www.canadianveterinarians.net/larounds

Large Animal VETERINARY Rounds®

DECEMBER 2006
Volume 6, Issue 10

AS PRESENTED IN THE ROUNDS OF THE DEPARTMENT OF LARGE ANIMAL CLINICAL SCIENCES OF THE WESTERN COLLEGE OF VETERINARY MEDICINE, UNIVERSITY OF SASKATCHEWAN

Anthrax – The Forgotten Plague

By Chris Clark, VetMB, MVetSc, Diplomate ACVIM

In the current world situation, it is difficult to consider anthrax without thinking in terms of biological warfare, weapons of mass destruction, and bioterrorism. It is easy to forget that anthrax, once the scourge of agriculture throughout the known world, has been almost completely controlled through a basic understanding of the disease, coupled with an effective vaccine. This issue of *Large Animal Veterinary Rounds* reviews the disease, the outbreak of anthrax in Saskatchewan during the summer of 2006, and provides some basic information on public health issues surrounding the disease.

Anthrax in history

Anthrax has perhaps one of the longest histories of any disease.[1] By examining ancient manuscripts, scholars have attempted to identify diseases based upon their descriptions. As described in the Old Testament, the plague of boils affecting the Egyptians in the time of Moses (circa 1490 B.C.), had many similarities with human cutaneous anthrax. The ancient Romans were also aware of anthrax and, as the following account demonstrates, had a good understanding of the basic epidemiology and public health implications.

> *For neither might the hides be used, nor could one cleanse the flesh by water or master it by fire. They could not even sheer the fleeces, eaten up with sores and filth, nor touch the rotten web. Nay, if any man donned the loathsome garb, feverish blisters and foul sweat would run along his fetid limbs, and not long had he to wait ere the accursed fire was feeding on his stricken limbs. (Virgil ~200 A.D.)*

Throughout the Middle Ages anthrax continued to be the scourge of agriculture. The disease was classically referred to as the "Black Bane," killing hundreds of thousands of head of livestock annually, as well as many humans. It is difficult to imagine the significance of this disease, although some idea of its magnitude becomes apparent with the realization that two of the greatest minds in microbiology of the 19th century began their careers with a focus on anthrax.

Robert Koch's discovery that anthrax is caused by the bacteria *Bacillus anthracis* was seminal (Germany, 1876). He cultured *Bacillus anthracis* for the first time, developed "Koch's Postulates" and, for the first time, demonstrated that a disease was caused by a microorganism. Five years later, Louis Pasteur publicly demonstrated his anthrax vaccine, the first live vaccine ever developed in a laboratory. The vaccine was a temperature-sensitive mutant, developed by culturing the bacteria in the laboratory at elevated temperatures. It was a great success and nearly 4 million doses were produced in just 13 years using simple 19th century facilities.

The current vaccine (Sterne vaccine) was developed in the 1930s. It is a live, unencapsulated, spore vaccine that has lost most of its virulence and it is highly effective with minimal risks.

Anthrax was not found naturally in North America. It appears likely that the disease was brought to North America by the French who settled in Louisiana.[2] The disease spread slowly north along the eastern seaboard. Settlers moving west into the interior appear to have taken the disease with them. The first published cases in animals and humans were reported in Bardstown, Kentucky in 1819.[3] The disease presumably entered native wildlife and was spread through their annual migrations. The disease is now found throughout the continent, from the Arctic Circle to Mexico.

Western College of Veterinary Medicine
Department of Large Animal Clinical Sciences
52 Campus Drive
University of Saskatchewan
Saskatoon, Saskatchewan S7N 5B4

The editorial content of *Large Animal Veterinary Rounds* is determined solely by the Department of Large Animal Clinical Sciences, Western College of Veterinary Medicine

The Canadian Veterinary Medical Association recognizes the educational value of this publication and provides support to the WCVM for its distribution.

Bacteriology

Bacillus anthracis is a non-motile, facultative anaerobic, Gram-positive, spore-forming rod.[4] In the spore form, the bacteria is incredibly stable and can survive for decades in appropriate climatic conditions. The spores are also very resistant to temperature changes and many disinfectants. In addition to protecting the spore in the environment, the spore capsule appears to play a role in establishing infection by protecting the vegetative form of the bacteria from the immune system. Mutant bacteria lacking the capsule are less virulent and form the basis of the Sterne vaccine.

Anthrax bacteria in the growth phase are not particularly hardy; however, when environmental conditions are appropriate, they sporulate. Sporulation occurs more easily *in vivo* than in culture. Although not entirely understood, the requirements for sporulation include a warm ambient temperature and oxygen. Under the right conditions, sporulation can occur in a matter of hours.

Pathogenesis

The anthrax bacteria secretes 3 distinct toxins: edema factor, lethal factor, protective antigen. These are responsible for the widespread damage to the reticuloendothelial system and the vasculature. There are also 3 distinct forms of the disease, depending on the route the spores take to enter the body: intestinal anthrax, cutaneous anthrax, and inhalation anthrax.

Intestinal anthrax is the most common form of the disease seen in livestock. Spores present in the soil are ingested through feed or water and germinate within the intestines. The infectious dose is relatively small and the incubation period can range from 1 to 14 days. The disease can occur in humans following the ingestion of contaminated meat. The classic signs of intestinal anthrax are sudden death[6] and, shortly before death, there may be a massively elevated body temperature and bleeding from the orifices.

Cutaneous anthrax occurs when the spores or bacteria penetrate through a break in the skin. The significance of this disease in animals is not clear and there is some evidence to suggest that biting flies can transmit the disease.[5] Cutaneous anthrax is the most important natural form of the disease in humans.

Inhalational anthrax does not generally occur in the natural setting because anthrax spores do not disperse well in air and the infectious dose is very high (10,000-20,000 spores in humans). The disease, known as "Woolsorter's disease," has occurred in humans who work in poorly-ventilated buildings, handle hides and fleece from affected carcasses, and inhale large amounts of dust. Inhalational anthrax is also the disease associated with biological weapons.

Postmortem examinations will demonstrate that the blood does not clot and the spleen is typically enlarged (if anthrax is suspected, a postmortem examination should be avoided). Diagnosis is made by examination of the blood for anthrax bacteria. A sample can be collected easily from a nick in the ear or the jugular vein because the blood does not clot. A blood smear is stained with polychromatic methylene blue to allow identification of the characteristic bacteria. The diagnosis is typically confirmed within 24 hours by culture of the organism.

Natural infection with anthrax can be readily treated with a wide variety of antimicrobials, if the disease is recognized early. In agricultural practice, the first choice of antimicrobials is usually penicillin or oxytetracycline.

Epidemiology

The epidemiology of the basic cycle of natural anthrax infection is well understood, but our understanding of the environmental factors that allow the organism to persist and then sporadically emerge to cause disease, is far from complete. Animals at pasture ingest spores from the soil, the spores germinate within the intestines and the animal dies. In nature, typically, the carcass is scavenged by predators and during that process the bacteria are exposed to oxygen and form spores. The spores are spread into the soil where, under the right conditions, they can survive for decades. Soils favouring the survival of anthrax spores typically have a mildly alkaline pH and a high organic content.

Factors that have been associated with anthrax outbreaks include:

- disturbance of the soil, such as ditch digging that exposes spores buried deep in the soil
- drought conditions, when animals may be forced to graze areas that are not normally grazed (eg, the bottom of dried-up sloughs)
- periods of flooding followed by drought; standing water allows spores to float to the surface and, when the flood waters recede, the spores become concentrated in small areas.

The significance of other mechanisms of spread such as carrion scavengers and flies is not entirely clear. The reasons for the sporadic large outbreaks of anthrax in North America have not been determined.[7]

Anthrax in humans

Humans are susceptible to all 3 forms of anthrax infection; however, the control of the disease in domestic animals has almost eradicated the disease in humans. Prior to this year, there had been only 25 cases of anthrax in humans in Canada, since records began in 1931. Most of these cases occurred in 1936 and there had only been 3 cases since 1961. Intestinal anthrax is almost unheard of in the developed world because animals that die of natural causes do not enter the food chain. The recognition of specific postmortem clinical signs such as an enlarged spleen is an important component of the meat inspection process and plays an essential role in safeguarding public health from an animal that is potentially incubating the disease at the time of death. Inhalational anthrax is rare because hides and fleece from affected animals are no longer salvaged.

Cutaneous anthrax, the least serious form of the disease, presents the greatest risk to human health. Anyone dealing with affected carcasses is at risk through accidental skin puncture. There are sporadic reports of cutaneous anthrax in artisans manufacturing drums using hides from Africa that were contaminated with anthrax spores. Cutaneous anthrax takes the form of a "malignant carbuncle." The lesion begins as a painful edematous swelling that becomes cold and painless when the center necroses, forming a black eschar. This eschar is said to resemble a piece of coal (hence the name, anthrax, from the Greek, anthrakis, for coal). The mortality rate from cutaneous anthrax is low and there is ample time to treat the infection after the development of the classic clinical signs.

A veterinarian and a farm worker developed cutaneous anthrax in Saskatchewan this past summer (2006), after performing a postmortem examination on an animal that had died of anthrax. Both were treated successfully with antibiotics. During this outbreak in Saskatchewan, prophylactic antimicrobials (amoxicillin) were only given to individuals who could demonstrate a puncture wound sustained during the handling of an anthrax-infected carcass.

Anthrax around the world

Anthrax is found throughout the world and most countries report cases to the World Health Organization.[8] Data reveal that anthrax tends to occur annually in the countries of Africa, Asia, Central and South America. The disease only occurs sporadically in developed nations. Because anthrax has an almost worldwide distribution, there are no trade barriers preventing the movement of agricultural produce on the basis of anthrax. In this respect, anthrax differs significantly from other reportable diseases.

In North America, anthrax has occurred in a number of large sporadic outbreaks: specifically, in Louisiana in 1971, in Texas in 1974 and 2001, in North Dakota in 2000, and in South Dakota in 2005.[7] In 2006, Minnesota suffered its worst anthrax outbreak on record.

Anthrax in Canada

Similar to other developed nations, anthrax occurs sporadically in western Canada. The scale of recent outbreaks is shown in Table 1. The disease typically occurs in animals grazing on pasture and most of the cases are associated with drought conditions in the late summer. The outbreak in 2004 was something of an anomaly because it occurred during the winter; however, an investigation of this outbreak traced the disease source to baled canola, where the baling had included a large amount of soil that contained anthrax spores.

Saskatchewan – Summer 2006

The first cases of anthrax were diagnosed at the beginning of July, east of Prince Albert. Over the next two months, the toll of cases rose steadily (Table 1), with a total of 806 animals on 153 premises. The cases ranged across the northeast corner of the province with two particularly heavily-affected areas north of Melfort (near where the first cases were diagnosed) and also south of Foam Lake. The remaining cases were widely spread across 44 rural municipalities (Figure 1).

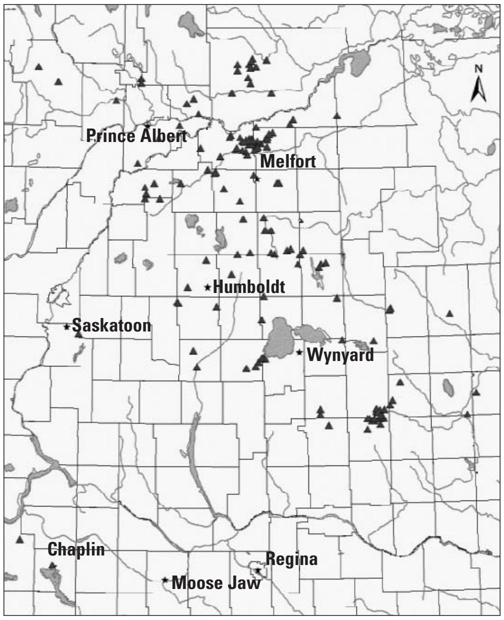
The reasons for the outbreak are not known at the current time. A combination of unusual events, including severe flooding in the fall of 2005 and again in the spring of 2006, followed by a very dry summer, may have precipitated the outbreak. A few of the cases appeared to be unconnected to the much larger outbreak. These cases occurred in areas that had not flooded in the spring and may simply represent the normal background incidence of the disease. Under normal conditions, such sporadic deaths at summer pasture might not have been reported. However, given the heightened public awareness associated with the outbreak, producers may have been more likely to contact their veterinarian following the death of livestock.

Cattle were the species most commonly affected by this outbreak of anthrax and this is consistent with previous outbreaks. The unusual aspect of this outbreak was the high number of bison affected. Although the number of bison in the province increased recently, their numbers are still low in comparison with the numbers of cattle. The reason that bison accounted for > 25% of anthrax deaths may be

Table 1: Recent anthrax cases in Canada

Year	Area	Animals affected
2006	Saskatchewan, 153 premises, 44 RMs Manitoba, 21 premises	493 cattle, 254 bison, 33 sheep, 13 white tailed deer and elk, 6 horses, 3 pigs, 2 goats 95 cattle, 3 horses, 39 bison
2005	Manitoba 12 farms	26 cattle, 10 horses
2004	Saskatchewan 1 farm	14 cattle
2003	Manitoba 3 farms	
2002	No cases reported	
2001	British Columbia Alberta Saskatchewan Manitoba NWT	2 cases 2 cases 2 cases 4 cases 5 cases
2000	Alberta Saskatchewan Manitoba NWT	9 cases 1 case 24 cases 1 case

Figure 1: **Distribution of anthrax cases in Saskatchewan during the summer 2006. Taken from CFIA website: http://www.inspection.gc.ca/english/anima/heasan/disemala/anthchar/mc/ske.shtml Accessed: December 7, 2006.**



explained, in part, by the timing of the anthrax outbreak. Bison herds were affected with anthrax at a time of year when prophylactic vaccination was not practical for safety reasons because calves were at side and the rut was in process. Producers tried a number of different options, including trying to move the animals to different pastures, or using medicated feed or water for prophylactic dosing of animals to prevent anthrax. The medicated feed and water did not appear to be particularly effective in preventing disease and many of the herds could not be moved.

Saskatchewan was not alone in dealing with anthrax this summer (2006). There was a significant outbreak in Manitoba involving 21 premises and 137 dead animals, as well as outbreaks in the USA.

Anthrax as a biological weapon

In the current political climate, the mention of anthrax evokes concern regarding biological weapons. The use of anthrax in this manner is not particularly new. In fact, the ancient Romans tried to break a siege of a fortified city by catapulting dead carcasses over the walls. There is some evidence to suggest that rudimentary attempts may have been made to use anthrax as a weapon during the First World War. Research into biological weapons really began in earnest during the Second World War. The British successfully detonated an anthrax bomb on Gruinard Island off the northwest coast of Scotland. This seeded the entire island with anthrax spores. The island remained uninhabitable until a massive clean-up operation (using 280 tonnes of formaldehyde and removal of the most contaminated topsoil) began in 1986. The island was declared free of anthrax in 1990, almost 50 years after the bomb was detonated.

The difficulty in using anthrax as a weapon (other than the longevity of the spores), is that the electrostatic charge of the spores tends to make them clump together and very difficult to disperse. Following World War II, a number of countries started to develop weaponized anthrax. This dried powder form of the spores dispersed into the air much more easily and made the delivery of effective anthrax spores possible. The goal of weaponized anthrax was to induce the inhalational form of anthrax. Although the infectious dose for inhalational anthrax is high (10,000-20,000 spores), the disease is extremely difficult to treat once it is diagnosed. In 1979, there was an accidental release of anthrax from a Soviet research facility in Sverdlosk resulting in at least 66 deaths and an extremely high mortality despite treatment. One characteristic of the outbreak was that the incubation period of the disease could be very long (up to 2 months in some cases). This experience with the disease led to the recommendation that individuals exposed to weaponized anthrax be treated prophylactically with a prolonged course of ciprofloxacin (more traditional antimicrobials were avoided due to concerns about engineered antimicrobial resistance). The "white powder," sent through the mail following the terrorist attacks in New York in 2001 was weaponized anthrax.

Controlling anthrax

The control of anthrax requires a two-pronged approach:

- rapid identification of the disease to allow environmental control measures
- vaccination.

It is vital that all clinical cases be promptly identified; however, because anthrax does not have characteristic clinical signs, it is necessary to consider all cases of sudden death as potential anthrax cases. When a case of anthrax is identified, control and disposal of the carcass to prevent further contamination of the environment are paramount. The carcass must remain intact and protected from scavengers. These measures not only limit contamination of the environment, but they also offer an additional advantage – if the carcass is not opened, the vegetative form of the bacteria cannot sporulate and it will eventually be destroyed as the carcass putrefies. Though potentially effective, putrefaction is not a practical method of controlling the disease; as a result, it is necessary to destroy the carcass by one of two approved methods: incineration and deep burial (at least 8 feet).

The method of disposal chosen will be somewhat dependent on local factors (eg, fire bans and depth of the water table). During the recent epidemic in Saskatchewan (2006), 70% of the carcasses were burned, 25% were buried, and 5% were deemed inaccessible (ie, the carcass could not be easily accessed). Based upon this experience in Saskatchewan, incineration is the preferred method of disposal. The technique is now well-defined and the Canadian Food Inspection agency (CFIA) has developed a great deal of experience in building appropriate pyres.[9] Incineration has the advantage that, even when the carcass has been opened and the bacteria have presumably sporulated, the entire carcass, the spores, and the surrounding area are all sterilized. After disposal, it is important to thoroughly disinfect all tools with 10% formaldehyde.

The second approach to controlling anthrax is use of the vaccine. The licensed vaccine in Canada is produced by the Colorado Serum Company.[10] Following the diagnosis of anthrax on a premises, all at-risk animals should be vaccinated (this vaccination is performed by the CFIA). The vaccine is licensed for use in cattle, sheep, goats, pigs, and horses and the dose is 1 mL administered subcutaneously. The label suggests that a second dose should be administered if animals are at high risk. Under normal circumstances, the CFIA recommends that animals be moved to a different pasture at the time of vaccination and that a single dose is usually sufficient. Annual revaccination is recommended for at least 3 years. Producers within a 10 km radius should contact their veterinarian for advice on whether to vaccinate their animals at their own expense. This recommendation is based on the findings of an international anthrax committee, and the understanding that the local veterinarian knows the local geography and can help a producer quantify the risk-benefit analysis of vaccination in their particular situation.

The vaccine may take 7-10 days to become effective. During that period, animals should be monitored closely and, if an animal shows signs consistent with possible anthrax infection, it should be immediately treated with antimicrobials. Treated animals must be clearly identified because the antimicrobials will also kill the vaccine strain of the anthrax bacteria. These animals will need to be revaccinated at least 8 days after the last dose of antimicrobial. All other use of antimicrobials in vaccinated cattle should be avoided for 8 days prior to and after vaccination. The vaccine has a 42-day withdrawal for meat and "zero"-day withdrawal for milk.

The CFIA also uses a quarantine system to further control the spread of anthrax. Premises are quarantined for 21 days after vaccination or the last case of anthrax, although milk can still be shipped from a dairy farm. The quarantine only controls the movement of animals; there is no limitation on human traffic.

Reporting requirements

Reporting anthrax cases to the CFIA is encouraged through a compensation program, in which producers are paid a sum of money for animals that are confirmed to have died of anthrax. The compensation differs from the compensation payments made for other diseases (eg, BSE and foot and mouth disease), in that no animals are ordered destroyed. The compensation is paid on animals that die of natural causes and helps to cover the costs of carcass disposal. The compensation is also administered under different legislation than the other reportable diseases. This is a relatively old piece of legislation and the values assigned to the individual animal species are very low by today's standards. In addition, the legislation did not recognize that bison, deer, and camelids are farmed animals and, therefore, no compensation could be paid on these species. This situation was rectified in September of this year (2006) when the Minister of Agriculture announced a change to the program.[11]

Summary

It is unlikely that anthrax will ever be entirely eradicated. As veterinarians, we must accept that the disease will continue to emerge sporadically. Eventually, it may be possible to more accurately predict the likelihood of such outbreaks. Our profession plays a vital role in protecting agriculture and public health from this disease. Further, the heightened sensitivity of the media and the general public to the possible use of anthrax as a biological weapon means that we also have a key role in educating our clients and the public to avoid over-reaction to outbreaks and to ensure the disease is quickly and effectively contained.

References

1. Klemm DM, Klemm WR. A history of anthrax. *J Am Vet Med Assoc* 1959;135:458-462.
2. Hanson RP. The earliest account of anthrax in man and animals in North America. *J Am Vet Med Assoc* 1959;135:463-465.
3. "American Farmer" in 1824.
4. Timoney JF, Gillespie JH, Scott FW, Barlough JE. *Hagan and Bruner's Microbiology and Infectious Diseases of Animals.* 8th ed. Ihtaca, NY: Comstock Publishing; 1988:206-213.
5. Cousineau JG, McClenaghan RJ. Anthrax in bison in the Northwest Territories. *Can Vet J* 1965;6:22-24.

6. Radostits OM, Gay CC, Blood DC, Hinchcliff KW. *Veterinary Medicine.* 9th ed. London, UK: W.B. Saunders Company; 2000:747-751.
7. http://www.aphis.usda.gov/vs/ceah/cei/taf/emerginganimal-healthissues_files/anthrax.pdf. Accessed: December 7, 2006.
8. http://www.vetmed.lsu.edu/whocc/mp_world.htm. Accessed: December 7, 2006.
9. http://www.svma.sk.ca/news/current.pdf. Accessed: December 18, 2006.
10. http://www.colorado-serum.com/biologics.html. Accessed: December 7, 2006.
11. http://www.inspection.gc.ca/english/reg/apppor/actloi/anthraxe.shtm. Accessed: December 7, 2006.

Dr. Chris Clark is an Assistant Professor of Internal Medicine in the Department of Large Animal Clinical Sciences at the Western College of Veterinary Medicine. His research interests are cattle lameness and the control and prevention of infectious disease. He has a particular interest in clinical pharmacology and is involved in the Canadian GFARAD initiative (Global Food Animal Residues Avoidance Databank).

Abstract of Interest

Past, imminent, and future human medical countermeasures for anthrax.

BAILLIE LW. BALTIMORE, MARYLAND

AIM: Anthrax is caused by the bacterium Bacillus anthracis. Although primarily a disease of animals, it can also infect man, sometimes with fatal consequences. As a result of concerns over the illicit use of this organism, considerable effort is focussed on the development of therapies capable of conferring protection against anthrax. This brief review will describe the efforts being made to address these issues.

METHODS AND RESULTS: A review of the literature and the proceedings of the sixth international conference on anthrax, held in Santa Fe, USA in 2005 shows intense activity, but there has been, as yet, no real progress. While effective antibiotics, antitoxins, and vaccines are available, concerns over their toxicity and the emergence of resistant strains have driven the development of second-generation products. The principal target for vaccine development is Protective Antigen (PA), the nontoxic cell-binding component of anthrax lethal toxin. While the recombinant products currently undergoing human clinical trials will offer considerable advantages in terms of reduced side effects and ease of production, they would still require multiple, needle-based dosing, and the inclusion of the adjuvant alum makes them expensive to administer and stockpile. To address these issues, researchers are developing vaccine formulations, which stimulate rapid protection following needle-free injection (nasal, oral or transcutaneous), and are stable at room temperature to facilitate stockpiling and mass vaccination programs.

CONCLUSIONS: An array of medical countermeasures targeting B. anthracis will become available over the next 5-10 years.

SIGNIFICANCE AND IMPACT OF THE STUDY: The huge investment of research dollars is expected to dramatically expand the knowledge base. A better understanding of basic issues, such as survival in nature and pathogenesis in humans, will facilitate the development of new modalities to eliminate the threat posed by this organism.

J Appl Microbiol 2006;101(3):594-606.

Upcoming Meetings

13 – 17 January 2007
The North American Veterinary Conference
Orlando, Florida
CONTACT: Website: http://www.tnavc.org/

19 – 21 January 2007
Western Canadian Association of Equine Practitioners Meeting
Calgary, Alberta
CONTACT: Ms. Sharon Stodler
Tel.: 306 966-7178
Email: sharon.stodler@usask.ca

18 – 22 February 2007
Western Veterninary Conference
Las Vegas, Nevada
CONTACT: Website: http://www.wvc.org/

Dr. Clark has stated that he has no disclosures to announce in association with the contents of this issue.

Change of address notices and requests for subscriptions to *Large Animal Veterinary Rounds* are to be sent by mail to P.O. Box 310, Station H, Montreal, Quebec H3G 2K8 or by fax to (514) 932-5114 or by e-mail to info@snellmedical.com. Please reference *Large Animal Veterinary Rounds* in your correspondence. Undeliverable copies are to be sent to the address above. Publications Post #40032303

This publication is made possible by an educational grant from

Schering-Plough Animal Health

117-057R

SNELL