



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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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**.
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- 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.