

ANTHRAX



Image from: <http://www.cdc.gov/anthrax/resources/history/>

Anthrax History:

While the true length of existence of Anthrax is unknown, some scholars believe descriptions of the disease date back to prebiblical times when knowledge was not as scientifically ranged as it is today (Simon 11).

It wasn't until 1876 that Robert Koch discovered Anthrax or *Bacillus anthracis* as the first proven bacterial cause of a human disease (Simon 11). The studies produced by Koch in those times led to the development of Koch's Postulates which is still widely used today in the world of microbiology as a set of diagnostic criteria. Five short years after Koch's findings, a man named Louis Pasteur developed a vaccine for the bacterial disease. This became known as the first effective vaccine for a bacterial disease (Simon 11).

Genome Type and Content:

Anthrax is a bacterial disease caused by the spore forming bacteria called *Bacillus anthracis* (Moayeri 186). Like all bacteria, *Bacillus anthracis* chromosomes consist of a circular shape and contain two large plasmids which encode the most important virulence factors. One is called the pXO1 plasmid while the second is called the pXO2 plasmid (Moayeri 187). Each plasmid has a certain encoding "job" but each helps in replication and protection.

Exchange of Genetic Material:

Anthrax first exists as a spore forming bacteria. Once the bacteria enter a living organism's systems. If the spores are able to find their way into an organism, the environment becomes conditional for the bacteria to multiply. *Bacillus anthracis* then releases a diffusible endotoxin into blood cells, body tissues and immune system macrophage cells. This toxin is composed of three components including and edema factor, a protective antigen and a lethal factor. If two or more of the proteins are apparent, the disease can become lethal. (Simon 13). It is important to remember that anthrax is not contagious: a victim must be directly exposed to the bacteria spores. (Simon 14)

Signs/Symptoms and Treatment/Prognosis:

Anthrax has three major clinical presentations with different signs, symptoms, treatments and prognosis. The first is cutaneous anthrax which is an itchy bump resembling a bug bite which progress to a vesicle that eventually ruptures to form necrotic tissue all within 1-2 days. If left untreated, the disease may spread causing serious internal issues in the lymph system and blood stream. However, it is easily treatable with a simple antibiotic and death is rare (fewer than 1% of cases) (Simon 13). The second type is pulmonary Anthrax which occurs from the inhalation of the Anthrax spores. Early symptoms resemble an upper respiratory infection along with fever, malaise, a cough and mild chest discomfort. The illness may seem to dissipate until the late stage (24 to 36 hours later) where labored breathing, stridor and shock usually occurs resulting in death. Because this is usually recognized too late, treatment is difficult and it typically leads to death. The final is gastrointestinal anthrax. This can be caused by eating contaminated or undercooked meat for humans. Early symptoms resemble food poisoning with nausea, vomiting, fever and abdominal pain. This form is extremely rare however, much like pulmonary anthrax, is rarely recognized as anthrax until antibiotics are no longer effective resulting in the disease being lethal (Simon 14).

Moayeri, Mahtab, Stephen H. Leppia, Catherine Vrentas, Andrei P. Pomerantsev, and Shihui Liu. "Anthrax Pathogenesis." *Annual Review of Microbiology Annu. Rev. Microbiol.* 69.1 (2015): 185-208. *Annual Reviews*. Web. 14 Nov. 2016.

Simon, Eric J. "Anthrax: A Guide for Biology Teachers." *The American Biology Teacher* 64.1 (2002): 11-19. *JSTOR*. Web. 14 Nov. 2016.

Modes of Transmission:

Anthrax infects a person when the spores enter the body through inhalation, digestion, or through an open wound or scrape in the skin. Anthrax spores are found in the soil, where they exist as dormant organisms up to 48 years. Anthrax is not contagious from person-to-person, though one can become sick by working with infected animal hides, hair, wool, or meat. The spores in animal hides become airborne upon processing, infecting those that inhale the spores. Gastrointestinal anthrax may result from eating raw or undercooked affected meat, though this form of anthrax infection is a rarity in the United States. Cutaneous anthrax, the most common manifestation and least lethal, is contracted through an opening in the skin, upon which the spores enter.

When anthrax spores are inhaled, the deadliest form of transmission, they enter the lungs and attach to macrophages. The small amount of spores that survive upon the macrophages ultimately reach the lymph glands in the chest. It is at these glands that the anthrax bacteria reproduce, spread throughout the body through the blood stream, and effectively release deadly toxins. While the anthrax bacteria may easily be killed through antibiotics, the toxins that they produce remain in the body, continuing to damage cells. Ultimately, it is the three different proteins that anthrax releases that make the bacteria efficient killers: protective antigen, lethal factor, and edema factor. The toxic proteins target macrophages, a primary unit of the immune system, and disrupt cell signaling pathways. The immune system shuts down due to lack of cellular communication, leading to patient death.

Protective antigen, one of the three released proteins, attaches to a receptor protein on the membrane surface of individual cells. Protective antigen then undergoes a conformational change into a ringed structure, allowing for lethal factor and edema factor to attach to the ring away from the protein receptor. The ringed structure containing the three killer proteins then enters the cell through endocytosis, allowing the proteins to work on immobilizing the cell. Edema factor increases the amount of cAMP in the cell, which disrupts osmosis and water homeostasis, effectively disrupting intracellular communication. Lethal factor kills macrophages, shutting down the immune system and allowing for anthrax bacteria to survive. Lethal factor also negatively affects protein kinases within the cell, altering cell signaling pathways and leading to cell apoptosis.

"How People are Infected." *Centers for Disease Control and Prevention*. Centers for Disease and Prevention, 01 Sept. 2015. Web. 13 Nov. 2016

Davis, Charles Patrick. "Anthrax." *MedicineNet.com*. Ed. William C. Shiel. N.p., n.d. Web. 13 Nov. 2016

Gau, Mu, and Klaus Schulten. "Molecular Basis for Anthrax Intoxication." *Molecular Basis for Anthrax Intoxication*. NIH CENTER FOR MACROMOLECULAR MODELING & BIOINFORMATICS AT THE UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN, n.d. Web. 13 Nov. 2016.

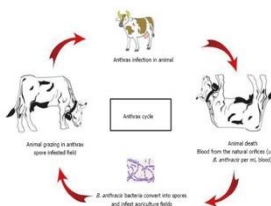


Image from: <http://www.wjnet.com/2307-8960/full/v3/i1/20.htm>

Alex Hasselbach, Jacob Thomas, Colton Kellogg and Joe Pinney

Research/Work in the Field:

The anthrax toxin is made of 3 separate parts: the oedema factor (OF), the lethal factor (LF), and the

protective antigen (PA) (Bradley et al.). These proteins are not toxic on their own (Stoppard), and so research into treating the disease generally focuses on stopping one of the three proteins. The research of Kenneth Bradley and his team confirms that PA is essential to the function of the toxin, for example, by identifying the anthrax toxin receptor (ATR) on mammalian cells and by identifying a protein that can bind to PA, stopping it from binding to the ATR and preventing infection. This kind of blockage is called competitive inhibition. This discovery was later used to develop a PA-based vaccine. Zeev Altboum and his team showed that this vaccine is not a cure, however. Using rabbits, they showed that while this treatment was effective in stopping the disease even after exposure, it was ineffective once the infection had begun and there was bacteria in the blood. However, there is some research that suggests that the anthrax toxin could be modified and used to inhibit blood flow to cancerous tumors, killing them (Stoppard).

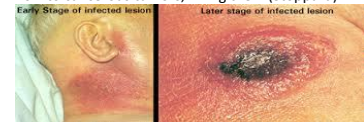


Image from:

<http://www.angelfire.com/scary/crocetti/anthrax.html>

Altboum, Zeev, Elad Bar David, Amir Ben-Shmuel, et al. "Revisiting the Concept of Targeting Only Bacillus anthracis Toxins as a Treatment for Anthrax." *Antimicrobial Agents and Chemotherapy*, vol. 60, no. 11, 2016, <http://aac.asm.org.proxy.lib.ohio-state.edu/content/60/8/4878.full#ref-list-1>. Accessed 15 Nov. 2016.

Bradley, Kenneth A., R. John Collier, et al. "Identification of the cellular receptor for the anthrax toxin." *Nature*, no. 414, 2001 pp. 225-229, <http://www.nature.com/nature/journal/v414/n6860/full/414225a0.html>. Accessed 15 Nov. 2016.

Stoppard, Miriam. "Scientists Want to Send in Anthrax in the Bid to Beat Cancer." *The Mirror*. 27 Oct. 2016. Web. 13 Nov. 2016.

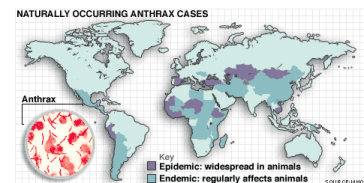
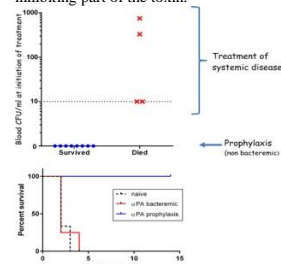


Image from: <http://pathogensanthrax.weebly.com/about.html>

Coursework Relevance:

Anthrax presents relevant information to our coursework because it hijacks cells through endocytosis, by utilizing protein receptors on the cell surface. This was talked about and taught in chapter 7. It has relevance through Biology Lab from looking through microscopes at live bacteria in which we learned and used those techniques during lab. During lab we observed living and moving bacteria such as the paramecium. Different treatments are being tested to treat anthrax. The vaccine works by competitively inhibiting part of the toxin.



The effectiveness of the anthrax vaccine decreases as the disease progresses. (Altboum et al.)