Study gives clues about how deadly bacterium gains foothold

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How a potentially deadly bacterium that could be used as a bioterrorist tool eludes being killed by the human immune system is now better understood, University of Iowa researchers report in the December issue of the *Journal of Leukocyte Biology*.

This bacterium, Francisella tularensis, is found naturally in the Northern Hemisphere and can be contracted through certain insect bites, contact with infected rabbits or ingesting contaminated food, water or air.

Francisella tularensis rarely infects people. However, because the bacteria has the potential to be used as a bioterrorist tool there is increased interest in understanding how it functions, said Lee-Ann Allen, Ph.D., associate professor of internal medicine and microbiology at the UI Roy J. and Lucille A. Carver College of Medicine.

"The rate of tularemia or 'rabbit fever' infection has significantly declined since the 1940s. However, the bacteria would be very deadly as an aerosolized terrorist weapon -- inhaling as few as 10 bacteria could be potentially deadly," said Allen, who also is a staff researcher with the Veterans Affairs Iowa City Health Care System.

"We wanted to better understand how Francisella tularensis can overcome the body's innate immune response and cause disease. In addition, learning more about this bacterium can help us learn more about the overall human immune response to bacteria," she said.

The team focused on how Francisella tularensis evades being killed by a form of white blood cells called neutrophils. Normally, neutrophils can be quickly activated in response to infection, making them the equivalent of "first responders" for the human immune system, Allen said.

"We knew that Francisella could live inside other white blood cells called macrophages and not be killed by them," Allen said. "But little research had been done on the bacteria's survival in neutrophils.

"Early data indicated that neutrophils did not kill Francisella well. With new techniques, many of them more sensitive than in years past, we were able to look at that scenario more closely," Allen added.

The team mixed bacteria with neutrophils taken from healthy volunteers and studied the results.

"We found the neutrophils could ingest the bacteria but were not able to kill them. The Francisella somehow inhibit the ability of the neutrophils to perform two defensive functions that otherwise would kill the bacteria," Allen said.

One of the defensive functions is dependent on oxygen, and the other is oxygen-independent. Ideally, the two functions will be activated and kill the bacteria while they are trapped in a particular compartment within the neutrophils.

"The bacteria prevent these two functions from working in part by blocking the assembly of certain enzymes. After a few hours, the bacteria can escape the compartment instead of being killed, which leaves it able to replicate and cause harm," Allen said.

The researchers now seek to identify how the bacteria prevent

neutrophils from mobilizing its defenses and learn more about how those defenses normally function. Additional insights could help with the eventual development of therapies or vaccines against tularemia.

A person infected with tularemia cannot pass the disease on to another person. Hunters are at an increased risk of infection if they skin an infected rabbit. Using blasts of water to clean machines, such as mowers, that have inadvertently come into contact with the carcasses of infected rabbits also can be a risk, as it makes the bacteria easy to inhale.

Allen noted that tularemia infections contracted though the skin are generally less serious to an individual. However, the inhaled form can be fatal if a person does not receive antibiotic treatment.

The Centers for Disease Control and Prevention (CDC) reported an average of 124 suspected cases of tularemia in the United States each year from 1990 to 2000, with nearly 60 percent of the cases confirmed. An investigation by the CDC into an outbreak of the disease in 2001 on Martha's Vineyard found that landscapers and gardeners who used power blowers and lawn mowers were at increased risk of being infected.

Source: University of Iowa