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## Of Young Life & Breath

By Roland Merullo

*Woe to that child who when kissed  
on the forehead tastes salty.*

— ANCIENT NORTHERN EUROPEAN  
FOLKLORE

With its comfortable houses set on small, neatly kept plots of land a few miles from Center City, this Cherry Hill neighborhood evokes ad-agency images of a certain kind of American dream. There are basketball hoops beside the driveways, new cars, flowerbeds out front. And inside one of these homes you find exactly the sense of security and middle-class comfort you would expect from the scene on the street. Well-dressed, well-educated parents. Two handsome boys sitting in soft chairs.

Except that these boys, Nicholas and Vincent Dell'Omo, suffer from cystic fibrosis, the most common lethal genetic disease afflicting Caucasian Americans. And these parents, Greg and Polly Dell'Omo, live every moment of every day with the knowledge that the median life expectancy of CF patients is 32 years. Despite improvements in diagnosis and treatment over the last two decades, some kids still don't make it out of grade school.

Nicholas, now 15, was diagnosed seven years ago. Until then, he had been healthy, suffering only from minor respiratory problems his family doctor diagnosed as asthma. When a case of pneumonia proved resistant to two courses of antibiotics, pulmonary specialists at Children's Hospital of Philadelphia suggested more tests. The day those test results came back is a day Polly Dell'Omo recalls with profound sadness: "We were called into a private room," she says.

"That didn't seem good. Then the doctor told us Nick had cystic fibrosis."

The Dell'Omos' youngest child, Vincent, 5 years old at the time, showed no symptoms at all, but he too was found to have cystic fibrosis. An older daughter tested negative for the disease.

"We had no idea what cystic fibrosis really was," Polly adds, "we were just completely shocked" — a typical first reaction to the diagnosis. Her second reaction was typical too: With the help of doctors at Children's, one of the premier CF treatment centers in the country, she and Greg set about learning everything they could about the disease.

What the Dell'Omos learned is that about 10 million Americans, roughly one in 30, are carriers of CF, which cannot be passed on to another person except through the genes, at birth. The child of two carriers has a one-in-four chance of being afflicted with the disease. This translates into about 30,000 cases nationwide, or about one in every 3,000 births for Caucasians, one in every 15,000 for African Americans, and one in every 100,000 for Asian Americans.

In people with cystic fibrosis, a gene common to everyone has mutated and produces a defective protein that results in abnormal movement of salt in and out of the cells. This seemingly small defect has enormous implications in the body because it dehydrates the mucous membranes that surround organs and exocrine glands. The thicker, stickier mucus causes some bodily systems, especially the lungs and pancreas, to function improperly. And, as Northern Europeans realized hundreds of years ago, the perspiration has a much higher salt content.



Nicholas Dell'Omo and brother Vincent (rear) take nebulized medicine. Nicholas is also undergoing the vest treatment.

In a normal respiratory system, the body's daily production of mucus along with damaging bacteria are flushed out of the lungs by minuscule hairlike structures called cilia. Working like small brushes, cilia push the bacteria out of the tiny air passages and the mucus is coughed out, or swallowed and removed from the body via the digestive process. But in people with CF the mucus is too thick to be easily cleared, the tiny air passages become clogged over time, the cilia aren't able to function, and the bacteria quickly colonize. Because of this, something as simple as the common cold — a mere aggravation for most of us — can, in the CF patient, carry deadly bacteria into the air passages. At some point virtually every person with cystic fibrosis develops chronic lung disease, which manifests itself as continual coughing, gradual loss of pulmonary function, and, eventually, respiratory failure.

Roughly 85 percent of CF patients also suffer from pancreatic

insufficiency. Children with this aspect of the disease often "fail to thrive," and are diagnosed at an early age because of lethargy, abnormal stools, or the inability to gain weight. Michael and Valerie Franklin, who live in Montgomery County, have a daughter, Jessica, now a pretty and vivacious 7-year-old. At age 3½, when she was diagnosed, she seemed almost like any other child. She had had no trouble gaining weight, and to this day displays so much energy that Valerie says, "Sometimes I think she was born with the off-button missing." But Jessica complained regularly of stomach discomfort, and Valerie noticed that she failed to digest her food properly. Though Michael told himself these were just the ordinary aches and ailments of childhood, Valerie took her daughter in for tests. The tests showed poor absorption of food, and further tests showed that this condition was caused by pancreatic insufficiency due to cystic fibrosis.

"Tell me," Valerie said to Jessica's doctor, "just tell me what

we have to do to fix it.” When he responded that although new treatments had doubled life expectancy, there is no known “fix” at this point, she started shaking uncontrollably and nearly passed out.

Michael, who operates an insurance business in Philadelphia, searches for words to describe those first weeks: “We went from the best lives you could have, normal everyday lives, to seeing all these medicines in our cabinet. I was angry. I was nuts. I would contact the bosses of the pharmaceutical companies and say, ‘Where are we on this?’ I got in e-mail contact with the CEO of the CF Foundation, with gene therapy researchers. I’m the problem-solver. I used to say, ‘I don’t understand why this is not resolved.’”

The Franklins’ way of dealing with the shock was to turn into human dynamos, educating themselves and others about the disease and hosting a regular event called Jessica’s Carnival of Fun, which has raised more than \$100,000 for CF research.

It was at one of those carnivals that they met Abby Schwartz, whose daughter, Samantha, had just been diagnosed. “Michael looked at me, gave me a hug and just said, ‘I know,’ and I broke down,” Abby says, recalling that first meeting. “When your child is diagnosed, your whole world just collapses.”

The Schwartzes and the Franklins have now become close friends and have formed part of a community of people whose lives have been touched by the disease. At the center of this extended family is the national Cystic Fibrosis Foundation (CFF), with headquarters in Bethesda, Md., and presided over by Robert Beall, a charismatic and energetic biochemist. In one physician’s words: “There isn’t enough hyperbole to describe how good CFF is.” And according to Smart Money magazine, the CFF ranks third in efficiency among all health-related charities in America, spending less than 12 percent of its income on administrative costs and advertising. The rest goes to fund the 115 cystic fibrosis care centers at hospitals across America — two, Children’s and St. Christopher’s, in Philadelphia — and to support research aimed at finding new treatments and new approaches to a cure.



As mother Valerie reads to her, Jessica Franklin, 7, takes medication through a nebulizer and wears a vibrating vest that loosens mucus in her lungs.

One reason for the CF Foundation’s reputation as a model health-care charity is the innovative incentives Beall and the organization have devised — matching grants, biotech investing — to inspire drug companies to pay attention to the disease.

Thanks to foundation funding, doctors now have a complete blueprint of the *Pseudomonas* bacterium, by far the most prevalent colonizer of the lungs of CF patients and one of the most deadly. New antibiotics that target *Pseudomonas* are in trials in animals and will be available in aerosolized form for humans in the next two to three years.

Beall speaks of the future with genuine optimism: “If these work,” he says, referring to new drugs that will repair what is called the “basic defect” in the CF protein, “we’re talking about adding decades to people’s lives.”

Since the CF mutation was identified in 1989, researchers have learned more about how cystic fibrosis disrupts the body’s normal functions. Doctors such as the University of Pennsylvania’s James Wilson and Cornell’s Ronald Crystal are using this knowledge to find ways of introducing a properly functioning gene into the body and having it replace the defective one.

Wilson’s work is centered in the Wistar Institute at Penn. The building has a quaint, old-fashioned feeling, but the work that goes on there is very much on the cutting edge of genetic research worldwide.

Wilson is a tall, trim 46-year-old whose blue eyes seem at once

focused on the conversation and off in some biochemical dreamscape of cell membranes and ion transport. “Cystic fibrosis is a complex disease,” he says, “with a very interesting biology. The beauty of it, from a researcher’s perspective, is that the cells you need to correct are accessible, right there in the lungs.”

Between February 1989, when Wilson was asked to address the annual North American Cystic Fibrosis Conference on the prospects of gene-replacement therapy, and October 1989, when the conference took place, the CF mutation was identified. Overnight, the talk of curing cystic fibrosis went from conceptual to real. “You could feel the energy in that room,” Wilson says of the October conference. Moved by the enthusiasm of the community and the prospect of a cure, he signed on for the battle.

Before the discovery of the defective gene, it was as if all the patients, their relatives and friends, and the ghosts of those who had slowly suffocated at age 5, or 8, or 11, had been standing at the door to a vault, behind a crowd of a thousand researchers with a million keys in their hands. Over the years, so many keys had been tried while children coughed and gasped and “failed to thrive,” and parents wrung their hands and wept in waiting rooms. And then suddenly a key worked, the door to the vault opened, and the struggle seemed to be over.

But between that bright moment in 1989 and now, the history of gene therapy as it relates to cystic fibrosis has been a checkered one. Doctors and scientists

have struggled to find a way to introduce a healthy gene into the body. In the early ’90s, Crystal, a pulmonary doctor at Cornell and the first researcher to test gene replacement in CF patients, came up with the idea of using a modified cold virus, or adenovirus, to transport the healthy gene into the lungs.

So promising was this new technology that it was moved quickly into human trials. Tragically, in 1999, a patient in one of Penn’s trials, Jesse Gelsinger, died when he suffered an acute immune reaction to the experimental treatment. Gelsinger suffered from liver disease, not CF, but his death sent waves of sorrow and concern through the gene-replacement community.

Wilson’s work now centers on producing a gene-carrying vehicle, known as a vector, that can “get in under the radar of the body’s immune system.” One of his current projects is a hybrid formed from the HIV virus “decorated” with proteins from the Ebola virus. “It works spectacularly well,” Wilson says, “a hundredfold better than anything else we’ve seen,” and has so far proved effective when aerosolized into the lungs of mice and monkeys. But doctors have not found the way — the key to another vault — of using this method without risking lethal infection in their patients.

While researchers continue to probe the mysteries of intracellular transport, other members of the CF community fight the same battle on a more visible front. Daniel Schidlow is chairman of the Department of Pediatrics at MCP Hahnemann School of Medicine, physician-in-chief at St. Christopher’s Hospital for Children, and a 25-year veteran in the battle against CF. Along with a team of respiratory therapists, nurses, nutritionists and social workers, he sees about 100 patients in the adult program at Hahnemann (people associated with cystic fibrosis count it as a victory that an adult program even exists), and 200 in the pediatrics program at St. Christopher’s.

Schidlow cites the “great variability” in the clinical manifestations of cystic fibrosis, noting that there are more than 1,000 known mutations of the CF gene, and that even two patients with identical

mutations can manifest the disease quite differently. While only 50 percent of people afflicted with CF will live beyond age 32, the oldest living patient on the CF registry is 75, and Schidlow and other doctors assert that it is entirely possible that a small number of people with extremely mild cases might never even know they have the disease.

Patients vary even in the way they respond to identical bacteria, including one lethal germ called *B. cepacia*, which, in most manifestations, is resistant to all known antibiotic treatments. Only about 3 percent of people with CF are afflicted with *cepacia* (as opposed to about 60 percent with the damaging, but more successfully treated, *pseudomonas* bacterium), but the infected patient's condition often deteriorates rapidly. While CF patients pose zero risk to the population at large, they can infect each other with the specific types of bacteria that thrive in compromised lungs. Because of that, except in cases of siblings, most doctors recommend that children with CF keep a distance of at least three arms' length when playing together, and never travel together in a car or other closed compartment. Good friends though they are, for example, the Schwartzes and Franklins have never introduced their daughters to each other, because of fear of infections such as *B. cepacia*.

Like Schidlow, Thomas Scanlin is a Philadelphia clinician who has been seeing CF patients for 25 years. Director of the CF Center at Children's Hospital and professor of pediatrics at Penn, Scanlin got into the cystic fibrosis field in medical school, after spending a summer working with sick children at the Children's Seashore House. "We're not looking for the needle in the haystack anymore," he says,

referring to the cloning of the CF gene. "We've found the bent needle and we're trying to fix it."

That said, however, he describes the last decade as a "plateau" in terms of CF breakthroughs and patient longevity and notes how difficult it has been for patients and parents that gene therapies have not yet yielded any results.

Even so, Scanlin is optimistic that in the coming years there will be, if not a cure, then at least a breakthrough in the drugs used to treat CF symptoms. His own research has produced a synthetic sugar-coated protein that has performed remarkably well in lab experiments and will soon go into animal testing. He notes, too, that the National Institutes of Health have recently issued a recommendation in support of prenatal CF screening, a sign of the raised consciousness about the disease. And perhaps an attempt to address the fact that non-specializing pediatricians and general practitioners often misdiagnose the disease. They see an otherwise robust person with respiratory symptoms and think asthma or allergies when in fact what they are looking at is CF.

Everyone associated with cystic fibrosis senses the shadow of premature death hovering around the edges of every conversation on the subject. One hears stories of 11-year-old children waiting in quiet desperation for a double lung transplant that might keep them alive until a cure is found. One visits a CF clinic and sees two unusually thin teenagers sitting close beside their mother in the waiting room, not mixing with the other kids, their faces revealing a seriousness beyond their years and the sense that college, marriage, and a career are things to dream about, rather than plan for.

But on any given day, for the vast majority of the 30,000 people suffering from cystic fibrosis, the question of life and death takes a back seat to the more pressing concerns of an exhausting therapeutic and physical therapy regimen. In addition to taking a dozen or more different medications, children such as Jessica Franklin, Samantha Schwartz, Nicholas and Vincent Dell'Omo and Tommy Clark endure two half-hour sessions daily during which their parents drum on their back and chest with cupped hands. Or they strap themselves into a \$15,000 vibrating vest that shakes the whole body, sometimes giving them painful chest cramps in the process.

"It's a full-time job to supervise his treatments," says Jonene Clark of Delaware County. Her stepson Tommy, 17, suffers from chronic sinusitis, and his lungs are currently harboring four strains of *pseudomonas* and two strains of staph bacteria. "I can't imagine single parents having to go through it."

"Words can't describe it," she adds, "but these kids are going through their own personal hell."

It isn't just kids, of course: In America, there are about 11,000 adults suffering from CF. One of them is a 50-year-old Aston, Pa., woman named Laura Watts, whose life was saved by a double lung transplant in 1998. Watts faces her disease with a hopeful stoicism typical of CF patients. "I'm thankful for each breath I take," she says.

Nicholas Dell'Omo shows a similar courage: "I hate having to get up early to do my treatment," he admits, "but after a while you just accept that this is your life. I feel there was a purpose for this."

And Tommy Clark advises other children with the disease to "do the best with what you've got and try to fight it every day."

Tommy plays left wing on a traveling hockey team (though he skates shorter shifts), and both Nicholas and Vincent Dell'Omo play in highly competitive soccer leagues (though if Nicholas misses a single treatment, he notices a difference on the field). Samantha Schwartz and Jessica Franklin are active kids, too, participating in ice skating, gymnastics, and the usual playground games. "We try to make our kids' lives as normal as possible," Greg Dell'Omo says. And Abby Schwartz agrees: "I will never tell Samantha there is a limit on her life or on the activities she can do."

But in spite of the courage of patients and parents, the hard work of doctors and researchers, and the determination of the people at the Cystic Fibrosis Foundation, the patients still suffer, people still wait for a new set of lungs, and parents such as Michael Franklin still compulsively check the CF Internet site ([www.cff.org](http://www.cff.org)) every morning before work, hoping for the breakthrough that will save their child's life.

"A doctor told me flat-out that we will have a cure within 10 years," Michael's wife, Valerie, says through a lens of tears. "So I set a sort of clock. Seven more years and I can think about world peace again."

Contributions may be sent to the Cystic Fibrosis Foundation, Marple Commons, 2004 Sproul Rd. Suite 208, Broomall, Pa. 19008, or the Cystic Fibrosis Foundation, 6931 Arlington Rd., Bethesda, Md. 20814.

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For more information about cystic fibrosis and the programs and services available please contact:



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