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*Silent Epidemic*

## **Defying Treatment, A New, Virulent Bug Sparks Health Fears**

**Drug-Resistant Staph Kills Quickly and Randomly; Antibiotics' Worrying Toll Simon Sparrow Wakes Crying**

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In April 2004, Simon Sparrow was a robust toddler, 17 months old and just learning to feed himself. Then he caught a cold.

He awoke with a cry at his family's Chicago home. His parents took him to the University of Chicago Children's Hospital. Emergency-room doctors X-rayed his chest and chalked up his symptoms to a virus and asthma. They let him go home at about 1 p.m. At 4:30 p.m., his mother called back and asked doctors to listen to his worsening breathing over the phone. Call 911, they said.

An ambulance whisked Simon back to the hospital where his condition rapidly deteriorated. Doctors scrambled to insert tubes and administer antibiotics and drugs to combat organ failure triggered by an overwhelming infection. Approaching midnight, he was taken off a regular ventilator in favor of a high-tech, heart-lung bypass system. Twelve hours later, he was dead.

What killed Simon Sparrow is a new form of an old foe: the staph infection. Identified as a lethal threat in 1999, this new strain is

resistant to drugs and is highly virulent, responsible for 60% of all skin and soft-tissue infections treated in the nation's ERs. Infections can recur and ping-pong through families. The germ can penetrate bones and lungs, and the abscesses it causes often require surgery. In severe cases, up to a quarter of patients die.

Public-health officials see a silent epidemic on the rise. Almost 1% of the population, or more than two million people, carry drug-resistant staph without symptoms, according to an article in this month's *Journal of Infectious Diseases* by Matthew Kuehnert, a medical epidemiologist at the U.S. Centers for Disease Control and Prevention. Carriers can spread the disease and suddenly become acutely ill themselves. In a separate study based on data from 1999 and 2000, Dr. Kuehnert estimates there are 292,000 hospitalizations a year for staph, of which 126,000 are for the resistant kind.

Public-health officials have warned for years that heavy use of antibiotics could breed drug-resistant bugs. This version, one of the most extreme so far, is breaking out as the attention of the federal health bureaucracy is focused on more explosive threats such as bioterrorism and bird flu. The test for drug-resistant staph may not be routinely covered by insurance, so many ER and family doctors don't administer it. Even if they did, the standard test takes up to 48 hours to complete, during which time the most serious cases have often turned fatal.

### **MORE INFORMATION**

Researchers studying staph say they are hamstrung by limited funds. Officials have also been slow to publicize the disease. The CDC held an expert meeting on the subject in summer 2004 but is only now editing the proceedings of that meeting for publication this spring. It has posted some information on its Web site. Surveillance is limited because the federal government and most

states don't require doctors to report such cases.

The CDC is now readying a call to doctors for increased vigilance. Its officials say the rapidly developing disease couldn't have been detected any sooner. "I can't point to anything and say that was a failure," says Fred Tenover, associate director for laboratory science in the Division of Healthcare Quality Promotion at CDC. "The organism's biological success...points out we can't have a surveillance system for each unique possibility."

### **Fierce Debate**

Now the nation faces a fierce debate over how to stop the bug. Some argue that all hospital patients should be screened, a position rejected by others on the grounds of cost and practicality. There's also little consensus on how to treat drug-resistant staph once it takes root.

No one knows exactly when or where bacteria become resistant to drugs. In general, public-health officials blame the heavy use of antibiotics, which kill off a disease's sensitive strains and leave the field open for its hardier cousins. Doctors have long prescribed popular drugs such as Keflex and Cipro to combat staph, which some feel may have contributed to the rise of the drug-resistant type. A number of such bugs have cropped up recently, but few with this one's combination of toxicity, resistance and reach.

Staph in its common form is a bacterium carried by nearly one-third of the U.S. population, usually harmlessly in their nostrils. Drug-resistant forms emerged decades ago in hospitals, where only those most impervious to treatment survive. Until recently, they afflicted mostly the elderly or sick patients with compromised immune systems.

But the new form -- known as community-associated methicillin-resistant staphylococcus aureus, or CA-MRSA -- has a distinct

package of resistance genes. Once it gets going, CA-MRSA can't always be reversed by antibiotics. It produces a nasty poison that kills white blood cells used to fight infection and destroys the body's tissue. Especially alarming to doctors, the strain is circulating in the broad community, striking healthy patients often seemingly at random.

At the University of Chicago hospital where Simon died, more than 10 adults and between one and three children have staph-related abscesses drained every day. "This is a huge epidemic," says Robert Daum, the hospital's chief of pediatric infectious diseases. "This is where resistance and virulence meet."

The 1999 deaths of four Midwestern children from CA-MRSA first suggested the arrival of a new, particularly violent form of staph. That piqued the interest of microbiologist Francoise Perdreau-Remington, who works out of a tiny lab at San Francisco General Hospital, where she has collected 7,800 tubes of staph bacteria.

In 2000, Dr. Perdreau-Remington identified the new variant, later dubbed USA300 by the CDC. She describes it as "an epidemic strain that has taken over the market." As part of an unexplained biological trade-off, most bugs weaken as they pick up resistance genes. This one, by contrast, was beating back an increasing number of drugs while at the same time gaining strength.

On a recent day, Dr. Perdreau-Remington pointed to a petri dish in her lab, where a colony of bacteria was busy devouring blood cells. The bacteria had a yellowish hue, which is how it gets the name "aureus," golden in Latin.

When drug-resistant staph first appeared beyond hospital walls, it seemed to thrive only in certain well-defined risk groups: people who had skin-to-skin contact and those sharing close quarters,

sports equipment or personal items such as towels.

At the Los Angeles County Jail, inmates suffered a mysterious plague of apparent spider bites in June 2002. Jail authorities ordered a bug eradication effort, thinking the problem was caused by bites that had become infected with staph. Health authorities determined the infection was staph alone, with no spiders involved, says Elizabeth Bancroft, an epidemiologist at the Los Angeles County Department of Health Services. "The misdiagnosis is so common," she says.

College and professional football teams, including the St. Louis Rams, experienced outbreaks as well, prompting doctors to test everything from Astroturf to whirlpools.

At the CDC in Atlanta, Dr. Tenover had an epiphany in 2004 when the same strain of CA-MRSA that infected prisoners in Georgia, Mississippi, and Texas cropped up in a Pennsylvania football team and among children in Tennessee. "That told me this thing had spread across the U.S. totally off our radar screen," he says.

Brad Frazee, an emergency room physician at Alameda County Medical Center Highland Campus in Oakland, Calif., recalls a 31-year-old man visiting his ER with a bloody cough. Writing in the November 2005 *Annals of Emergency Medicine*, Dr. Frazee says the man was discharged with a prescription for levofloxacin, a cousin of Cipro that doesn't work against CA-MRSA. He returned 15 hours later after his shortness of breath worsened.

Doctors gave him a drug to combat resistant staph but despite that "aggressive treatment the patient died 38 hours after his second presentation," Dr. Frazee wrote. Tests showed he had CA-MRSA.

Most people who get the new strain suffer skin or tissue infections. Such cases can be painful, prolonged or disfiguring, though much less likely to be fatal.

In Houston, 7-year-old Angela Salinas collided with the bumper of the family truck while playing in her driveway last July. Despite having no visible wound, Angela complained of leg pain and ran a fever. Her mother, Cynthia Ruiz, sought care in two hospital trips and from her family physician. Doctors offered Motrin and Tylenol with codeine. Angela's family doctor alerted the hospital to a possible underlying problem with infection in the family, according to Ms. Ruiz.

After five days of unrelenting pain, Angela was transferred to Texas Children's Hospital where scans revealed a deep bone infection and muscle inflammation, plus a dangerous blood clot. The cause: CA-MRSA.

The girl was hospitalized for 16 days during which she underwent an operation to drain pus and blood from her leg and to remove a bone chip for testing. After being discharged, for the next two-and-a-half months she had to take a powerful antibiotic, which was delivered through a tube in her arm, and a blood thinner to treat the clot.

Ms. Ruiz says she believes a bout of skin boils introduced staph into the family. Dr. Sheldon Kaplan, chief of the infectious-disease service at Texas Children's Hospital, says it's likely that staph somehow got into Angela's bloodstream, perhaps through a small scratch, and then infected tissue damaged by the fall.

"Everybody is seeing lots of these cases," said Dr. Kaplan. "Once it came in, it took off like wildfire."

The CDC plans soon to publish the findings of an expert panel on CA-MRSA it held in July 2004, along with educational materials for doctors and the public. It has designed a poster depicting a huge spider: "When in doubt, check it out," the poster says. Another advises against sharing towels and razors. The CDC will

also urge doctors to send infected tissue for testing so it can better understand the disease's pattern. The strains in Houston, Chicago and parts of the West coast show high levels of resistance.

In western Australia, hospitals test patients for MRSA and place the infected in separate wings, notes Stuart Levy, a Tufts University professor and specialist in antibiotic-resistance. Similar efforts are also common in Northern European countries, he says.

In the U.S., such efforts would be controversial because testing everyone and isolating the infected would be costly. Doctors also contend that testing every patient entering a hospital is impractical. Dr. Perdreau-Remington, the microbiologist, says even if it were possible to test everyone and cleanse them of the bug, patients often get re-infected within six weeks. "Do you know how many times a day people touch their nose? About 800."

Conventional tests that identify staph strains take up to two days to complete. Faster tests cost up to \$30 per patient, and they're not comprehensive. Some test only a patient's blood. They also can't determine the entire range of drugs to which the strain is resistant.

### **Without Warning**

Like many staph victims, Simon Sparrow was struck without warning and rapidly deteriorated before medical professionals could get a handle on his condition.

The morning of April 16, 2004, he woke about 6 a.m. with a "primal, terrified shriek," recalls his mother, Everly Macario, who is a consultant in public-health. Simon's father, James T. Sparrow, an assistant history professor, took him to the ER at about 7:30 a.m. His wife joined them an hour later. The doctors assured them that Simon's oxygen was within the normal range. They remained in the ER until 1 p.m., with Simon inconsolable and his lips blue.

Tracy Koogler, a pediatric critical-care doctor who later cared for Simon, says X-rays taken during this visit showed simply a child with a viral cold and asthma.

As the afternoon wore on, Simon's breathing grew more labored, his chest heaving with the effort. At about 4:30 p.m., Ms. Macario had a doctor listen to Simon's labored breathing over the phone. The doctor said, "hang up and call 911," she recalls.

As Simon was taken into the intensive-care unit, after the administration of antibiotics and other drugs, his eyes were open and he looked around. Wasn't that a good sign, Ms. Macario asked? The doctors' expressions told her something was seriously wrong. "They seemed confused, scared, frantic and helpless themselves," she wrote in a later essay detailing the day's events.

Dr. Koogler doesn't contradict the mother's assessment. "This child was dying before our eyes," she says.

The hospital suggested putting Simon on a high-tech respirator to oxygenate his blood, a process called extracorporeal membrane oxygenation, or ECMO. On the ECMO machine, Simon's small body grew bloated and purple and drops of plasma "tears" seeped out of his eyes, Ms. Macario recalls.

By late Saturday morning, Simon was no longer responding to the treatment. His parents decided to shut off the machine. At 12:45 p.m., he was pronounced dead. There was still no precise cause of death.

Dr. Koogler says the hospital examined its treatment of Simon "with a fine-toothed comb" and concluded, after consulting a number of physicians, that "no one would have done anything differently." The progression of Simon's condition was exceptionally rapid. The tests, which came back after his death, confirmed Simon had CA-MRSA.

After Simon's funeral, his parents were assailed by questions. "Why him? Where did he get it? Did he breathe it in?" says Ms. Macario. She wondered whether past steroid treatment for asthma lowered his immunity, or if visits to a family acquaintance on dialysis exposed him to staph. Dr. Koogler says there's no way to know where it came from.

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