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This Man Was Dead.

He Isn't Anymore.

How Science Is Bringing More Heart-Attack Victims Back To Life

PHOTOGRAPH BY ETHAN HILL

Brian Duffield, 41, whose heart stopped after a swim in May 2006

Doctors are reinventing how they treat sudden cardiac arrest, which is fatal 95 percent of the time. A report from the border between life and death.

BACK FROM THE DEAD

BY JERRY ADLER

BILL BONDAR KNOWS EXACTLY WHERE he died: on the sidewalk outside his house in a retirement community in southern New Jersey. It was 10:30 on the night of May 23, a Wednesday, and Bondar was 61—a retired computer programmer with a cherry red Gibson bass guitar, an instrument he had first picked up around the same time as Chuck Berry. He was 6 feet 1 and 208 pounds, down about 50 pounds over the last several years. On that night he had driven home from a jam session with two friends and, as he was unloading his car, his heart stopped. That is the definition of "clinical death," one of several definitions doctors use, not always with precision. He wasn't yet "brain dead," implying a permanent cessation of cerebral function, or "legally dead," i.e., fit to be buried. But he was dead enough to terrify his wife, Monica, who found him moments later, unconscious, not breathing, with no pulse. His eyes were open, but glassy—"like marbles," Monica says, "with no life in them. They were the eyes of a dead man."

In a general sense, we know what happened to Bondar. His doctor at the University of Pennsylvania Hospital, Dr. Edward Gerstenfeld, later determined that Bondar's left anterior descending artery was 99 percent blocked by a coating of plaque, leaving a passage "the width of a hair." A blockage in that vessel, the largest artery feeding the heart, is known

to cardiologists as the widowmaker. A tiny clot lodging there would have sent his heart into a brief burst of the ineffectual rhythm known as fibrillation, before it stopped altogether. Within 20 seconds the hundred billion neurons in Bondar's brain would have used up their residual oxygen, shutting down the ceaseless exchange of electrical charges that we experience as consciousness. His breathing stopped as he entered a quiescence beyond sleep.

About 250,000 times a year in the United States, someone's heart stops beating on the street, or at home or at work. This can be the result of a heart attack, when a clot chokes off a coronary artery, or a host of other conditions including congenital defects, abnormal blood chemistry, emotional stress and physical exertion. Without CPR, their window for survival starts to close in about five minutes. Life or death is mostly a matter of luck; response time to a 911 call varies greatly by location, but can exceed 10 minutes in many parts of the country. In rough numbers, they have a 95 percent chance of dying.

Oxygen deprivation is merely the start of a cascade. Dying turns out to be almost as complicated as living.

HOW LONG HAS IT been since you've read an article about heart attacks that didn't mention saturated fats? Our age is obsessed with "health," but when health fails, the last line of defense is in the emergency room, where doctors patrol the border between life and death—a boundary that they have come to see as increasingly uncertain, even porous. This is a story about what happens when your heart stops: about new research into how brain cells die and how something as simple as lowering body temperature may keep them alive—research that could ultimately save as many as 100,000 lives a year. And it's about the mind as well, the visions people report from their deathbeds and the age-old questions about what, if anything, outlives the body. It begins with a challenge to something doctors have always been taught in medical school: that after about five minutes without a pulse, the brain starts dying, followed by heart muscle—the two most voracious consumers of oxygen in the body, victims of their own appetites. The emerging view is that oxygen deprivation is merely the start of a cascade of reactions within and outside the cells that can play out over the succeeding hours, or even days. Dying turns out to be almost as complicated a process as living, and somehow, among its labyrinthine pathways, Bondar found a way out.

Monica tried to recall what she had learned in a CPR class decades earlier. She bent over Bondar and began pushing down on his chest, then rushed back to the kitchen to dial 911. "My husband is dying!" she gasped to the operator.

Compressing Bondar's chest would have sent a trickle of blood to his brain, supplying a fraction of its normal oxygen consumption, not enough to bring him back to consciousness. But the West Deptford police station was only three blocks away, and within two minutes of Monica's call three officers arrived with a defibrillator. They placed the pads on Bondar's chest, delivered two jolts of electricity to his heart, and got a pulse back. Soon paramedics arrived with oxygen and rushed him to a nearby community hospital. The report Monica received there after an hour was equivocal: Bondar was "stable"—his heart rate and blood pressure back to near normal—but he was still in a coma. It was then that Monica made a decision that may have saved his life. She asked that her husband be moved the 15 miles to Penn, the region's leading university hospital.

Dr. Lance Becker, director of Penn's year-old Center for Resuscitation Science, frequently dreams about mitochondria: tubular structures within cells, encasing convoluted membranes where oxygen and glucose combine to produce the energy the body uses in moving everything from molecules across cell membranes to barbells. Recently mitochondria have been in the news because they have their own DNA, which is inherited exclusively down the female line of descent, making them a useful tool for geneticists and anthropologists.

But Becker is interested in mitochondria for another reason: he believes they are the key to his audacious goal of tripling the time during which a human being can go without a heartbeat and still be revived. That the five-minute rule is not absolute has been known for a long time, and the exceptions seem to involve low temperatures. Children who fall through ice may survive unexpectedly long immersions in cold water. On Napoleon's Russian campaign, his surgeon general noticed that wounded infantrymen, left on the snowy ground to recover, had better survival rates than officers who stayed warm near the campfire. Becker is hoping to harness this effect to save lives today.

BECKER IS 53, SLENDER and boyish in a way that belies his thinning hair; his typical greeting to colleagues is a jaunty "What's up, guys?" For his lab he has assembled a high-powered team from a wide range of specialties, including a brilliant young neuroscientist, Dr. Robert Neumar; an emergency-medicine specialist, Dr. Ben Abella; plus cardiologists, biochemists, bioengineers and a mouse-heart surgeon. His associate director, Dr. Vinay Nadkarni, comes from pediatrics. Becker has in effect re-created at Penn, on a more ambitious scale, the laboratory he founded in 1995 at the University of Chicago, with a grant of $50,000 from the philanthropist Jay Pritzker. Ten years earlier Pritzker had walked into the emergency room at Chicago's Michael Reese Hospital complaining of chest pains, and crumpled to the floor. Becker resuscitated him, the beginning of both a rewarding friendship (Pritzker lived for 14 more years) and a new direction for Becker's career. "Every day since then," he says, "I would go home and wonder why Jay

People have a hard time believing that something as simple as cooling the patient can make such a difference.

Pritzker got a second chance and so many other people didn't."

Becker's interest in mitochondria reflects a new understanding about how cells die from loss of circulation, or ischemia. Five minutes without oxygen is indeed fatal to brain cells, but the actual dying may take hours, or even days. Doctors have known for a long time that the consequences of ischemia play out over time. "Half the time in cardiac arrest, we get the heart going again, blood pressure is good, everything is going along," says Dr. Terry Vanden Hoek, director of the Emergency Resuscitation Center at the University of Chicago, "and within a few hours everything crashes and the patient is dead." It took some time, though, for basic research to supply an explanation. Neumar, working with rats, simulates cardiac arrest and resuscitation, and then examines the neurons at intervals afterward. Up to 24 hours later they appear normal, but then in the next 24 hours, something kicks in and they begin to deteriorate. And Dr. James R. Brorson of the University of Chicago has seen something similar in neural cells grown in culture; deprive them of oxygen and watch for five minutes, or even much longer, and not much happens. "If your car runs out of gas, your engine isn't destroyed, it just needs fuel," he says.

Cell death isn't an event; it's a process. And in principle, a process can be interrupted. The process appears to begin in the mitochondria, which control the cell's self-destruct mechanism, known as apoptosis, and a related process, necrosis. Apoptosis is a natural function, destroying cells that are no longer needed or have been damaged in some way. Cancer cells, which might otherwise be killed by apoptosis, survive by shutting down their mitochondria; cancer researchers are looking for ways to turn them back on. Becker is trying to do the opposite, preventing cells that have been injured by lack of oxygen from, in effect, committing suicide.

It's a daunting problem. "We're asking the questions," says one leading researcher, Dr. Norm Abramson of the University of Pittsburgh. "We just haven't found the answers." Until recently, the conventional wisdom was that apoptosis couldn't be stopped once it was underway. It proceeds by a complex sequence of reactions—including inflammation, oxidation and cell-membrane breakdown—none of which seems to respond to traditional therapies. Becker views cell death in cardiac arrest as a two-step process, beginning with oxygen deprivation, which sets up the cell for apoptosis; then the heart starts up again and the patient gets a lungful of oxygen, triggering what is called reperfusion injury. The very substance required to save the patient's life ends up injuring or killing him.

Researchers have ransacked their arsenal of drugs looking for ways to interrupt this sequence. Over the years they have tried various techniques on nearly 100,000 patients around the world. None has shown any benefits, according to Dr. A. Michael Lincoff, director of cardiovascular research at the Cleveland Clinic. But one thing does seem to work, something so obvious and low-tech that doctors have a hard time accepting it. It's hypothermia, the intentional lowering of body temperature, down to about 92 degrees Fahrenheit, or 33 Celsius. Research by a European team in 2002 reported favorable results from a controlled study of several hundred cardiac-arrest patients; subjects who were cooled both had better survival rates and less brain damage than a control group. The first big international conference on cooling took place in Colorado this February. Despite favorable studies and the endorsement of the American Heart Association, "we were concerned that [hypothermia] still wasn't catching on," says the conference organizer, Dr. Daniel Herr of Washington Hospital Center in Washington, D.C. The two leading manufacturers of cooling equipment—Medivance, Inc., and Gaymar Industries—say only about 225 hospitals, out of more than 5,700 in the United States, have installed machines for inducing hypothermia. Herr says the treatment requires a "paradigm shift" by doctors. "People have a hard time believing that something as simple as cooling can make such a big difference." Perhaps that's because no one quite understands how cooling works. It appears to work globally on apoptosis, rather than on any of the individual biochemical pathways involved in it. "The short answer is, we don't know," says Neumar.

Researchers have also been looking into the way patients get oxygen during resuscitation, and afterward. The treatment goal in cardiac arrest has been to rush oxygen to the heart and brain at maximum concentration; the mask the paramedic pops on your mouth supplies it at 100 percent. "The problem with that," says Dr. Ronald Harper of UCLA, "is it does some very nasty things to the brain." Harper believes a mixture containing 5 percent carbon dioxide would buffer those negative effects, but the idea is still controversial. At the University of Maryland, Dr. Robert Rosenthal and Dr. Gary Fiskum have been looking into whether oxygen concentrations should be dialed down much more aggressively. In their lab, dogs with induced cardiac arrest recovered better when they were taken off full oxygen after just 12 minutes, compared with an hour in the control group. Rosenthal says in practice patients sometimes are left on pure oxygen for much longer than an hour—in one hospital he studied, for as much as 121 hours.

At Penn, Becker's Resuscitation Center coordinates with the Emergency Department on a protocol for cooling patients in cardiac arrest. "We look at their prior mental state," says Dr. Dave Gaieski. "If someone was in a coma in a nursing home, we're not going to cool them." The same goes for patients whose hearts stopped for longer than an hour. Since 2005 just 14 patients have met Penn's criteria for hypothermia. Eight survived, six of them with complete recovery. No one knows how many others were saved by cooling around the country.

Bondar arrived at Penn at about 1:30 a.m., still comatose, minutes ticking away while he was evaluated for cooling. Once the decision was made, the team sprang into action, injecting him with an infusion of

chilled saline—two liters at about 40 degrees—then wrapping him in plastic tubes filled with chilled, circulating water. Becker believes, based on animal work, that cooling patients even sooner—ideally, on their way to the hospital—would be even more effective, and part of the work of his lab involves perfecting an injectable slurry of saline and ice that could be administered by a paramedic. Bondar was kept at about 92 degrees for about a day, then allowed to gradually return to normal temperature. He remained stable, but unresponsive, over the next three days, while Monica stayed at his bedside. She finally went home Sunday evening, and was awakened Monday by a call from the hospital that she was sure meant bad news.

"Guess what?" said the voice on the other end. "Bill's awake."

Bondar's first words were, "How did I get here?" He had lost track of a full week, from about two days before his heart attack until he woke up. That's not unusual; short-term memory is often the first casualty of cardiac arrest. Neumar says certain cells in the hippocampus, the part of the brain that forms new memories, are for unknown reasons especially sensitive to ischemia. Another Penn patient, Sean Quinn, was 20 and a student at Drexel University when he went into unexplained cardiac arrest in 2005. He was one of the earliest patients cooled at Penn, and there's reason to believe that it saved his life, but the continuing memory deficit has prevented him from returning to college.

Certainly, people do not form memories while they're in a coma. Exactly one year before Bondar had his heart attack, Brian Duffield, then 40, a salesman in Tucson, collapsed in the shower after a swim. Luckily for him, he was on the campus of the University of Arizona, whose hospital uses a cooling protocol similar to Penn's. "I was there one minute and the next thing I know, it's a few days later and people are telling me I was dead and came back," says Duffield. But Duffield's memory and intellect and personality all returned intact from his brush with death, as did Bondar's. This is, on some level, deeply mysterious. We experience consciousness embedded in time, a succession of mental states continually re-created in our brains, even during sleep. But when the brain shuts down, where does the mind go?

That is the crux of one of the oldest debates in philosophy. The materialist view is that Bondar's memories resided in the physical state of the cells and synapses of his brain, a state that is preserved for some period after the heart stops beating. Becker has pronounced perhaps a thousand deaths in his career, but often with the feeling that—despite the lack of pulse, breathing or discernible brain function—something vital remains in the body on the bed. He felt it most strongly when his own father died of cardiac arrest at the very hospital where Becker was working in 1993. When Becker saw him, he was already dead, but something seemed preserved. "I just had the sense he wasn't really dead yet," Becker says. "He was dead. He had been pronounced. But he hadn't left."

This is the belief motivating people who pay to have their bodies frozen in liquid nitrogen after their deaths, in the hope that they can someday be thawed and restored to life. The Alcor Foundation, in Scottsdale, Ariz., has signed up about 825 prospective patients, and has preserved 76 of them, including Ted Williams. These aren't all whole bodies; some people opt for just their heads, which, apart from being cheaper, freeze faster than an entire body, reducing the danger of frost damage to the cells. Of course, we are a long way from knowing how to reanimate a frozen body, let alone just a head. One possibility, according to Tanya Jones, chief operating officer of Alcor, is to take a cell from the head and clone a new body to attach it to. The other is to scan the entire three-dimensional molecular array of the brain into a computer which could hypothetically reconstitute the mind, either as a physical entity or a disembodied intelligence in cyberspace. This, obviously, is not for the impatient. The physicist Ralph Merkle, an Alcor board member, has used this idea to popularize a fourth definition of death: "information-theoretic" death, the point at which the brain has succumbed to the pull of entropy and the mind can no longer be reconstituted. Only then, he says, are you really and truly dead.

Consciousness is a series of mental states. But when the brain shuts down, where does the mind go?

BUT THERE'S ANOTHER answer to the question of where Bondar's mind was during the last week of May. This is the view that the mind is more than the sum of the parts of the brain, and can exist outside it. "We still have no idea how brain cells generate something as abstract as a thought," says Dr. Sam Parnia, a British pulmonologist and a fellow at Weill Cornell Medical College. "If you look at a brain cell under a microscope, it can't think. Why should two brain cells think? Or 2 million?" The evidence that the mind transcends the brain is said to come from near-death experiences, the powerful sensation of well-being that has been described by people like Anthony Kimbrough, a Tennessee real-estate agent who suffered a massive coronary in 2005 at the age of 44. Dying on the table in the cath lab during angioplasty, he sensed the room going dark, then lighter, and "all of a sudden I could breathe. I wasn't in pain. I felt the best I ever felt in my life. I remember looking at the nurses' faces and thinking, 'Folks, if you knew how great this is, you wouldn't be worried about dying.'" Kimbrough had the odd sensation of being able to see everything in his room at once, and even into the next room. He is one of about 1,200 people who have registered their experiences with a radiation oncologist named Dr. Jeffrey Long, who established the Near Death Experience Research Foundation in 1998 to investigate the mystery of how unconscious people can form conscious memories.

That's also what motivates Parnia, who has begun a study of near-death experiences in four hospitals in Britain, aiming for 30 by the year-end. The study will test the frequently reported sensation of looking down on one's body from above, by putting random objects on high shelves

above the beds of patients who are likely to die. If they later claim to have been floating near the ceiling, he plans to ask them what they saw. Parnia insists he's not interested in validating anyone's religious beliefs; his idea is that death can be studied by scientists, as well as theologians.

As for Bondar, his mind stayed put during his ordeal, which ended when he went home with Monica on June 1, nine days after he died. Gerstenfeld had given him an implantable defibrillator, cleared his blocked artery and inserted a stent to keep it open. "He came back fully intact," says Gerstenfeld. "He was dead, if only for a few minutes. But it could have been much worse. He could have been dead-dead."

We are, Becker believes, at the forefront of a revolution in emergency medicine destined to save millions of lives in the years ahead. This is doctoring at its most basic, wresting people back from death. "I have been fighting with death for 20 years," he says. "And I'll keep doing it, I think, until I meet him in person."

With MATTHEW PHILIPS, JOAN RAYMOND and JULIE SCELFO

There's a New CPR

BY JOAN RAYMOND

The good news: millions of Americans know how to perform CPR. The bad news: when confronted with an apparent victim of cardiac arrest, most bystanders won't do it because it includes mouth-to-mouth breathing.

Now Dr. Gordon Ewy, director of the University of Arizona's Sarver Heart Center, is championing a new form of CPR called cardio cerebral resuscitation, or CCR, which focuses on rapid, forceful chest compressions, about 100 per minute, minus the mouth to mouth. "Mouth to mouth inflates the lungs, but it's not the lungs that need oxygen, it's the heart and the brain," says Ewy. "Chest compressions alone will help save those organs."

The Sarver researchers have developed two separate CCR protocols. Bystanders who witness a cardiac arrest are urged to perform chest compressions until help arrives. Paramedics are to attempt CCR for two minutes, before they use a defibrillator. Several Arizona fire departments have adopted the new approach. An analysis of that data shows survival rates have nearly tripled.

Current American Heart Association and American Red Cross guidelines do recommend compression-only CPR for anyone who is unwilling or unable to provide mouth to mouth. The AHA also encourages emergency dispatchers to give instructions for compression-only CPR to bystanders at the scene of a presumed cardiac arrest. "People want to do the right thing," says Ewy, "and we are giving them an easier way to do the right thing."