Public release date: 20-Feb-2006
Contact: Michelle Brandt
mbrandt@stanford.edu
650-723-0272
Stanford University Medical Center

Most effective anthrax treatment: VA-Stanford study finds

When spores sent through the mail in 2001 caused 11 people to contract anthrax - ultimately killing five of them - infectious disease specialists noted that the death rate was substantially lower than the historical mortality rate, which approached 100 percent. Many assumed that access to modern intensive care units and more powerful antibiotics made the difference.

But after completing the most comprehensive review of anthrax cases ever conducted, researchers at the Veterans Affairs Palo Alto Health Care System and Stanford University School of Medicine have found that what most likely saved lives from the various anthrax mailings in Sept. 2001 was not advanced hospital care: It was rapid diagnosis and initiation of antibiotic treatment within the first few days of symptoms.

The researchers found that once anthrax progresses to its advanced stage, which typically occurs four days after the first symptoms, patients are almost certain to die from it, even if they receive the best care modern medicine has to offer. They also found that drainage of fluid from around the lungs is a key procedure associated with anthrax patients' survival.

The study findings, published in the Feb. 21 issue of the Annals of Internal Medicine, underscore the importance of detecting anthrax early, educating medical personnel about its symptoms and treatment and ensuring efficient distribution systems that can deliver antibiotics to patients within hours of a bioterrorist attack. The findings also indicate that bioterrorism response stockpiles should include ample supplies of chest tubes used to perform fluid drainage - an intervention that has received relatively little attention in bioterrorism planning.

"Even with our modern intensive care, once you've reached the advanced stage of this disease, you're probably going to die. That's why it's crucial to start antibiotics within the first few days," said lead author Jon-Erik Holty, MD, a fellow in pulmonary and

critical-care medicine at Stanford, who did the research during a fellowship in health services research at the VA Palo Alto Health Care System.

Complicating matters, Holty noted, anthrax is difficult to diagnose. The disease's early symptoms mimic the flu, and even in the later stages there is no quick, definitive test for it. For this reason, he said, "Doctors in the ER need to have a high degree of suspicion. They need to ask questions and notice patterns: Are a lot of patients getting flu symptoms in the summer? Is there a group of patients with these symptoms who were all in the same place?"

Anthrax is an acute infectious disease caused by the spore-forming bacterium Bacillus anthracis. "It's one of the main agents we're worried about for bioterrorism, because it's available, it can be weaponized, and it can do a spectacular amount of damage in a short period of time," said study senior author Douglas Owens, MD, a senior investigator at the VA Palo Alto and an associate professor of medicine at the Center for Health Policy/Center for Primary Care and Outcomes Research at Stanford. A few grams of anthrax spores could kill thousands of people within a week.

Anthrax progresses in two phases: an initial phase lasting about four days (called the prodromal phase), which produces flu-like symptoms including cough, fever, and chills; and an advanced phrase (the fulminant phase), which causes respiratory distress and shock.

While previous studies have examined up to 40 anthrax cases, the Stanford and VA researchers conducted a more comprehensive review, seeking all published reports of inhalational anthrax from 1900 to 2005 (anthrax could not be accurately diagnosed before 1900). The researchers sought to determine how patient characteristics, type of treatment given and the timing of treatment affect the course of the disease. They also aimed to compare the 2001 anthrax cases with all previous cases.

From an exhaustive search, they obtained reports of 82 confirmed cases of inhalational anthrax from 15 countries, including Russia, Germany, Uganda, Iran, Croatia, Turkey and Nairobi. All non-English reports were translated from their original languages. For each case, the researchers documented the year; the patient's age, sex and nationality; the presenting symptoms and the stage at which anthrax was diagnosed; the type of treatment given and the timing of treatment; and whether the patient survived.

From their statistical analyses of all 82 cases, they found that the overall death rate was 85 percent, but for patients who progressed to the fulminant phase, the death rate was 97 percent, even among patients who received supportive care in a hospital ICU.

Timely antibiotic treatment was the key to patients' survival. When antibiotics were begun within two days of initial symptoms, approximately 20 percent of patients died. When treatment was begun at four days, mortality was about 58 percent, and at six days it was nearly 80 percent. Multi-drug regimens were found to be more effective than single-drug regimens. And among all the anthrax patients who survived, 80 percent had fluid drained from around their lungs, a procedure known as pleural fluid drainage.

Comparing the 2001 anthrax cases with all others previously reported, researchers found that the 2001 patients were more likely to have started antibiotics during the prodromal phase, to have used multi-drug treatments and to have received pleural fluid drainage. Likely as a result, these patients were less likely to have progressed to the fulminant phrase and to have died.

###

BROADCAST MEDIA CONTACT: M.A. Malone at (650) 723-6912 (mamalone@stanford.edu)