BACTERIOLOGY

Flesh-Eating Bacteria: Not New, But Still Worrisome

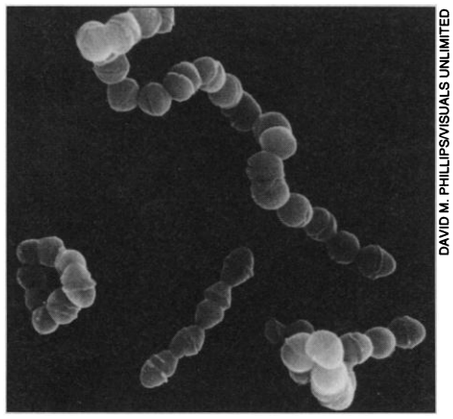
"Killer bug ate my face" screamed a headline last month, as Britain's tabloids created panic with graphic descriptions of the effects of a strain of Group A streptococcus, a bacterium that, in severe cases, can destroy tissue as fast as surgeons can cut it out. An unexplained proliferation of seven cases around the city of Gloucester had the press predicting an epidemic, and British public health officials had to fight to bring the panic under control.

In fact, the outbreak of necrotizing fasciitis and myositis—the flesh-eating conditions that so fascinated the tabloid papers—is simply the latest twist in a series of apparent changes in the virulence of streptococcus A. Those changes have concerned bacteriologists on both sides of the Atlantic for the past 5 years. (A virulent strep A infection claimed the life of Muppeteer Jim Henson in 1990.) The flesh-eating aspect isn't new either, although some experts think it could be on the rise. And although there aren't enough good epidemiologic data to tell whether the virulent strep A strains are actually spreading, researchers are zeroing in on a powerful combination of two toxins that enables them to do their deadly work.

Streptococcus A is best known as the cause of streptococcal pharyngitis, or strep throat. But unlike the docile strains that cause strep throat, the virulent strains penetrate deep into the body, with catastrophic results. Since 1986, it's been recognized that invasive strep A infections can trigger a toxic shock syndrome, characterized by a precipitous drop in blood pressure, failure of multiple organs, and a raging fever. Sometimes the invasive strep A also chews up muscle (myositis), or destroys the sheath that covers the muscle (necrotizing fasciitis).

Concerned because the incidence of invasive streptococcus A infections was unknown, the Centers for Disease Control and Prevention (CDC) in Atlanta conducted surveillance in four states between 1989 and 1991. Extrapolating from the four states, CDC researchers concluded that up to 15,000 cases of invasive strep A infections occur annually in the United States and that between 5% and 10% of them are associated with necrotizing conditions. (Their results were published 2 weeks ago in the *Morbidity and Mortality Weekly Report.*)

The CDC data provide no inkling of whether the invasive form of strep A is on the rise, but a spate of reports documenting outbreaks over the past decade in the United States, Canada, Australasia, Scandinavia, and the United Kingdom suggest to some investigators that it is. "There was an increase in the late '80s," says Patrick Schlievert of the University of Minnesota in Minneapolis, whose lab is the U.S. testing center for the invasive strains of strep A. "Then it took a dip, and now it's gone back up above what it was before." Schlievert says that in 1991 and 1992 his lab received about two samples a week; this year, even before all the media attention, the rate has shot up to about two samples a day.



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Dots of death? Type A streptococcus bacteria, which may be increasing in virulence.

Dennis Stevens of the Veteran's Affairs Medical Center in Boise, Idaho, who specializes in treating invasive strep A infections, agrees. "Something is different. If you look through the literature [before the 1980s], there's only a few reports of necrotizing fasciitis, and they weren't as severe." Necrotizing fasciitis was described in China in 1924, for example, but it was less aggressive, felling only about 20% of its victims, even though antibiotics weren't available then. In contrast, the recent British outbreaks killed 70% of their victims.

But case histories and anecdotal evidence simply aren't enough to close the case—and conclusive epidemiologic data are lacking. World Health Organization spokesperson Thomson Prentice says surveillance for invasive strep A infections is grossly inadequate throughout the world—including the United States, where the CDC has abandoned active surveillance—and so it is impossible to tell whether virulent strep A and necrotizing fasciitis and myositis are increasing or whether researchers are simply more aware of the problem.

While the trends in virulent strep A infection are still being debated, researchers are beginning to discover what makes the infection so deadly. The new strains wreak their damage, in part, by secreting a protein called pyrogenic exotoxin A, which acts as a "superantigen." Ordinary antigens, the protein fragments that kick the immune system into gear, stimulate one in 10,000 of the key immune cells called T cells. Superantigens, on the other hand, stimulate as many as one in ten, triggering an out-of-control production of cytokines, chemicals that carry signals between cells. The cytokines in turn damage the cells that line the blood vessels so that fluid leaks out, blood flow dwindles, and tissues die from lack of oxygen.

Exotoxin A seems to be one of the hallmarks of the invasive strep A infection. Of the invasive strep A strains studied in the United States, 85% carry the exotoxin A gene, compared with 15% of all strep A strains, according to a 1992 report by Schlievert and his colleagues. Moreover, patients with severe invasive strep A infections—toxic shock with or without necrotizing fasciitis and myositis—have depleted numbers of T cells bearing the superantigen receptor, according to studies reported last year by a team led by Malak Kotb of the Veteran's Affairs Medical Center in Memphis, Tennessee. According to animal studies, T cell depletion (following T cell proliferation) is a characteristic of a superantigen reaction.

But the most horrifying aspect of severe strep A infections—the rapid destruction of tissue—is localized, so it is unlikely to be caused by a general overstimulation of the immune system, says Schlievert. Instead, the invasive strains of strep A probably have more than one weapon in their armory, and the second main weapon may be another deadly toxin. James Todd of the University of Colorado Medical Center in Denver and his colleagues found that strains associated with necrotizing fasciitis and myositis secrete abnormally high amounts of a cysteine protease (also called exotoxin B), an enzyme that destroys tissue by breaking down protein.

Since this one-two punch seems so deadly and strep is highly contagious, it's unclear why more people haven't fallen prey to the virulent strains. One possible answer is that they're extremely rare (although that could change, warns Schlievert). Another possibility is that the majority of people are immune. Both are reassuring explanations, but because of the devastating nature of the disease, strep A specialists warn that it's better to err on the side of caution and step up education, research, and surveillance. That is something all can agree on. But most other aspects of this renewed virulence among strep A bacteria—particularly its incidence—remain wide open to scientific debate.

–Rachel Nowak