

Khristy Nicholas
Biochemistry 118Q: Genomics & Medicine
Douglas Brutlag

A History of the Development of Anthrax Vaccines and a Look into the Future

What is Anthrax?

Anthrax is an infectious disease that is caused by infection of the bacteria, *Bacillus anthracis*. It is usually more prevalent in animals, and is not a common human infection. Those most at risk are the people who work or live around animals a lot. If infection does occur in humans, it typically involves the skin, gastrointestinal tract, or lungs. There are three main paths that humans can become infected with anthrax. The first is Cutaneous anthrax, the most common type. It occurs when the anthrax spores make their way into an open wound. The second type is Inhalation anthrax. It becomes manifested when the spores enter someone's lungs through the respiratory tract. It is important to keep in mind that though it is not imminent that inhaling spores will indefinitely result in infection, the incubation period of anthrax cannot always be predicted. The third mode is Gastrointestinal anthrax which develops when a person eats meat that is infected with anthrax (Pub Med health, 2012). Anthrax spores can remain dormant for long periods of time in soil, seemingly resistant to intense environmental conditions. This could explain why anthrax is primarily an issue for herbivores. (Grabenstein, 2008).

The symptoms of anthrax depend on the mode of contraction. They can include, but are not limited to, an itchy sore that eventually leads to a scab that then falls off, fever, shortness of breath, abdominal pain, and bloody diarrhea. The diagnostic methods also depend on the type of anthrax that was contracted. Some of the methods include a biopsy, blood culture, chest X-ray, and spinal tap. Regarding treatment of anthrax, a patient may be prescribed antibiotics and even

combinations of antibiotics that can be taken by mouth or injection. The real discrepancy comes from vaccinations. This paper will explore the history of anthrax vaccines and take a glimpse into its future potential as well.

A History of Anthrax and its Vaccines

Anthrax is not a new infectious disease, but it's most recent danger occurred in 2001 when a Florida resident contracted inhalational anthrax. This was the first documented case of anthrax since 1976. At first, the man was thought to have just had a unique exposure to anthrax and that there was no need to worry about anyone else contracting the disease. This belief, however, was soon proved wrong. It turned out that there were other confirmed or suspected cases of inhalational and cutaneous contraction. The source was most likely letters and packages that were polluted with the bacteria. When these people came into contact with the bacteria, they contracted it. (Grabenstein, 2008)

In the late 1800s and into the early 1900s, the predominant vaccine against anthrax consisted of less intensified strains of the *Bacillus anthracis*. Active anthrax bacilli were cultured in order to provide immunity (Kaur & Bhatnagar, 2011). It was tested in animals and found to result in antibodies to the three main components of anthrax. Other studies were conducted that varied the degree of virulence of the bacteria in culture and in most cases, the results were promising. It is important to keep in mind that there would be very little data on human vaccinations at this time because of its prevalence in animals.

In the 1950s to 1980, *Bacillus* spores came in to the spot light in an attempt to improve anthrax vaccination. The western world did not accept this vaccine and it was deemed unsuitable and toxic. It did not meet the standards of safety for human use and remains restricted for animal

use only, except in Russia. Recently, because of the advances on recombinant DNA technology, there has been great improvement in a spore related vaccine, but non-toxic! (Kaur & Bhatnagar, 2011). One of the major new discoveries was that "... spore antigens can be used to augment immunity against anthrax (Kaur & Bhatnagar, 2011). In addition, for the first time, it was possible to have an oral vaccine. Normally, vegetative cells had been used in evaluating the efficacy of vaccinations but this time, the vaccine was delivered in the sporogenic form. Contrary to the vegetative cells, this new method allowed survival through the gastrointestinal tract, displaying the success of mucosal immunity, tested in guinea pigs (Kaur & Bhatnagar, 2011).

The next attempt at the ideal vaccine was in the form of a cell free filtrate. Acellular culture supernatant vaccines were accepted more than its predecessors. In the U.S., it was called AVA for Anthrax Vaccine Adsorbed. A lot of the animal studies done with this vaccine reflected positive safety results as well as effectiveness. AVA proved to be effective in fighting off cutaneous and inhalation anthrax as well as being able to probe the development of antibodies in order to combat the anthrax toxin. However, it was realized that the vaccine might lead to undesirable reactions, so a lot of people shied away in advocating for it. In addition, the vaccination process was one that was extremely lengthy and costly. It was concluded that a more efficient and cost sensitive vaccination was needed.

Safety, being the main issue regarding vaccines that worried people, caused the development of the next line of vaccinations against anthrax-- subunit vaccines. Some of the advantages that were promising of using subunits as vaccines included "increased safety, less antigenic competition as only a few components are included in the vaccine, ability to target the vaccines to the site where immunity is required." (Kaur & Bhatnagar, 2011) An enormous

downside to this vaccine is that the immunity period may be shorter than with the other, live vaccines.

Even though there have been a few studies centered around using the whole protein or subunit of a vaccine (though not all is known about this in subunit vaccines), it may be possible to "...identify individual epitopes and subunit vaccines ..." (Kaur & Bhatnagar, 2011). This new vaccine is the immunodominant epitope vaccine. Though there are some issues regarding the difficulty in making B cell versus T cell epitopes, the vaccines are very economical. But, there are some issues regarding the impact this vaccine has on the ability to generate immune responses and its effect on the immune system. There has also been research done on the effectiveness of capsule based vaccination. It was proven in a previous study that a capsule was important in protection against the anthrax virus. This presence of a capsule was then combined with protective antigen (PA) that proved to enhance protection. In fact, this combination protected against a lethal and completely virulent strain of the bacteria! Another study in mice showed that the addition of PA was not really needed. Thus, it is clear that there is a great deal of uncertainty when it comes to the most efficient, safe, and cost effective way of making a vaccine of this nature (Kaur & Bhatnagar, 2011).

The next big type of vaccine is using transgenic plants as an edible vaccine! Plants are very safe, clean, and can be gathered in large harvests. "Initial studies towards developing edible vaccine against anthrax were based on the expression of PA in tobacco and tomato by agrobacterium mediated by transformation" (Kaur & Bhatnagar, 2011). What was very interesting was that mice were injected with chloroplast- derived PA and it was found that they had complete protection against a deadly toxin dose. What this case showed was that there is a

great possibility that an edible plant vaccine could be used in the future. For now, there still needs to be more research done on it.

The final vaccine to be discussed here is the DNA vaccine. DNA vaccines are safe, reliable, and there is little difficulty involved in their production. “They hold enormous potential as they can induce both cellular and humoral immunity...” (Kaur & Bhatnagar, 2011). This method of vaccination seems to be widely advocated for. In an analysis of anthrax vaccines by Leslie Baillie, she calls it “vaccination at its simplest” (Baillie, 2009). One of its major advantages is the fact that there is no need to create costly protein expression because the person receiving the vaccine will make their own vaccine antigen! (Baillie, 2009). There have even been clinical trials on humans that reflect its safety and effectiveness as a vaccine. However, studies done on guinea pigs suggested that their protection was not significant enough and both papers advocated for the need of more research.

What does the future hold?

Currently, much work is being done to discover the most efficient, safe, and cost effective anthrax vaccine, but some worry that it is not being done fast enough. Previously in this discussion, it was mentioned that there was a problem regarding the length of protection vaccines offer and in the future, a vaccine with immunity for a few weeks is ideal. It is suggested in an article by John Grabenstein that passive immunization which takes place after infection and involves administering antibodies might take precedence over active immunization. It seems as though it is more predictable to treat anthrax than using a vaccine to prevent it at this point in time. There has been a great deal of disappointment expressed regarding the slow nature of creating a new vaccine for anthrax. There has been a lot of money invested in research for a new

generation of vaccines, but it has been about two decades and we are still without a novel vaccine (Baillie, 2009). At this point, it may be smart to start working on a more efficient antibiotic for the infection as research on vaccination ensues.

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