

INFLUENZA

**THE HUNDRED-YEAR HUNT
TO CURE THE DEADLIEST
DISEASE IN HISTORY**

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*To prevent the spread of Spanish Influenza, sneeze, cough
or expectorate into your handkerchief. You are in no danger
if everyone heeds this warning.*

—SIGNS POSTED IN PHILADELPHIA RAILCARS, OCTOBER 1918

There's nothing quite like flu in terms of the risk.

—TOM FRIEDEN, FORMER DIRECTOR OF THE CENTERS FOR
DISEASE CONTROL AND PREVENTION, JANUARY 2017

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PROLOGUE: AUTUMN

Autumn Reddinger was deathly sick. Her lungs were not working. Her heart was so weak that it could no longer pump blood through her body. The only thing keeping her alive was a heart-lung machine. She lay corpse-like in the intensive care unit. Her parents had called their pastor to administer last rites. How would they tell Autumn's young children that their mom, who was raising them alone, was dying from influenza, an illness that was usually shrugged off as a minor inconvenience? That a vibrant young woman who went to the gym twice a week was now, in December 2013, at death's door?

During the Christmas break, Autumn thought she had a cold but soldiered through the holiday with her parents and two young children at her home in western Pennsylvania. Two days later she felt much better and went to dinner with a friend, Joe. When she returned to her house she began texting him, but the messages he received were jumbled and made no sense. She had been totally coherent at dinner, and Joe knew she hadn't had any alcohol. Alarmed, he got in his car and drove to Autumn's home, where he found her confused and weak. He called her parents to watch the kids and drove her to the local hospital in Punxsutawney. She told the emergency room nurses that her lungs were on fire.

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The ER physician went through every test: Autumn's lungs sounded clear when he listened to them with a stethoscope. Her pulse and blood pressure were perfect. She had no fever. Her chest X-ray showed no infection in her lungs. Her blood tests were normal, and a rapid test for influenza came back negative. But something wasn't right, so he admitted Autumn to the hospital for observation, just to be safe, and started her on antibiotics.

Autumn's condition quickly worsened. Over the next few hours she became increasingly disoriented and found it harder and harder to breathe. The antibiotics didn't seem to make a difference. The staff made a call to Mercy hospital in Pittsburgh, a two-hour drive away. Autumn's condition was now critical. Transferring her by ambulance was too risky. Mercy sent a medevac helicopter. By the time it arrived, Autumn could no longer breathe on her own. She was sedated, a tube was put into her throat, and she was connected to a ventilator.

Autumn was taken directly to the intensive care unit at Mercy. By now she was coughing up blood, and it became almost impossible to get enough oxygen into her to keep her alive. A chest X-ray showed that her lungs—which had sounded clear and looked entirely normal a few hours earlier—were now filled with pus and fluid. She was given more antibiotics and hooked up to IV medications to keep her blood pressure from dropping. At one a.m. the ICU team called in Dr. Holt Murray, who had trained as an emergency physician and now specialized in critical care. He was Autumn's last hope.

Murray was an ECMO specialist. ECMO, or extracorporeal membrane oxygenation, is the medical term for the technique used by a heart-lung machine. It takes dusky and dark blood, scrubs it of carbon dioxide, fills it with oxygen, and sends it back, red and healthy, into the body. Doctors use it when they perform heart or lung transplants. Since Autumn's lungs were not functioning at all, the machine could step in and do their work.

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When Murray talks to family members about putting a patient on ECMO, he has very little time—perhaps only a few minutes—to explain the procedure and get their permission. “I don’t think we have other options,” he will say, though he is careful to be cautious. “ECMO is potentially lifesaving, but it comes with a host of complications.”

Families are usually in no state to make an informed decision, and are highly dependent on the doctor to guide them. Autumn’s parents, who had arrived at Mercy, agreed with the ECMO plan.

Very quickly Murray inserted a big needle into a vein in Autumn’s groin. This would remove her blood and send it to the machine to be scrubbed and filled with oxygen. Another needle went into her neck, where the blood would return. It didn’t take long for the ECMO machine to improve her oxygen levels. But then her heart stopped.

Murray and his team of nurses and specialists began continuous chest massage and gave an injection of epinephrine to restart the heart. Brief success. Then another episode. More epinephrine. The heart kicked back into action, but it was barely working. Murray did an ultrasound of Autumn’s heart that showed it was functioning at less than 10 percent of capacity. It was no longer able to pump blood through her body.

Doctors have a rather unsavory term for patients in Autumn’s condition: “circling the drain.” It describes, in cold and colloquial terms, that hopeless feeling when every attempt to save a patient is failing. Autumn was circling the drain.

Even though the initial influenza test had been negative, Murray now repeated it using a much more sensitive technique. It revealed that Autumn had the H1N1 influenza virus, the same virus behind the swine flu outbreak of 2009. In a matter of hours, the virus had destroyed her lungs and was now attacking her heart muscle. The ECMO machine that had taken over for her lungs was no longer good enough. It now needed to take over the work of her failing heart. To do that, the machine needed to be replumbed. And that meant transferring Autumn four blocks to

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the University of Pittsburgh's Presbyterian hospital, where a cardiothoracic surgeon could do the procedure. Murray traveled with her in the back of an ambulance, carefully monitoring the portable ECMO machine. Autumn was taken directly to the operating room. The surgeon cracked open her sternum with a surgical saw, and then inserted one catheter into her right atrium, one of the four chambers of her heart. A second catheter went directly into her aorta, and her sternum was wired back together. Her chest now had a long, fresh vertical wound and two large tubes sticking out from it, connecting Autumn to the heart-lung machine. This was the end of the road. There were no more machines, no better interventions or heroic measures that Murray could offer. She would either pull through or die.

Autumn's parents, Gary and Bambi, sat with their pastor in a small family room near the ICU. "We got together and prayed," Gary says. "Then the pastor told us that she saw two angels, and that things would be okay."

The pastor was right. Autumn stabilized. Her heart, stunned by the influenza virus, returned to normal over the next few days. Antibiotics cleared up a secondary bacterial pneumonia, and her blood pressure no longer took sudden nosedives. On January 10, 2014, she was disconnected from the ECMO machine, though she was still sedated and attached to a ventilator. A week later she had improved enough to be discharged from the cardiothoracic intensive care unit. After another month of slow improvements, she left Presbyterian hospital on February 13 for a rehabilitation center closer to home. She had beaten influenza, but now had another battle to fight. Patients who have a long stay in the ICU often develop a profound generalized weakness. At the rehab hospital, Autumn had to learn how to walk again, to climb stairs, and to perform a host of other daily activities that she had once taken for granted. After two weeks of rigorous exercise, she left rehab and came home. In the fall of 2014, nine months after she first caught influenza,

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Autumn was finally strong enough to return to work. Her medical bills were close to \$2 million, but she was fortunate to have good medical insurance and was only on the hook for her \$18 copay.

She was left with scars on her neck and chest. As a result of nerve damage from the needles in her groin, she cannot bend her left ankle, and her left leg sometimes goes numb. But her survival and recovery were a triumph of modern medicine. She pulled through because she was close to a medical facility that was able to offer her the best of today's interventions.

Autumn's fate would have been far different during the influenza pandemic of 1918, the worst in recorded history. The best medicine at the time was aspirin, but it was new, misunderstood, and often given in fatal doses. Desperation and ignorance produced plenty of awful methods of "healing," from barbaric bloodletting to treatments with toxic gas. It is estimated that between 50 and 100 million people died during that influenza pandemic. In the United States there were 675,000 deaths, ten times as many as had died in combat in the Great War, which was ending at the same time the flu was peaking.

The flu is something we have all experienced at some time: the winter cough, the fever, the body aches and chills that knock us out for three or four days and then disappear. As an ER doctor and as a patient, I have experienced it from both bed and bedside. The one and only time that I have visited the emergency room as a patient was when I was sick with a particularly nasty bout of the flu. I had a high fever and was delirious. I was too weak to drink or get out of bed, and I was dehydrated. But even the modern medicine that pulled me through my relatively minor infection—and that which brought Autumn back from the brink of death—isn't always enough. The flu is still a serial killer.

We all harbor the desire to see cancer cured and heart disease eliminated. I obviously share these hopes, but as an ER doctor I have found myself wishing for something far more modest: a cure for influenza.

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We tend to shrug off the flu as just a nasty cold, but in the United States alone it kills between 36,000 and 50,000 people each year. That's an astonishing and depressing number. But here is even worse news: If a pandemic strain of influenza as deadly as the 1918 virus were to infect the United States today, more than 2 million people could die. No conceivable natural disaster would compare. And it's not something we can just pretend won't affect us. In early 2018 newspapers warned that the flu season was "the worst in nearly a decade." All across the country there were reports of young, healthy people dying. Several hospitals were so overwhelmed with the influx of flu patients that they had to set up triage tents or turn patients away.

Flu is certainly not "the emperor of all maladies," as cancer was described by the oncologist Siddhartha Mukherjee, but it is the malady of all empires. It has been with us since the dawn of time, and it has afflicted each civilization and society in every corner of the globe.

We've had several close calls with major viral outbreaks since 1918. The Hong Kong avian flu outbreak in 1997 killed few people, but only because 1.5 million infected chickens were slaughtered before they could spread the disease. In 2003 there was the SARS outbreak that infected at least 8,000 people and killed about 10 percent of them. More recently we have encountered MERS, Middle East respiratory syndrome, which infected 1,400 people between 2012 and 2015. That disease entered the human population courtesy of infected dromedary camels. (Here's some free medical advice: before taking a swig, make sure your camel milk has been pasteurized.) These viral diseases all originated in animal hosts (we think) and somehow jumped into humans—which is what happened in 1918 (we think). We don't know when or where the next viral pandemic will occur, but it *will* occur. There is little doubt that, unless we plan for it, we are in for rather a rough ride.