Don't Mess With MRSA



Magnified 20,000X, this colorized scanning electron micrograph shows a grouping of methicillin resistant Staphylococcus aureus (MRSA) bacteria.

Photo credit: Janice Carr Public Health Image Library

▶ On October 15, 2007, Ashton Bonds, a 17-year-old high school senior from Lynch Station, Virginia, died after being hospitalized for more than a week. Ashton went to the hospital October 4 complaining of a pain in his side. After ruling out appendicitis, the doctors sent him home where his condition deteriorated. Three days later he was admitted to Bedford Memorial Hospital and diagnosed with a bacterial infection called MRSA that had spread to his kidneys, liver, and lungs. He was sedated and put on a ventilator. Doctors were about to perform surgery to clear the infection from his lungs when they found a blood clot near his heart and could not operate. "His lungs didn't recover," said Aston's mother Veronica Bonds. "I want people to know how sick [this disease] made my son."

It's one of those things that's not supposed to happen—a bacterial infection that seems to come from nowhere striking down a healthy teenager. ►

Although contracting a life-threatening MRSA infection outside of a hospital setting is unlikely, the number of such cases is rising, and doctors and healthcare officials around the world are concerned. A day before Ashton's death, a 12-year-old boy from Brooklyn, New York succumbed to an identical infection. The following spring, the Duke University Medical Center in Durham, North Carolina had four cases of MRSA infection in a single month—one involved a 13-year-old girl, whose bout with the infection led to a life-and-death struggle with necrotizing ("flesh-killing") pneumonia.

These illnesses were all caused by a particularly nasty strain of bacteria called methicillin-resistant *Staphylococcus aureus* or MRSA (pronounced mer-sah). MRSA is commonly known to the general public as a superbug—a bacterium that is resistant to many antibiotics, and thus hard to kill once it has infected the human body. MRSA infections do not respond to a class of antibiotics doctors call beta-lactam antibiotics. (Commonly prescribed drugs in this set that include methicillin, as well as penicillin, oxacillin, amoxicillin, and cephalosporins.)

In 2007, researchers from the Centers for Disease Control and Prevention (CDC) estimated that MRSA is responsible for the deaths of nearly 19,000 Americans each year, a number comparable to the U.S. death toll from HIV/AIDS.



No need to panic! Most people who become infected by the MRSA strains found outside of hospitals develop treatable skin and soft tissue infections.

Where do staph (and MRSA) infections come from?

Lots of bacteria are naturally present on and in your body.

Your body is like a whole ecosystem where bacteria play important roles that scientists are learning more about all the time. And while these common bacteria usually don't cause illnesses, virtually any of them can become a problem if they get into the wrong place and are able to multiply. For example, *Escherichia coli* (*E. coli*) are bacteria that inhabit the human gut and are important in food digestion, but if they leak from the intestine into the abdominal cavity they can cause peritonitis, a potentially fatal inflammation of the abdominal lining.

Similarly, ordinary *Staphylococcus aureus* (*S. aureus*), usually shortened to staph, is commonly found on the skin and in the nostrils. Around 25% to 30% of the population naturally carries *S. aureus* without illness. A smaller number of people (approximately 1% of the population) carry the MRSA form of staph in the same way. When a staph or MRSA



infection does occur, probably through a break in the skin, it usually produces skin conditions such as boils or rashes. Most staph infections, including MRSA, appear as a bump or infected area on the skin that may be:

- RED
- SWOLLEN
- PAINFUL
- WARM TO THE TOUCH
- FULL OF PUS OR OTHER DRAINAGE

While rare in healthy people, invasive MRSA infections can occur if MRSA bacteria get into the bloodstream and attack other tissues and organs. These infections can cause serious and even fatal disease, such as sepsis (blood poisoning), necrotizing pneumonia, joint infections, and endocarditis (heart valve infections). The CDC estimates that the number of invasive MRSA infections in 2005 was around 94,400. About 20% of those with invasive MRSA infections die.

People with more serious MRSA infections may also have a fever, muscle aches, chills, and other flu-like symptoms. If you think you might have a staph or MRSA infection, visit a healthcare provider. You won't be alone! Americans seek medical attention approximately 12 million times each year to get checked for suspected staph or MRSA skin infections. (www.cdc.gov)



An abscess, located on the back, caused by MRSA. Photo credit: Gregory Moran, M.D.

What are the types of MRSA?

You expect to get better when you go into the hospital, not sicker. **>**

Around 1.7 million patients in U.S. hospitals and healthcare facilities contract hospitalrelated (nosocomial) infections annually, and nearly 100,000 people die from these infections—more than the number of Americans killed annually by homicides and car accidents combined. (www.cdc.gov) MRSA was first identified as a nosocomial infection in the United Kingdom in 1961. Today, most serious invasive MRSA infections still occur in hospitals and other healthcare settings. This kind of MRSA infection is commonly termed healthcare-acquired or HA-MRSA.

When you stop and think about it, the spread of HA-MRSA in hospitals is not so surprising. Healthcare environments provide ideal conditions for the evolution and spread of drug-resistant bugs like MRSA. Healthcare facilities have a lot of sick people, many of whom have weakened immune systems and are loaded with a spectrum of germs. Hospital staff moves from patient to patient, sometimes carrying germs inadvertently. The quantities of antibiotics, antiseptics, and other anti-microbial agents used provide strong selection pressure for bacteria to evolve resistance. Germs that can survive these onslaughts are usually pretty hardy. The CDC estimates that 70% of the infections Americans acquire while in the hospital are resistant to at least one of the common antibiotics used against them. Hospitals also provide many pathways for germs to enter the human body, including IV lines, catheter tubes, ventilators, and incisions.

Until recently, nearly all MRSA cases were limited to the healthcare settings. However, since the 1990s, physicians have reported an increasing number of cases among the general population. Known as community-associated methicillin-resistant staph or CA-MRSA to distinguish it from its hospital-acquired cousin, it is now the most frequent cause of skin and soft tissue infections appearing in emergency rooms across the U.S.

Most CA-MRSA infections in the U.S. are skin and soft-tissue infections that appear as boils, impetigo, or abscesses. Necrotizing skin lesions caused by MRSA are often mistaken for spider or insect bites. CA-MRSA made headlines in 2005 when Miami Dolphins Junior Seau and Charles Rodgers contracted limb-threatening MRSA skin infections.

The CDC estimates that about 14% of CA-MRSA cases are of the more serious type of infection in which the MRSA bacteria invade the bloodstream and other organs. Invasive CA-MRSA infections were responsible for the deaths of four children in Minnesota and North Dakota in 1997. In 2005, college football player Rickey Lannetti died of MRSA pneumonia after contracting flu.

A genetic variant or subtype of a microorganism is called a strain. Genetic analysis has shown that CA-MRSA is not just the same bacteria as HA-MRSA that people happen to contact outside of hospitals; it is actually a different strain. This suggests that CA-MRSA strains may have evolved in the community separately from the healthcare environment.

How did MRSA become resistant to antibiotics?

Bacteria such as MRSA become resistant to antibiotics because they evolve through natural selection. ►

Here's how it works: Each bacterium's DNA is a little different than its neighbor's ... just like each person's DNA is different. Some of the bacteria in a patient's body will have DNA that gives them resistance to an antibiotic and therefore a slightly better chance of surviving. As the antibiotic kills off the majority of bacteria, the few resistant ones continue to multiply, passing this resistance along to their offspring. If these bacteria are later exposed to the same antibiotic, then the most resistant of these already resistant bacteria multiply even more.

Eventually, a population of bacteria evolves that is completely unaffected by the antibiotic. To make matters worse, some bacteria are able to transfer their resistant genes to other bacteria by exchanging small segments of DNA. In effect, the bacteria not only "learn" for themselves how to resist antibiotics, they can "teach" the trick to others. For example, *Staphylococcus aureus* is thought to have acquired an antibiotic-resistant gene, called mecA, from another species of bacteria that is common on the skin of domestic and wild animals.



Schematic circular diagrams of the MRSA252 and MSSA476 chromosomes. Image credit: Complete genomes of two clinical Staphylococcus aureus strains: Evidence for the rapid evolution of virulence and drug resistance, Matthew T. G. Holden, et. al, Proceedings of the National Academy of Sciences

Can antibiotic resistance be stopped?

Antibiotic resistance is a natural outcome of using antibiotics to treat disease. >

Antibiotics were seen as miraculous in the 1940s, when they were first widely used. Infections that were once deadly or crippling could be cured in days, if not hours. Penicillin, the first mass-produced antibiotic, saved the lives of many thousands of American soldiers during World War II. Soon, infected wounds, septicemia (blood poisoning), pneumonia, and scarlet fever were no longer death sentences for millions. However, almost as soon as penicillin was introduced, strains of bacteria

appeared that produce an enzyme, called penicillinase, which destroys the penicillin molecule. Bacteria with this enzyme were thus resistant to penicillin. Early resistant strains of staphylococci and streptococci (another common infectious bacterium) occurred most commonly in hospitals and other healthcare facilities, where they were responsible for many deaths.

Many people unrealistically assume that science will come to the rescue and solve the problem of antibiotic resistance. They think that if pharmaceutical companies just keep making more and better antibiotics, infectious diseases will soon be a thing of the past. Unfortunately, this attitude has vastly underestimated the extreme versatility and adaptability of microorganisms.

Overuse and misuse of antibiotics have worsened the problem of antibiotic resistance. Even though antibiotics don't work against viral infections such as colds and flu, patients often demand them, and doctors prescribe them to satisfy patients. In other cases, doctors prescribe an antibiotic "just in case" when they're not certain if the microbe causing the patient's illness is a bacteria or a virus. Millions of Americans end up taking unnecessary antibiotics every year.

Even when antibiotics are needed and prescribed appropriately, many people stop taking the medicine as soon as they feel better, instead of completing their treatment. Consider this scenario: One of your classmates is

sick. She goes to the doctor, who prescribes a 10-day course of antibiotics. However, after three days, your classmate feels fine and stops taking the antibiotics. A few days later, she's sick again. She goes back to the doctor, who prescribes more of the same antibiotic, but after three days, she feels no better. If your classmate had completed her first antibiotic treatment, more of the resistant bacteria would have eventually died, and her immune system would have been able to take care of the remaining infection. Because she ended her treatment too early, plenty of resistant bacteria were left to reproduce and make her sick again. The same antibiotic did not help against this resistant population.

Awareness of antibiotic resistance is starting to change medical thinking. Official medical guidance now warns against treating sore throats and ear aches with antibiotics until it can be established that the source of the infection is bacterial, not viral. Plus, doctors are learning that some bacterial infections clear up just as fast without antibiotics.



This figure shows the penicillin core structure. "R" is variable group.

Alexander Fleming discovered penicillin in 1928 when mold from the genus Penicillium, being grown for other research in Fleming's building, accidentally contaminated petri dishes in his lab and killed the Staphylococcus bacteria in them. Fleming named the antibacterial substance "penicillin," but believed it had little practical application.

Years later, Howard Florey, Ernst Chain, and Norman Heatley worked out how to isolate and concentrate penicillin, leading to its practical use in medicine. In 1945, Fleming, Florey and Chain shared in the Nobel Prize. The contributions of Heatley, the junior member of the team, were not fully recognized for another 50 years. In 1990, he was awarded an honorary Doctorate of Medicine from Oxford University.



Am I at risk of MRSA infection?

First of all, be informed, but don't be scared.

Recent data suggest that MRSA in the community is increasing. (www.cdc.gov) The good news is that most staph and MRSA skin infections can be effectively treated by drainage of pus by a doctor (don't try this yourself!), with or without antibiotics. More serious invasive infections, such as pneumonia, bloodstream infections, or bone infections, are very rare in healthy people who get MRSA skin infections. The people most at risk for contracting invasive MRSA are people who have recently spent time in the hospital. Especially prone to infection are elderly people and people whose immune systems have been suppressed due to HIV/AIDS or chemotherapy.

Remember, a certain percentage of people are walking around with MRSA bacteria on their skin. So, it makes sense that CA-MRSA is transmitted by skin-to-skin contact or contact with shared items such as towels or razors that have touched the bacteria on someone's skin. You can assess your own risk of contracting MRSA if you consider the 5 C's-the factors that allow staph and MRSA to spread:

- **CROWDING** •
- frequent skin-to-skin CONTACT .
- **COMPROMISED** skin (cuts or abrasions)
- **CONTAMINATED** items and surfaces
- lack of CLEANLINESS.

The risk for young people in school of contracting a MRSA infection is higher if they live in a dormitory (hmm, crowding and lack of cleanliness come to mind!) or are athletes participating in contact sports such as football or wrestling. Athletes should be particularly careful to avoid sharing personal items that have touched sports-related wounds. In 2003, five members of the St. Louis Rams contracted MRSA infections on areas of the skin where they had suffered "turf burns." The skin damaged by turf burns gave the bacteria a place to take hold, and the disease was likely spread from one person's infected skin to another person through shared towels, whirlpool baths, and weightlifting equipment. Other groups at higher risk of getting CA-MRSA infections include childcare workers, athletes, prison inmates, people with poor hygiene, and IV drug users.

What can I do to lower my risk?

Careful attention to personal hygiene is key to avoiding MRSA infections:

- Wash your hands often, especially if you are visiting someone in a hospital.
- Speak up and ask healthcare providers to wash hands or use hand sanitizer before examining you.
- **Don't share personal items** such as towels or razors with another person.
- Cover a wound with a clean bandage, and avoid contact with other people's soiled bandages.
- Clean shared sports equipment with antiseptic before using.
- Avoid using common whirlpools or saunas with someone who has an open sore.
- Check that shared bathing facilities are clean.
- Wear clean clothes daily especially important when clothes have become sweaty.
- The nose is a MRSA breeding ground. Keep fingers out.

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