herself.

"What did you do to get such a nice bald head?" the woman asked.

"Oh, that's easy. All I did was just take two doses of chemo, and it came right out."

In a 2001 article in the *Montgomery Advertiser*, Annie Mae said, "Cancer was the way God chose to use me. I could show people that God is in control."

By that time, her cancer was in remission again.

THE MYELOMA INSTITUTE IS JUDGED by numbers: survival statistics. Behind the numbers, however, are human beings, like those who gathered at Little Rock's Peabody Hotel on the night of Dec. 1, 2007.

The Institute held a tribute dinner for patients who had survived myeloma for 10 years or more. Thirty-seven patients and their families attended. Annie Mae was among them. She had survived 13 years. She had seen son Earnest marry at the family home, with Echol Sr. officiating as minister. Pam had deployed to Iraq with the Air Force, and Echol Jr. had finished his PhD (Doctor of Philosophy) at Boston University.

Barlogie spoke at the dinner, as did some of the survivors. Each patient had a picture taken with Barlogie, and the group of 37 survivors gathered for a photo. One of the survivors, Barbara Nero of Louisiana, called the evening a "brilliant celebration" of what the Institute had accomplished in its then 18-year history. But even more impressive is what is missing from the group photo—the more than 350 other 10-year survivors around the world who did not attend the event.

It had been a revolutionary era in myeloma treatment. Thanks to Barlogie and other researchers, new drugs and techniques had multiplied the options available, improving patient outcomes. But a controversial split had developed over how to approach the disease. Should practitioners think in terms of control, or had the time come to consider myeloma curable?

Barlogie and the Institute had become the leading force on the "cure" side of the debate. True to the Total Therapy philosophy, this approach front-loads treatment, hitting the cancer with multiple high-dose drugs usually followed by marrow transplantation, in the hopes of delivering a decisive blow to the cancer. In baseball terms, Total Therapy is a swing for the fences.

Asked whether myeloma is curable, Barlogie points to data showing Institute patients who have survived a dozen years and more without a relapse. He says the idea of curability is gaining more acceptance, thanks in large part to the Institute's survival data.

The competing approach to curing myeloma, led by people like James Berenson at the Institute for Myeloma and Bone Cancer Research in southern California, focuses on controlling the disease. Where Total Therapy swings for the fences, the control approach plays small ball. Berenson views myeloma as a chronic condition, and aims to give patients the longest life span with the best quality of life possible. That can mean using only a couple of drugs up front, holding others in reserve to deal with future relapses. Highly intense, toxic regimens may be avoided for fear of complications down the road. And while Berenson does not believe myeloma is curable today, he does believe advances are bringing that day closer.

"My goal is to keep people in the game long enough to get to a cure," he says.

Trials have not established whether the cure or control approach is best. Passionate—and sometimes angry—

debate echoes from the lecture halls of medical conferences, down to the lowest comment threads of myeloma blogs. There are physicians on both sides of the debate, including both Barlogie and Berenson, who are producing exceptional survival data. Ultimately, however, until more is learned, patients and their doctors have to decide which approach seems best for them.



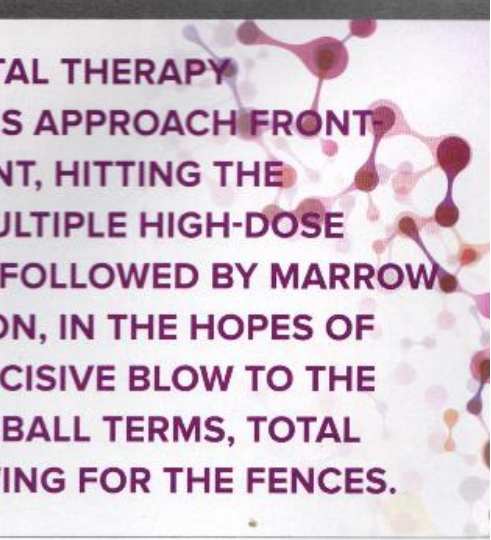
WAKING UP IN BED IN APRIL 2008, Echol Sr. heard a popping sound, then Annie Mae's cry. Her collarbone had broken as she rolled over. Soon the family would learn the worst. The cancer was back.

Annie Mae returned to Little Rock. Three more rounds of chemo, more stem cell collection and two additional marrow transplants drove the disease back into whatever recesses it hid in during remissions. But, as happens in many cases of myeloma, Annie Mae's remissions were becoming shorter-lived. In the spring of 2010, she was in Little Rock yet again. Dr. Barlogie gave her an experimental drug in hopes of breaking the relapse cycle.

Over the years she had grown close to Institute staff, not to mention people like Tommy Lee with Pilots for Christ. His young son, who rode along on that first flight in 1995, was now a young man studying in seminary. All of these people formed a sort of extended family for Annie Mae, though not as important as the one back home. It was only a matter of weeks until Keturah, who was only 6 when Annie Mae was diagnosed, would graduate from Tuskegee University. As the date approached, Annie Mae was still in Little Rock. She became adamant about one thing.

"I'm going to my daughter's graduation," she said.

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TRUE TO THE TOTAL THERAPY PHILOSOPHY, THIS APPROACH FRONT-LOADS TREATMENT, HITTING THE CANCER WITH MULTIPLE HIGH-DOSE DRUGS USUALLY FOLLOWED BY MARROW TRANSPLANTATION, IN THE HOPES OF DELIVERING A DECISIVE BLOW TO THE CANCER. IN BASEBALL TERMS, TOTAL THERAPY IS A SWING FOR THE FENCES.

A STORY OF LIFE
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She managed to get approval to return home the weekend before the ceremony. Though not in full remission, Annie Mae wanted to make the celebration a special time for everyone. She bought platters of food and decorated the family home in Montgomery.

That weekend, watching Keturah walk across the stage, Annie Mae saw her youngest child stride symbolically into adulthood. The dinner at the Nix home after the graduation ceremony doubled as a Mother's Day celebration. Annie Mae took the opportunity to make a surprising announcement. She had decided not to continue treatment. It had become too hard, she said.

At first, the family figured it was just one of those times they had seen before, when Annie Mae got down, when the strength had drained out of even her. "Come on," they countered, "don't say that."

"This is my body. After 16 years, I'm tired," was Annie Mae's response.

Barlogie, upon hearing the news, wanted Annie Mae to come back to Little Rock to continue treatment, as most of the family did. Finally, Annie Mae compromised by agreeing to take medication, but only by mouth and nothing experimental. And—she was staying in Montgomery.

By this time, Pam, still in the Air Force, had returned from Iraq and started nursing school in Mobile. Echol Jr. was in South Carolina, a professor at Furman University. Earnest was raising a family in Montgomery. Keturah was set to begin graduate school in the fall at Purdue University. Annie Mae and Echol Jr. made a trip to Indiana with Keturah that summer to find an apartment. When Annie Mae returned to Montgomery she stayed at home until Oct. 10, when she could no longer walk and had to be taken to the hospital.

One day in November, still in the hospital, she had hardly spoken or moved all day. It was on that day that Keturah, sitting on the floor of her apartment in Indiana, heard the phone ring. It was her father, saying her mother wanted to talk to her.

"Hey, Mama's baby," Annie Mae said. Her voice sounded clear and strong, almost like she wasn't sick. Keturah decided to ask one more time, did she want to go to Little Rock?

"No."

"I love you."

"I love you, too."

Annie Mae seemed at peace, which helped Keturah feel at peace. Not long after that conversation, Annie Mae became unresponsive. She died in the hospital on Dec. 11, 2010, Echol Sr. in the room with her.

THERE HAS BEEN TALK OF BARLOGIE stepping down as the Myeloma Institute's director. It is hard to imagine the Institute without him. But on this blustery, overcast day, in his leather jacket and red scarf, he looks like he might be ready to do it—pull the helmet on and ride into the sunset. When asked, however, he says there is only more research in his future—trying to better understand the mechanisms of success and failure in curing myeloma—the puzzle that has occupied so much of his life.

When he does leave, the Institute he has nurtured and grown in Little Rock will continue to build on what he began. The Institute's survival statistics are among the best in the world. Five-year survival of newly diagnosed myeloma patients is 43 percent for the entire U.S. At the Institute it is 74 percent. The median survival time for patients of the Institute is 8 1/2 years. But the people behind such numbers are the real story of the Institute's work.

One of these people, Annie Mae Nix, roughly doubled the survival figure above. For her, it was time enough to ensure that all her children grew up with a mother.

In Sept. 2008, Annie Mae's sixth grandchild was born—Echol Jr.'s daughter, McKenzie. Annie Mae had held the baby in her arms.

"Junior," she whispered. "Make sure you tell McKenzie about me."

This year, McKenzie Nix will turn 6 years old. She can tell you all kinds of things about Annie Mae. **AL**

