Medical Xpress

Answering crucial questions about anthrax exposure

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If terrorists targeted the United States with an anthrax attack, health care providers and policy makers would need key information – such as knowing the likelihood of an individual becoming infected, how many cases to expect and in what pattern, and how long to give antibiotics – to protect people from the deadly bacteria.

Those questions gained urgency when anthrax-laced letters killed five people and infected 17 others in the wake of the terror attacks of September 2001. Now, using information from prior animal studies and data from a deadly anthrax exposure accident in Russia in the late 1970s, University of Utah and George E. Wahlen Department of Veterans Affairs Medical Center researchers have developed a mathematical model to help answer critical questions and guide the response to a large-scale anthrax exposure.

In an Aug. 15, 2013, study in *PLOS Pathogens* online, the researchers use their model to estimate that for an individual to have a 50 percent chance of becoming infected with anthrax (known as ID50), he or she would have to inhale 11,000 spores of the bacteria. A 10 percent chance of being infected would require inhaling 1,700 spores and a 1 percent chance of infection would occur by inhaling 160 spores. The researchers also found that at ID50, the median time for anthrax symptoms to appear is 9.9 days and that the optimal time to take antibiotics is 60 days.

"Anthrax is a well-studied disease and experimental animal data exist, but there is no real good information on dose response for the disease in humans," says Adi V. Gundlapalli, M.D., Ph.D., an infectious diseases specialist and epidemiologist, associate professor of internal medicine at the U of U School of Medicine and staff physician at the Salt Lake City George E. Wahlen Department of Veterans Affairs Medical Center. "We don't want to be overly fearful, but we need to be prepared in the event of a bioterrorism attack with anthrax."

Although studies with animals at other institutions have looked at anthrax, the data are limited and usually involved vaccine testing and not exposure amounts for infection. Gleaning information from accidental exposures in isolated cases is difficult and not often helpful. So, Toth and Gundlapalli gathered what useful information from animal studies reported in the medical literature and then combined it with data from an accidental exposure at a Soviet Union bioterrorism plant that occurred in the city of Sverdlovsk, Russia, in 1979.

Gundlapalli, who as a postdoctoral fellow at the U of U helped build a bioterrorism surveillance system for the 2002 Winter Olympics in Salt Lake City, and Damon J.A. Toth, Ph.D., a mathematician and assistant professor of internal medicine at the U of U, are co-first authors on the study.

Anthrax is found on the skin of dead animals and its spores can live thousands of years. People can become infected when they are in close proximity to anthrax, such as a farmworker who might be exposed to a dead animal and inhales spores of the bacteria. But it also can be manufactured in laboratories and spread in other ways, such as when people opened letters containing anthrax or when the spores are put into an aerosol and dispersed over large areas by wind currents.

Previous studies at other institutions had provided widely varying estimates of the chance of becoming infected with anthrax with low dose exposure. For example, one model based on animal data estimated a 1 percent chance of becoming infected from inhaling one spore, while another study estimated that healthy humans would have virtually no chance of becoming infected after inhaling up to 600 spores. But analyzing the results from a better documented, non-human primate study at another institution, in combination with a carefully constructed mathematical model appropriate for humans, Toth estimated that the number of spores required for a 1 percent chance of infection is 160. These estimates were derived by developing and refining a competing-risks model in which the inhaled bacteria is trying to set up an infection in the lungs and the human body is trying to expel or control the bacteria. Toth then used available experimental animal data to optimize the working of the model to produce results that matched the timing of cases at Sverdlovsk.

"Our study, for the first time, takes all the best data and modeling techniques available on dose response and evaluates them critically," Toth says. "No one study satisfied all our criteria to be the best model, so we refined the available information to develop our model."

"When the Institute of Medicine was asked to look at the effectiveness and costs of different strategies to respond to an anthrax in 2012, the Committee identified a critical need for accurate information on the time from exposure until people became ill and how this would change depending on the dose," said Andrew Pavia, M.D., professor and chief of pediatric infectious diseases at the University of Utah and a member of the IOM committee that wrote the report, "Prepositioning antibiotics for Anthrax," and a consultant to CDC on anthrax. "The time between exposure and when symptoms develop is the most effective time to administer antibiotics to prevent illness. This study adds a thoughtful approach to using all of the available data to improve these estimates, but considerable uncertainty will remain." Pavia was not involved in the study

Along with existing animal studies, data gathered from the accident at Sverdlovsk proved invaluable. Up to 100 people died when a filter was accidently left off a piece of equipment at a plant that was developing anthrax as a bioterrorism weapon. Spores of the bacteria were released into the air near the town of Sverdlovsk. The Soviets eventually let outside experts in to study the accident. From publicly available accounts, despite limited records and a substantial delay before the investigation, it would appear that scientists were able to estimate when the release happened, plot where people were in the surrounding area when it occurred and then look at weather records to identify wind currents. With that information, they plotted how the spores were scattered in relation to people who became infected.

The timing and geographic pattern of the best documented cases from Sverdlovsk were consistent with both the shape of the dose-response curve and the distribution of incubation periods produced by the new model. The model also sheds light on how long antibiotics should be given after an exposure to decrease the chances of infection. The model's predictions match so well with publicly available Sverdlovsk data that Gundlapalli and Toth believe they can use the model to reasonably estimate how exposures to anthrax would unfold, especially at low doses of the bacteria.

"By combining the data from Sverdlovsk and prior studies, we can make defensible estimates on how scenarios might play out if anthrax were released in a terrorist attack," Gundlapalli says. "How many cases could we expect? When would be expect to see the cases? How long should we treat those exposed with preventive antibiotics? Our model provides real answers to help policy makers when they need that information."

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