



## LOOKING FOR THE *FAINT* OF HEART

**Jessica Martineau** was just 25 years old when her heart stopped for the first time. A professional dancer, she was rehearsing with a contemporary ballet company for an upcoming show. Caffeine from a double latte was in her system, and she was still stressed and sleep deprived from a week spent helping her boyfriend finish his graduate thesis. “I was exhausted,” she says, “but I was just going as hard as I could.” In the middle of her solo, she felt her heart race out of control. Suddenly, her muscles stopped obeying her commands. “Then, everything went black, and I hit the floor.” As she lay there turning white, Jessica had no pulse. Yet just as the paramedics arrived, charging up a defibrillator, her heart managed to restart on its own. Gradually, she recognized the crowd of dancers gathered around her. “I saw the looks of horror on all their faces, and I just burst into tears.” • At the hospital, after a night of diagnostic tests, a cardiologist delivered the news: **Jessica has what is known as long QT syndrome, an inherited condition that can lead to cardiac arrest—in which the heart’s pumping rhythm goes suddenly awry before stopping altogether.** The cardiologist immediately put Jessica on a beta blocker, a drug that dampens the excitability of the heart. He also urged her to get an implantable cardioverter defibrillator (ICD). The small titanium box would sit just below Jessica’s left collarbone, under the skin, with wires feeding down into her heart. If it detected a dangerous rhythm, it would deliver a revitalizing shock. To the dismay of all her doctors, Jessica

NYU Langone cardiogenetics researcher Silvia Priori is identifying children and adults at risk for sudden cardiac death.

By **KYLA DUNN**

Illustration by **AUDE VAN RYN**

**NYU PHYSICIAN** 13  
+ SPRING 2009

refused.

“On my frame, it would be very visible. You could see the box sticking out, and you’d see the scar,” she says. Even worse, for a dancer, the surgery would slice through her pectoral muscles, restricting arm movement. “I really don’t want to go through that surgery every few years to replace the battery,” she says. She fears device malfunctions, and a modification to her body that she rejects as unnatural—even freakish. “I’d rather live with the risk of dying from this disorder than to have this alien machine in my body that could potentially shock me uncontrollably,” she says. “I know it’s irrational. But in the end, I’m the one who has to live in this body.”

Jessica’s choice is extreme. “Clearly, anybody who has survived a cardiac arrest should be implanted,” says Larry Chinitz, M.D., associate professor of medicine and director of the Leon H. Charney Heart Rhythm Center. Still, he adds, there’s no denying that ICDs can have serious drawbacks. “Younger patients in general seem to have a higher rate of complications,” Dr. Chinitz explains, ranging from infections to broken wires to inappropriate shocks, “and many of the patients with these genetic disorders are so young . . . 10 years old or 15 years old.” Many will have devices for their entire lives and discover that they never need them. If a patient has not yet had a cardiac arrest, says Dr. Chinitz, “it’s very difficult within a long QT family to judge who’s at risk.”

Patients are starting to get better answers than ever before, however, since the creation of the new Cardiovascular Genetics Program at NYU. The program is directed by Silvia Priori, M.D., Ph.D., professor of medicine. “Dr. Priori and her team are really the world’s leaders in exploring the basis for some of these inherited heart rhythm disorders,” says Glenn Fishman, M.D., the William Goldring Professor of Medicine, professor of physiology and medicine and pharmacology, and director of the Leon H. Charney Division of Cardiology. “She and her team have seen literally thousands of individuals and families at their home base in Italy.”

That expertise is crucial, as the symptoms can be subtle enough to escape detection even by seasoned cardiologists. Since being recruited to NYU in 2008, Dr. Priori and her team have been using the newfound power of genetics not only to diagnose these heart conditions, but to help determine the best kind of treatment for each patient. “This is really a vision for the future,” Dr. Priori says. “We will see more and more in cardiology and in other branches of medicine related to genetics.”

## Sudden cardiac death kills some 450,000 Americans each year,

and for people under 40 years old, the leading cause is an inherited disorder such as Jessica’s. Some of the deaths are high profile: the Olympic hopeful whose heart stops at the beginning of a marathon, the college basketball player whose heart stops on the court. Others are more private tragedies: the young girl who dies when she is startled by a telephone or a doorbell. In most cases, a single defective gene is to blame and has often been passed down through many generations of a family before anyone realizes they are at risk.

“It is not by coincidence that most of the families here have long QT syndrome,” Dr. Priori told a roomful of patients gathered at an NYU-sponsored event in January. Discovered in the late 1950s, it is the best understood and most familiar of these diseases to physicians, so the most likely to be diagnosed. “Other such diseases are much more recent discoveries,” she continued, and “until a couple of years ago were not even in the textbook of cardiology.”

It is now clear that two distinct types of inherited disease can cause cardiac arrest. In one group of conditions, the physical structure of the heart is abnormal. These so-called “cardiomyopathies” are visible on an echocardiogram or an MRI. In the

second group of conditions, the physical structure of the heart looks completely normal. What’s abnormal is its flow of electrical current. A normal heart rhythm relies on a very precisely timed opening and closing of ion channels—pores that control the flow of electricity in and out of individual heart cells. Even a minor change in how these channels function can create life-threatening problems. Diagnosing these “channelopathies”

involves careful analysis of a patient’s electrocardiogram (ECG), that familiar jagged tracing of the heart’s electrical activity.

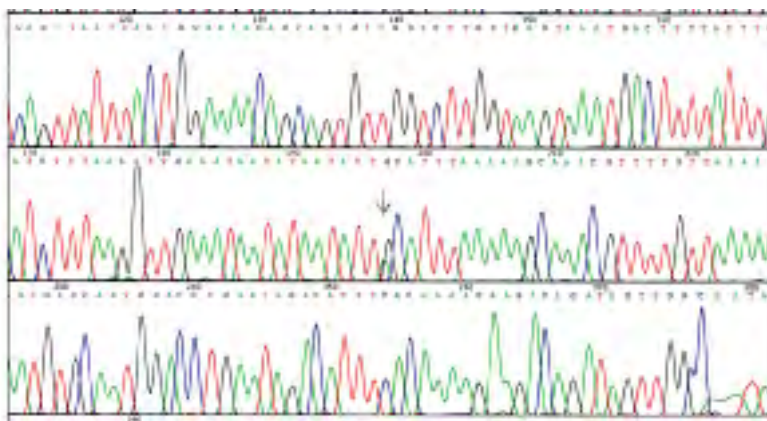
Long QT syndrome, Jessica’s disease, is a channelopathy whose symptoms emerge at times of stress, exercise, or emotion. Symptoms typically first appear in children and teenagers. The syndrome’s name comes from the portion of a patient’s ECG called the “QT interval,” which indicates how long it takes the heart

cells to reset, electrically, in preparation for the next beat. In patients like Jessica, this interval is too long. The highest-risk patients have an interval above 500 milliseconds. Jessica’s was 600. (Beta-blocker medication has since reduced this somewhat.)

Without the protection of an ICD, she says, her doctors—including Sabrina Wilbur, M.D., assistant professor of medicine, who referred her to Dr.



Las Vegas showgirl Jessica Martineau has been diagnosed with long QT syndrome.



Ion channels control how our heart muscle cells contract, and therefore the heart’s overall pumping rhythm. The body’s instructions for building this particular ion channel (above) consist of almost 15,000 DNA subunits: As, Cs, Gs and Ts. Yet a change to just one of them can cause a fatal change in heart rhythm. The black arrow indicates where a G-nucleotide (black peak) has mistakenly converted to an A-nucleotide (green peak) on one of the patient’s chromosomes, making cardiac arrest likely.

Priori—would prefer that she give up dancing. “For most long QT patients, they recommend only moderate exercise,” Jessica says, “and my life is anything but moderate.” For the past two years, Jessica has been working as a showgirl in Las Vegas. During the 12 shows she does each week, a defibrillator sits at her dressing table.

Doctors’ concerns proved justified when—a year and a half after her first cardiac arrest—Jessica’s heart stopped again. Her boyfriend had just proposed, and to celebrate, she went to her favorite café in SoHo for a hot chocolate. She had been too excited to sleep the night before and had eaten no dinner. Fueled only by sugar and caffeine, she stopped by a friend’s house to announce the news. “She saw my ring and she screamed,” Jessica recalls. “And the scream set off my arrhythmia.” Jessica’s new fiancé could not detect a pulse as he phoned for an ambulance. Once again, however, Jessica’s heart restarted on its own. “My doctors have said that basically it’s just luck that that happened,” Jessica says. “They say a third of people who have an episode come right back on their own, another third come back with defibrillation, and another third just don’t come back at all.”

**One goal of the Cardiovascular Genetics Program, says Dr. Priori,** is to limit the use of ICDs as much as possible by better identifying who is at serious risk. “I have seen the impact of genetics come into this field,” says Dr. Priori, who started seeing long QT patients in the clinic even before the first gene was identified in 1995, “and the field has just exploded.”

Long QT syndrome can result from defects in over a dozen different genes. The three most common forms of the disease are conveniently named LQT1, LQT2, and LQT3, each involving a different gene. The likelihood of a life-threatening cardiac event follows a simple formula: The longer a patient’s QT interval, the greater the risk. However, two patients with the same QT interval can be distinguished by their genes. As it turns out, an LQT1 patient is at less risk than a patient with LQT2 or LQT3. What’s more, LQT1 patients tend to respond well to beta blockers, while patients with LQT2 and LQT3 get less protection and may more often need an ICD. “These are important distinctions,” says Dr. Priori, whose program is supported by a grant from the family of the late Harold Snyder.

“I’m anxious to get that genetic testing done,” Jessica says. “It would give me a better idea of just how much danger I really am in.” Not only might the results



Silvia Priori, M.D., Ph.D.

change her mind about an ICD, they could also help her better understand which situations to avoid. “I’d like to know if it was the caffeine that triggered my cardiac arrest, or if it was really the loud noise,” she says. LQT1 patients, Dr. Priori explains, have most of their life-threatening events during sports activity. LQT3 patients, by contrast, tend to experience heart arrhythmias at rest—so restricting their physical activity may not be as crucial. LQT2 patients often have arrhythmias when startled by loud sounds: a telephone ringing or an alarm clock going off. Knowing this, “we’ll advise them not to keep a telephone on the night stand,” says Dr. Priori. “It’s a simple thing, but may play an important role.”

“That’s why I’m so passionate in saying that patients with long QT syndrome should get access to genetic testing,” Dr. Priori adds. Coverage of the cost of the test will vary among some insurance companies, while others will deny coverage altogether. What these companies need to understand, says Dr. Priori, is that the value of genetic testing now goes far beyond identifying other affected family members or knowing if one’s children could inherit the disease. “That by itself is already very important. But really it’s because the clinicians cannot do a good job of treating that family unless they know if they are dealing with an LQT1, 2, or 3.”

**Half of all children who die “suddenly” of a heart rhythm disorder** first have symptoms that go unrecognized. One goal of the Sudden Arrhythmia Death Syndromes Foundation, or SADS ([www.sads.org](http://www.sads.org)), a patient advocacy group, is to raise awareness of these early warning signs. Children and teenagers who have a history of fainting during exercise, excitement, or when startled by a loud

noise should be evaluated by a heart specialist. “Not everyone who faints once,” says Dr. Priori. “But definitely the child who has repeated episodes, especially associated with turning blue.” So should families with a history of unexpected, unexplained sudden death. This might include drownings, mysterious single-car accidents, or sudden infant death syndrome (SIDS). “At least 10 percent of these unexplained deaths in the first year of life are caused by one of these genetic diseases,” says Dr. Priori.

In hindsight, Jessica sees that there were some warning signs. When she was an infant, the noise of a train going by once caused her to pass out in her mother’s arms. During college, she could feel her heart racing when she drank too much coffee during the stress of finals. Concerned, she finally went to the campus health clinic. When her ECG came back abnormal, however, “they said, ‘It’s probably just the caffeine—don’t worry about it,’” she recalls.

Because so many cases go unrecognized, and cardiac arrests can happen unexpectedly, SADS also focuses on the critical first response: it urges all schools and workplaces to have portable defibrillators handy, and wants graduating high school students to be trained in how to use them, as well as in CPR.

Another need is for better communication within families. “A lot of families don’t know their family history,” Pam Husband, a cofounder of The Canadian SADS Foundation ([www.sads.ca](http://www.sads.ca)), observed at NYU’s January meeting. Yet when patients start to ask questions of their aunts, uncles, and grandparents, “the initial response, ‘No family history of sudden death,’ has actually become, ‘Yes, we have a history of sudden death.’”

In Jessica’s case, the dangerous gene clearly comes from her father’s side. Only recently did she learn that two generations ago a relative did die unexpectedly. “My grandfather’s brother, my dad’s uncle, died when he was 19 or 20 when he was in the service,” she says. It’s quite possible that the cause was long QT syndrome. For years, Jessica had also heard vague talk of one of her father’s cousins having heart problems—but the understanding that others might need to be tested never worked its way through the family. “Now we realize that we both have the same thing,” Jessica says.

Since Jessica’s diagnosis, several relatives have gone in for ECGs. One of her aunts, her father’s sister Cherie, is definitely affected. Typically, a parent will pass the diseased gene on to half of their children, and Cherie has *(continued on page 34)*

### 1980s

**WILLIAM J. COLE, M.D. ('80)**, has been named Physician of the Year by the NYU Langone Medical Center Auxiliary and was honored on October 27, 2008, at the auxiliary's 50th anniversary celebration at the Metropolitan Club.

**ROBERT M. AARONSON, M.D. ('88)**, received the 2008 Arizona Laureate Award from the American College of Physicians (ACP), Arizona chapter. He is the executive director of the Tucson Hospitals Medical Education Program, clinical associate professor of medicine at the University of Arizona, and associate director of the University of Arizona Internal Medicine Residency Program.

### 1990s

**JESSICA COOPER FOLTIN, M.D. ('90)**, director of the Pediatric Emergency Medicine and Transport Program at Tisch Hospital, and her husband, George Foltin, M.D., director of Pediatric Emergency Medicine at Bellevue Hospital, were honored by KiDS of NYU at its Springfling Gala for their contributions to both institutions.

**IN-KYU YOON, M.D. ('93)**, is a lieutenant colonel in the army, serving as assistant chief of the Department of Virology at the Armed Forces Research Institute of Medical Sciences in Bangkok, Thailand.

**RICHARD A. FALCONE, JR., M.D. ('95), M.P.H.**, is assistant professor of surgery in the Division of Pediatric and Thoracic Surgery, associate director of the Pediatric Trauma Program, and director of the Extracorporeal Membrane Oxygenation Program at Cincinnati Children's Hospital Medical Center.

**FRITZ FRANCOIS, M.D. ('97), ('07 M.S. MED.) '93 WSC**, has been appointed assistant dean for academic affairs and diversity. He completed his residency and gastroenterology fellowship at NYU. During his chief residency, he created the Department of Internal Medicine Organization for Nurturing Diversity (DIAMOND) to help with resident recruitment, mentoring, development, and retention.

**ANTHONY SHIH, M.D. ('97)**, has rejoined IPRO, an independent quality improvement and evaluation organization, as chief quality officer and vice president of strategic planning. He spent the past two years at The Commonwealth Fund, a national foundation working to improve U.S. health system performance, and held senior-level positions at IPRO from 2001 to 2006,

including vice president of healthcare quality improvement.

**NICOLE SUTTON, M.D. ('98)**, and her husband, Robert Sutton, are the proud parents of twin girls born on April 7, 2008.

### 2000s

**GERARD J. TEPEDINO, M.D. ('00), ('96 CAS)** and his wife, Jackie, welcomed the newest addition to their family, a baby girl, on November 5, 2008.

**DIANA LYNN ASCHETTINO-MANEVITZ, M.D. ('01), ('93 STEINHARDT)**, finished a fellowship in adolescent medicine at Schneider Children's Hospital and is now assistant professor of clinical pediatrics in the Division of Adolescent Medicine at Stony Brook University.

**CHIRAG R. KAPADIA, M.D. ('02)**, completed an endocrine fellowship at Children's Hospital of Philadelphia in July 2008.

**CHRISTINA A. TENNYSON, M.D. ('02)**, married Richard J. Naddeo on August 9, 2008, at St. Francis de Sales Church in Belle Harbor, NY. She began working at New York-Presbyterian Hospital in Manhattan in September 2008 after completing a fellowship in gastroenterology at Mount Sinai School of Medicine. Her husband is a counsel for the New York City Economic Development Corporation.

**JEANINE A. DALY, M.D. ('03)**, and Andrew H. Gillette were married on August 30, 2008 at the Woodbury Country Club in Woodbury, NY. She is a chief resident in dermatology at the State University of New York Downstate Medical Center in Brooklyn. Her husband is a marketing manager at American Express in Manhattan.

**RICHA AGARWAL, M.D. ('05)**, married Dr. Rajiv Seth Swamy on October 4, 2008, at the River East Art Center in Chicago. She is a fellow in cardiovascular medicine and her husband is chief resident for internal medicine at the University of Chicago Medical Center ●

#### Faint of Heart

*(continued from page 15)*

five children. "They've all been screened, and they don't have it," Jessica says. Yet genetic testing is the only way to know for sure. Even family members with normal ECGs may in fact be at risk: up to 35% of gene carriers have no symptoms—and a normal QT interval.

Even these "silent carriers" need to know their status so they can limit aggressive physical activity. What's more, certain prescription and over-the-counter medications—ranging from cold and

allergy products to antibiotics—can be life threatening to them. By prolonging the QT interval, some of these drugs can send people with long QT syndrome into cardiac arrest. For Jessica, familiarizing herself with this list has become crucial.

Family planning issues also loom large for everyone involved. One reason these genetic diseases continue to spread so widely throughout families is that people have children before realizing they are affected. In many cases, parents barely have time to process the tragedy of losing one child to long QT syndrome before learning that another of their children—or a grandchild, or a sibling—is also at risk. "We definitely want children," Jessica says. "And that's something definitely to consider: Do we want a kid who has this heart condition? So we've also considered adoption."

"The future is to try to cure these diseases," Dr. Priori adds. The promise of gene therapy is that a physician may someday be able to replace the defective gene in a patient's heart with a healthy one. That type of cure, however, is a long way off. In the meantime, Dr. Priori's team will continue to search for better drugs and therapies, and try to raise the level of awareness among physicians. "We need to be proactive and reach out," she says, "because every month, every year lost can mean more victims of sudden cardiac death." ●

#### Theo's Story

*(continued from page 27)*

to do after she took Theo home. How to handle reflux? The bassinet is on an incline—should I do that at home? When they bathed Theo and the other babies at night, they invited Audrey to come and observe. At first, Theo got a sponge bath, but eventually they put him in a round metal basin. "I hesitate to call it a tub," she says, laughing.

Finally, Theo was ready to go home. He was so ready that a nurse had nicknamed him Houdini. One day, she looked into his crib and saw an empty blanket. Theo was lying at the top of the bed, having shed the blanket he was swaddled in as if it were a cocoon he no longer needed.

On June 4, 119 days after he arrived in the NICU, Audrey buckled her seven-pounder into his car seat for the first time and carried him downstairs to the street where his father was waiting in the Jeep, dreaming about teaching his boy to swim and ride a bike, just as his father had taught him. ●