Advancing Regulatory Science

Individual bacteria could play critical role in spread of anthrax through body

The spread of inhalational anthrax in the body slows when a temporary immune system bottleneck traps the bacteria. But it appears that some bacteria escape, suggesting that a single bacterium could continue to spread the infection. This makes rapid treatment especially important.

“Dissemination Bottleneck in a Murine Model of Inhalational Anthrax”

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Roger D. Plaut, Vanessa K. Kelly, Gloria M. Lee, Scott Stibitz, Tod J. Merkel
Division of Bacterial, Parasitic, and Allergenic Products, Office of Vaccines Research and Review, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, Maryland

Inhalational Anthrax: Old Scourge & Modern Bioterrorism Threat

- Inhalational anthrax is the most severe form of the disease.
  - Rapid disease progress
  - Mortality rates approach 100% even when treated
- Anthrax mail attacks of 2001 caused five deaths; two letters were sent to US Senators.

Inhalational anthrax: Immune system transport of spores from respiratory system to organs throughout the body

- Macrophages and dendritic cells transport inhaled spores from nose and lungs to the lymph nodes.
- Anthrax spores germinate and multiply within immune cells, then escape and multiply in the lymph nodes.
- Vegetative anthrax bacteria enter the bloodstream and spread throughout the body.

Previous FDA study suggested the presence of a bottleneck in spread of anthrax in a mouse model

- Disease progression beyond lymphoid tissue occurred at significantly different times in different animals.
- Evidence suggested bottleneck in spread of bacteria: only one or very few bacterial cells appeared able to pass the bottleneck at one time.

New FDA study tracked anthrax spread in mice to study hypothesized bottleneck

- Inoculum of B. anthracis consisted of a mixture of three strains of B. anthracis, each one tagged with a fluorescent protein of a different color, but otherwise identical.
- Each strain was also tagged with bioluminescence to allow tracking of infection in live mice.
- Mice were infected through inhalation into the lungs.
  - Inoculum consisted of approximately equal numbers of each of the three colors of strains.
- Mice were sacrificed when luminescence was apparent in the area of cervical lymph nodes.

- Bioluminescence imaging of mice showed when anthrax infection reached the cervical lymph nodes.
- Mixtures of anthrax bacteria strains recovered from nasal lymphoid tissue and lungs remained near the same equal ratio as the inoculum (1:1:1).
- Dominance of one strain occurred quickly in the cervical lymph nodes and continued as the infection spread to other organs.
  - CFU recovered from kidneys were nearly always dominated by one strain, with the dominant strain varying among mice.
- This demonstrates that although host defenses are successful in containing and neutralizing most of the infectious spores, a single bacterium breaking through those defenses can cause systemic lethal infection.

The potential for a single anthrax spore to germinate, escape the immune system bottleneck, and seed a body-wide lethal infection emphasizes the importance of prevention, detection, and early treatment to reduce the incidence and severity of inhalational anthrax.