

THE GERM LURKS IN UNEXPECTED PLACES:

The patient's TV remote // A visitor's handbag // The doctor's gown // A nurse's computer keyboard // A thousand other spots from which it could be erased but isn't—and so kills tens of thousands of Americans each year.

A Killer Called Staph

■ BY WENDY ORENT

The 84-year-old patient, “Mr. S.,” has been transferred from a nursing home in Atlanta to one of the city’s large public hospitals. He lies in bed, barely conscious, wearing a diaper and a urinary catheter. An IV delivers heparin to ward off blood clots, and a solution of dextrose and water to prevent dehydration. His leg has been amputated below the knee, a result of the diabetes. He shivers while his student nurse, “Christian,” perspires in the overheated room. Mr. S. retains enough awareness and gentility to thank the young man who has spent 40 minutes helping him coax down bits of food.

Christian wears a disposable gown and double gloves but no mask, a fact that makes him uncomfortable. Mr. S.’s skin is sloughing off because of two infections—MRSA, or methicillin-resistant *Staphylococcus aureus*, and VRE, or vancomycin-resistant *Enterococci*. Both infections, but especially the first, are rampant in U.S. hospitals, and they’re very hard to cure.

Before leaving the room, Christian sheds his gown and gloves, dumps them into the biohazard disposal unit and rubs his hands thoroughly with disinfectant. Outside, before going on to his next patient, he stops off at the bathroom to scrub his hands with hot, soapy water.

In this single instance, the relentless chain of transmission that has made MRSA a lethal threat in most U.S. hospitals has presumably been broken by the attentiveness of one young man. But Christian is only a student. He isn’t yet subject to the intense pressures that send nurses in his big-city hospital dashing from one patient to the next, caring for 10 when four is supposed to be the limit. Nor is he a harried physician who, striding quickly through the corridors on morning rounds, may not notice that his gown has brushed against a patient’s bed and does not realize that he could be transmitting an infection from the last patient to the next, even if he touches neither.

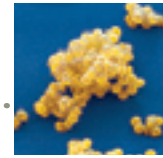
Carried from person to person in a thousand ways, MRSA and other hospital-borne infections exact a monstrous toll.

A Brief History of Staph



1860s

THE ENGLISH SURGEON JOSEPH LISTER, influenced by Louis Pasteur's work on infectious agents, uses carbolic acid directly on wounds and surgical dressings, preventing most post-operative infections.



1881

STAPHYLOCOCCUS IS IDENTIFIED AS A CAUSE of wound infection by the Scottish surgeon Sir Alexander Ogston, who named it for the grape-like clusters (in Greek, *staphyle*) he observed under the microscope.

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According to the U.S. Centers for Disease Control and Prevention (CDC), each year these virulent bugs afflict 2 million patients and take some 90,000 lives. Those who survive may suffer debilitating illnesses for months or years.

Though rates of MRSA infection in many European hospitals have dropped to almost undetectable levels, multidrug-resistant staph is widespread in the United States. It doesn't get the media attention of avian flu, SARS or Ebola, but it is a far deadlier and more insidious threat—all the more so because the spread of staph infections in hospitals is a product of the way medicine is practiced in this country.

"If God wanted to send us a plague to expose the weaknesses of American medicine, that plague would be MRSA," says Peter Perreiah, managing director of the Pittsburgh Regional Healthcare Initiative (PRHI), a 42-hospital collaborative that has worked to eliminate the MRSA scourge. According to Perreiah, MRSA has become "a leading cause of hospital-acquired infection" in the United States. "Preventing it is about fixing our health-care system," he says.

The genus *Staphylococcus* consists of several related species, of which two, *S. aureus* and *S. epidermidis*, are human pathogens. These spherical bacteria, which cluster in irregular bunches (*Staphylococcus* is derived from *staphyle*, the Greek word for a bunch of grapes), frequently colonize the skin and nostrils of their human hosts.

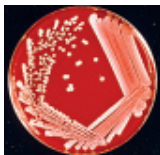
Only the severely immunocompromised fall victim to *S. epidermidis*, which is normally harmless. But *S. aureus*, named for the golden-yellow colonies it grows on agar and other media for growing bacteria, can infect otherwise

healthy individuals, attacking a range of human tissues. Any cut or abrasion may allow *S. aureus* an entrance. Sometimes only a small pimple results; at other times, *S. aureus* produces boils (a hair-follicle infection), abscesses, impetigo (a potentially serious, spreading skin condition) or cellulitis (another skin infection). Staph infection in the bloodstream produces often-fatal septicemia; osteomyelitis (infections in the bone) may not be fatal but can persist for decades.

One reason hospital-borne staph strains have evolved toward greater virulence—even deadliness—is their durability in the external environment. *S. aureus* is what Paul W. Ewald, an evolutionary biologist at the University of Louisville, calls a "sit and wait" pathogen. Though, unlike anthrax—another deadly and resilient agent—staph doesn't produce spores, it can persist under adverse conditions. It can survive for days or even weeks on fomites (objects contaminated by germs) such as computer keyboards, TV



FROM TOP LEFT: BETTMANN/CORBIS; EYE OF SCIENCE/PHOTO RESEARCHERS, INC.; IMAGESOURCE.COM (GLOVES); HOLOS/GETTY IMAGES (HANDPRINTS)



1884

STAPHYLOCOCCUS AUREUS IS ISOLATED BY

German scientist Anton Rosenbach, who grows the two strains, *S. aureus* ("golden staph," for the golden colonies it grows on bacterial media) and *S. albus* (white colonies), in pure culture.



1930s

A "COAGULASE" TEST ENABLES SCIENTISTS TO

detect a plasma-coagulating enzyme secreted by *S. aureus*, still the most common cause of wound infections in hospitals. Coagulase-positive staph is the most virulent strain.



1941

THE MORTALITY RATE OF *S. AUREUS*

bacteremia is reported as 81% in a Boston hospital. The same year, a British policeman seriously ill with *S. aureus* is cured by penicillin.

remotes and telephones. "In long-forgotten petri dishes in the lab, you could still scrape up live *S. aureus*," says Ewald.

And while flu and other infectious diseases require mobile hosts who sneeze or cough on the next victim, staph is happy to hitch a ride on unaffected nurses, doctors, aides, even visitors. Attendant-borne infections are like those carried by mosquitoes, says Ewald; both can maintain great virulence because they don't depend on host mobility for transmission.

To further complicate control of staph in the hospital, some strains now appear to be resistant to common hospital disinfectants. According to a 2002 article that appeared in *Lancet Infectious Diseases*, "In versatility of pathogenic strategies, numbers of virulence factors, and capacity to survive and multiply in a wide range of environments, *S. aureus* is unsurpassed by any other human pathogen."

That leaves American hospitals with a grievous problem: an insidiously spreading, often deadly disease that is very hard to treat. According to Perreiah, vancomycin, now the "drug of last resort," doesn't work all that well on MRSA infections, and resistance to it may be increasing. "If we lose vancomycin as a drug, we have limited options," he says.

As formidable an enemy as *S. aureus* has become, controlling its spread is not impossible, nor is there much mystery about what needs to be done. It won't be defeated by drugs but rather by interrupting the chain of its transmission in hospitals. The history of the bacterium—and its successful control in a few places—points the way.

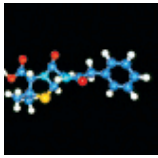
First recognized during the late nineteenth century as a common cause of infection at surgical sites and wounds, staph had become the most frequent cause of hospital-borne infections by the 1930s. After a short-lived rout by antibiotics, particularly penicillin, during the 1940s—when *S. aureus* seemed to disappear—new, antibiotic-resistant staph strains began to emerge in hospitals all over the world. Penicillin quickly became ineffective; another drug, methicillin, was

substituted, but resistance to that and several other widely used drugs soon followed. The resistant strain of *S. aureus* that has become the scourge of hospitals spread worldwide from its apparent origin in Europe during the early 1960s.

But since the 1970s, a strict no-tolerance policy has driven down infection rates in much of Europe—particularly in the Netherlands, Iceland, Norway, Denmark and Sweden—to extremely low levels. In Dutch hospitals, patients are routinely tested to see whether they're harboring MRSA strains. Even those who merely have transient bacteria in their nasal passages are isolated in single rooms, and visiting family members must be gowned and masked. Meanwhile, physicians and others who come in contact with affected patients are constantly monitored through nasal swabs to make sure they're not carrying the bacteria. Hospital workers in these northern European countries wash their hands often and use alcohol-based sanitizers, which are even more effective than soap and water—and easier on the hands. Floors and other surfaces are frequently disinfected.

In the United States, the PRHI has also begun to make measurable headway against MRSA. Inspired by former U.S. Treasury Secretary Paul O'Neill's success at improving worker safety when he was CEO of Alcoa, PRHI has adopted principles of the Toyota Production System in declaring a systematic war on MRSA. Like workers in Toyota plants, all employees in participating Pittsburgh-area hospitals—from physicians and administrators to aides and the cleaning crew—have been given the authority to take action whenever they spot a problem. And just as Toyota produces virtually defect-free vehicles, PRHI hospitals have sharply cut infection rates among patients.

According to Richard P. Shannon, chairman of the department of medicine at Allegheny General Hospital and an executive committee member of PRHI, 236 patients had documented MRSA infections during the three years preceding the MRSA initiative. Those infections cost the hospital



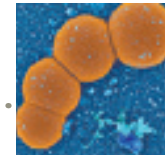
1940s

WIDESPREAD USE OF BENZYL PENICILLIN cures many staph infections. But having a “cure” leads to lapses in antiseptic and aseptic protocols. By the late 1940s, penicillin-resistant staph outbreaks begin to occur.



1959

WHEN PENICILLIN PROVES NO LONGER able to control staph infections, a new drug, methicillin, is developed. Introduced in Europe, it has a short-lived usefulness as the bacterium evolves to resist it.



1961

METHICILLIN-RESISTANT *S. AUREUS*, NOW known as MRSA, is detected in a British hospital; during the next 10 years, multidrug-resistant staph becomes widespread in Europe, Australia and the United States.

\$3.2 million, or almost \$14,000 per patient. Patients with MRSA infections spent an average of 31 days in the hospital, and 49% were readmitted at least once for MRSA-related complications. Thirty-eight patients died.

At Allegheny, patients are now swabbed nasally when they are admitted to intensive-care units to make sure they aren't harboring MRSA. “About 8% come in with MRSA,” says Shannon. “We never would have known that before.” As in northern Europe, infected patients, four out of five of whom have been hospitalized previously, are isolated and treated; health-care workers and visitors must wear disposable gowns, gloves and masks; and anyone walking into these patients' rooms must use a hand sanitizer. Shannon and his team rely on a long list of little things that, taken together, can be remarkably effective. “There is no magic bullet, no vaccine,” he says. “This is not about technology; it's about process.”

MRSA by the Numbers

119.3 Number, per million, of the population of Ireland infected with MRSA in 2003, according to an antimicrobial surveillance study of European hospitals; doctors blame poor hospital hygiene and overcrowding

46.5 Number, per million, of the population of Portugal infected with MRSA in 2003 (the European study's runner-up)

<1 Percentage of tests at two Icelandic hospitals that were positive for MRSA in 2002

51 Percentage of tests at 36 Greek hospitals that were positive for MRSA in 2002

95 Percentage of clinicians who think antimicrobial resistance to infections such as MRSA is a problem in the United States

77 Percentage who think antimicrobial resistance is a problem in their institution

It is also about getting physicians and other hospital personnel to take responsibility for halting the spread of MRSA—and in most U.S. hospitals, that hasn't happened. Part of the problem, according to Perreiah, is that most doctors seem to think that the main culprit is overprescription of antibiotics. But if that were indeed the case, with new strains of MRSA constantly developing to evade attack by overabundant antibiotics, researchers would expect to find a great number of clones—distinct genetic lines—with diverse ancestry. Yet 70% of MRSA strains are descendants of just two clones, one of which originated in Denmark during the late 1950s.

The resistance of *S. aureus* to some important drugs—the so-called beta-lactams—is based on a gene called *mecA*, part of a cassette of DNA that *S. aureus* acquired from some unknown bacterial donor. The *mecA* gene itself probably originated in *S. sciuri*, a germ that lives on the skin of many animals. Though it's not known where the cassette came from or how it entered *S. aureus*, it may have been through conjugation—a direct exchange of bacterial DNA through physical contact between a donor cell and *S. aureus*—or by some other means, such as with the help of a bacterial virus.

The *mecA* gene is now integrated into the *S. aureus* chromosome, making its association with the bacterium more stable. Whatever the ultimate source of their drug resistance, these clones have proved extraordinarily effective in their ecological niche: the hospitals of the world. Their inexorable spread underscores that hospital attendants, rather than mosquitoes, fleas or other disease-carrying vectors that aren't present in hospitals, are responsible for transmitting the disease. Still, while overuse of antibiotics is not the major reason why MRSA strains constantly evolve, it does contribute to the continued replacement of antibiotic-susceptible strains by multidrug-resistant clones.

But a misconception about the cause of the MRSA plague isn't the only reason physicians and other health workers have fallen short in efforts to defeat *S. aureus*. While many understand that hospital-borne infections are a national crisis, they tend to think it's not their problem, says Ronda Cochran of the CDC. “In order for clinicians to be part of

FROM LEFT: LAGUNA DESIGN/PHOTO RESEARCHERS, INC.; NICHOLAS EVELEIGH/GETTY IMAGES; DR. GARY GAUGLER/PHOTO RESEARCHERS, INC.



1970s

DENMARK, THE NETHERLANDS AND OTHER

European countries establish stringent infection-control regulations; MRSA rates begin to drop there while holding steady or climbing in the United States and Britain.

the change, we need to understand their perceptions. If they think antimicrobial resistance is a problem elsewhere but not in their own backyards, they are not going to take the problem as seriously. They need to be aware of the impact that their individual actions have on their patients.”

Nancy White, an infection-control nurse at Grady Memorial Hospital in Atlanta, enforces that kind of awareness. “You have to be autocratic,” says White, who insists that nurses and other staff wear gowns and gloves every time they visit patients with resistant infections, and use hand sanitizers every time they leave a patient’s bedside. She counts herself



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lucky because she has three infectious-disease doctors on staff: “A lot of smaller hospitals have only one nurse on this.”

But it will take more than individual nurses and physicians, no matter how engaged and well schooled in fighting *S. aureus*, to reduce the awful toll on hospital patients. The PRHI, like the health systems in the Netherlands, Denmark and other countries, has systematized infection control. The PRHI model, or something like it, needs to be in place in every hospital in the country.

S. aureus has haunted humanity for millennia. It isn’t going anywhere: Because the germ can live happily in the environment and on our skin, it won’t be eradicated, as smallpox has been. What’s more, a further complication has emerged as new strains of MRSA have begun flourishing outside hospitals. That’s a problem not only for those who pick up these “community associated” bugs in health-club locker rooms but also for patients in the hospitals where the victims show up. In some parts of the United States, community-associated

MRSA now accounts for about a fifth of the *S. aureus* strains causing skin infections. Even so, MRSA infections in hospitals can be controlled, and the chain of transmission broken. “No one expects to live forever, but they don’t expect to die needlessly,” says Shannon. “We want to be able to say, ‘No one will come into my hospital and be harmed.’” ■

→ DOSSIER

1. *The Doctors’ Plague: Germs, Childbed Fever, and the Strange Story of Ignác Semmelweis*, by Sherwin B. Nuland [Norton, 2003]. A moving account of Semmelweis’s fierce campaign to eliminate one lethal kind of hospital-acquired infection, puerperal fever, before germs were even recognized as the agents of disease.
2. *Hospital Infection: From Miasmas to MRSA*, by Graham A.J. Ayliffe and Mary P. English [Cambridge University Press, 2003]. An excellent introduction to both the history of hospital-acquired infections and the present problems, including the evolution of antibiotic resistance.
3. *Evolution of Infectious Disease*, by Paul W. Ewald [Oxford University Press, 1994]. An indispensable text for anyone who wants to understand how bacteria like *S. aureus* evolve to become deadly threats.

FROM LEFT: A. HUBERU, STARKE/CORBIS; JACK SULLIVAN/LAMY