Unveiling Anthrax: From Historical Pandemics to Modern Day Threats

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Abstract

Bacillus anthracis, the pathogen that causes anthrax, has been a powerful force throughout history, influencing sociopolitical environments and public health regulations. This chapter explores the history of anthrax, from its role as a deadly zoonotic disease to its current ramifications as a worldwide bio threat. It looks at the scientific turning points that revealed the biology of *B. anthracis*, including its spore-forming ability, transmission dynamics, and virulence mechanisms. Highlighting the role of anthrax in early germ theory and vaccine development, the chapter also examines historic anthrax outbreaks, ranging from ancient plagues to catastrophic agricultural losses. In light of bioterrorism, the emergence of antibiotic resistance, and the ongoing threat posed by anthrax spores in environmental reservoirs, contemporary viewpoints are examined. The critical analysis is given to developments in the diagnostics, treatment, and prevention, including the creation of vaccines and new antimicrobial agents. This chapter emphasizes the need for ongoing attention and creativity to lessen the complex threats of anthrax in a globalized world by connecting historical understanding with current issues.

Keywords: *B. anthracis*, Anthrax, Biological weapon, Bioterrorism, Emergence, Antibiotic resistance, Antimicrobial agents.

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Introduction

Louis Pasteur and Robert Koch were among many researchers who conducted extensive research on anthrax in 1870s. Understanding the disease and its pattern was made easier by the findings of these studies (Carter, 1988). After the discovery of the letter anthrax crisis, which led to a significant bacterial warfare program in the USSR, anthrax returned to scientific agenda. Both the general public and microbiologist were unaware of this prior to these events. The bible mentions a disease that affects herbivores and was a leading cause of animal mortality until the late 1800s (Schwartz, 2009).

History of Anthrax

The definition of anthrax dates back thousands of years, beginning with the fifth outbreak in Egypt around 1500 BC. In the middle ages, anthrax was first described lyrically by Black Bane and Virgil in 25 BC (Driks & Setlow, 1999). Since anthrax first appeared in bibilic times, it has been referred to as one of the great plagues throughout history. Additionally, it has been proposed that Athens plague was an anthrax epidemic caused by inhalation. In the 18th century, anthrax remained a problem in Europe, affecting both middle-aged humans and animals (Dirckx, 1981). Anthrax was not as well-known prior to the middle of the 20th century, but it became a serious issue when it was discovered in textile industry workers who sorted wool. Anthrax was discovered to be a medical advancement in the 19th century. wherein Casimir-Joseph Davaine and Pierre Rayer stated that filiform bodies are found in sheep blood (Carter, 1988).

While Louis Pasteur's 1881 test in sheep for a heat cured anthrax vaccine became the first use of live vaccine, William Greenfield's successful anthrax vaccination of livestock soon came to an end in 1880 (Tigertt, 1980). Human inhalational anthrax was first documented in 1900, which lead to the discovery that wool and hair which are used in industries, are the sources of infection (Jernigan et al., 2001). For the first time *B. anthracis* spore contamination in small ruminants is being studied in Pakistan's Tharparkar district. Samples were taken from the abdomen, neck and face, fore and hind limbs and other body parts of randomly chosen sheep and goats. According to the overall findings, 28% of the samples had anthrax spore contamination (Rajput, 2017).

As a result of immunization and effective management techniques, anthrax began to decline in farms during the 20th century. A new vaccine that was authorized and licensed in 1970 took the place of the 1950 human vaccine (Morris, 1999). There were extremely few human instances reported in the 20th century (Dixon, 2002). A few human and animal cases were reported in the Jhang district of Pakistan in 1961 and 1962 (Khan & Ahmad, 1962).

Anthrax spores, which cause the inhalational and cutaneous forms of the disease in humans, were purposefully released in the United States in October, November 2001, and March 2002 (Sternbach, 2003). A 63-year-old picture editor was admitted to the hospital on October 2, 2001. Meningitis was the original diagnosis made for the patient. His CSF fluid and blood were later revealed to contain gram-positive

Bacillus anthracis. On October 1, another 73-year-old newspaper mail room clerk was found to have some of the same symptoms. Patients which get extensive antibiotic therapy survive (Jernigan et al., 2001). According to Control and Prevention (Barlet J.G 2002) these instances verified the first instance of purposeful biological agent discharged in the United States. The majority of these cases were postal workers who were exposed to anthrax spores found in letters or mail, and there were 11 confirmed instances of inhalational anthrax and 11 suspected or confirmed cases of cutaneous anthrax (Bell et al., 2002). Accessibility, ease of administration, resistance to spores, high potency, and low visibility are some of the traits of *B. anthracis* that increase its potential as a biological weapon (Jamie, 2002).

Taxonomy

Bacillus anthracis belong to domain Bacteria, phylum *Firmicutes*, class *Bacilli*, order *Bacillales*, family *Bacillaceae*, genus *Bacillus* and specie *Bacillus anthracis* (Handistatus, 2005)

Epidemiology

The global distribution of anthrax is poorly understood, and it is a neglected illness. There are very few studies which have created regional maps. According to Blackburn et al. (2016) these maps are essential to the planning process for public health. According to reports, anthrax may be widely distributed throughout the North America, specifically in Australia, China, and Kazakhstan. Additionally, it has been proposed that *B. anthracis* thrives on the European continent, the Anatolian peninsula, and parts of the neighbouring areas. The *B. anthracis* thrives in soil that is alkaline, organic, and rich in calcium (Carlson et al., 2019).

Livestock

Disease outbreaks have a negative influence on a nation's economy and livestock output; the two are intimately correlated (Ndiva Mongoh et al., 2008). The herbivores like goats, sheep, and cattle are susceptible to anthrax, but pigs are also affected to a lesser extent. Numerous characteristics, including organic content, pH greater than 6.0, high soil nitrogen levels, and temperatures above 15°C, appear to be associated with environmental endurance. Two significant variables that cause its spores to germinate in potentially infectious quantities are dryness and heavy rain. Anthrax was originally common in countries with cattle, but due to extensive animal immunization, it is now only seen in Asia and Africa. However, rare outbreaks also happen in many other nations, including the United States, where the great plains are covered by a "anthrax belt" (Brachman, 1980). The epidemiology of anthrax involves environmental elements in addition to animal, human, and wildlife components (Bengis & Frean, 2014). According to reports, 1.1 billion animals are either in anthrax-endemic areas or at risk of contracting the disease. The majority of animals are at risk due to improper immunization. According to reports and observations, anthrax vaccination for cattle is not a prophylactic tool in East and South Asia. Instead, they only vaccinate during outbreaks, failing to consider that a significant portion of the rural livestock reside in these areas (Carlson et al., 2019). The graphic depicts the life cycle of *B. anthracis*. Animals that graze on polluted soil that contains *B. anthracis* spores become infected. It finds favourable conditions inside the host cells and begins to germinate, which, if left untreated or misdiagnosed, can be fatal (Setlow et al., 2003). *Bacillus anthracis*, the causative agent of anthrax, is a serious pathogen affecting livestock such as cattle, sheep, goats, and horses. The bacterium forms highly resilient spores that can persist in soil for decades, posing a continual threat to grazing animals. Livestock become infected by ingesting or inhaling spores from contaminated soil, water, or feed. Outbreaks often occur after heavy rains or soil disturbances, which bring buried spores to the surface. Once inside the animal, the spores germinate and multiply rapidly, releasing toxins that lead to severe systemic disease. Infected animals typically die suddenly with minimal signs, although symptoms like fever, difficulty breathing, or bleeding from orifices may be observed. Death often occurs within hours, leaving little time for intervention.

Anthrax in livestock is a major concern in endemic regions such as parts of Africa, Asia, and the Middle East. Carcasses of infected animals pose additional risk as they can release millions of spores into the environment if improperly handled. Therefore, safe disposal (incineration or deep burial) is critical. Vaccination is the most effective preventive measure in endemic areas. Strict biosecurity, surveillance, and reporting are essential to control outbreaks and minimize economic losses in the livestock industry caused by *B. anthracis*.

Human

There are two types of human cases: industrial and agricultural. The cases involving industries infect people who handle animal products such as infected bone meal or animal hair processing, while cases involving agriculture are caused by direct contact (slaughterhouse workers, herders and butchers) with infected animals (Glassman, 1958). However, anthrax illness is not known to exist throughout half of Africa (Balogh et al., 1994). Exposure to contaminated animal hair or wool was the cause of many US cases (Whitford, 1990). According to Walker et al. (1994), the two well-documented human pandemic outbreaks occurred in 1978–1980 and 1979 in Zimbabwe and Sverdlovsk (the former Soviet Union). A zoonotic disease is anthrax. Animals and people can contract diseases via improper handling of contaminated animal carcasses. When herbivores come in touch with contaminated soil, grass feed, or water, outbreaks of the disease can occasionally happen shown in the figure 1. It can take on the appearance of an epidemic in some areas and pose a major threat to the human population. Both humans and animals may be at danger due to incorrect diagnosis and inadequate care (Fasanella et al., 2010).

Microbiology

The *Bacillaceae* family includes *B. anthracis*, which has a rod-like structure and varies in size from 1-1.5 μm to 3-6 μm. It is non-motile and aerobic in nature. It can be found in chain forms, and its chain form assembly involves various parts. The development of a clear capsule around the organism's body during infection is unique to the infectious form and absent from culture media; it is thought to be a defence mechanism of bacilli. Although it can grow well in culture media under aerobic or microaerofillic conditions and temperatures ranging from 12°C to 44°C, this Gram-positive organism grows best at temperatures close to 37°C and pH values between 7.0 and 7.4 (Pile et al., 1998).

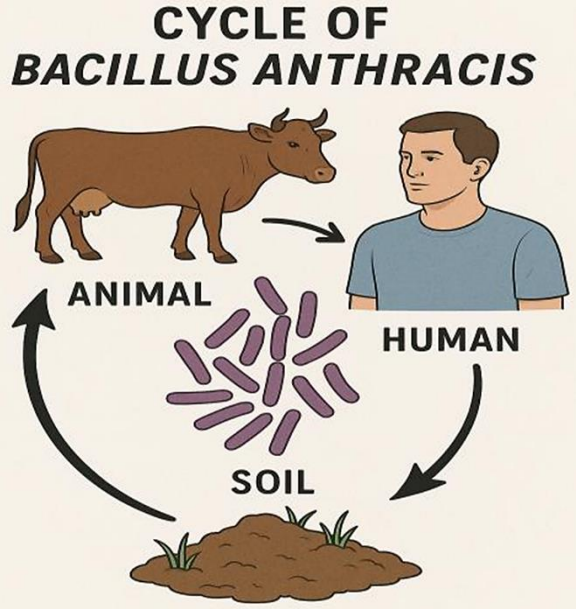

Fig. 1: Anthrax transmission cycle

To comprehend the behaviour of spores in aerosol form, it is crucial to consider their size, derived magnitude, spore volume, and aspect ratio. According to published research, the major and minor axes of *B. thuringiensis* spores have diameters of 1.07 and 1.38µm, respectively (Westphal et al., 2003). According to Leuschner and Lillford (2000), *B. subtilis* has lengths of 1•40 ± 0•14 µm and widths of 0•55 ±0•035 µm. The carbon source in the growth medium has an impact on *B. megaterium* spores, with the volume of spores varying 1.17 μm^3 when the carbon source is acetate and 0.38 μm^3 when it is citrate (Hitchins et al., 1972). The *B. anthracis* spores were observed to be around 2 µm long and 1 µm broad, similar to those of other Bacillus species (Turnbough Jr, 2003).

The thick peptidoglycan, S-layer, membrane, and capsule are all present in *B. anthracis*. According to certain data, *B. anthracis* contains lipoteichoic acid, which may play a significant role in its pathogenicity. The surface protein of gram-positive bacteria may be peptidoglycan-anchored, and this bond may or may not be covalent. Both kinds of associations exist in *B. anthracis* (Fouet, 2009).

Because of its structure, the S-layer can function as molecular sieves, cell adhesion, and molecule or ion traps. The cell surface is entirely covered by them (Sára and Sleytr, 2000). The capsule of *B. anthracis* is peptidic in nature rather than polysaccharide, and it contributes to both pathogenicity and immune system evasion (Fouet, 2009).

The *B. anthracis* spores are made up of several concentric shells. The chromosome and densely complex proteins known as small acid soluble proteins (SASP) are found in the core, the interior component of the spore (Driks & Setlow, 1999). The core is surrounded by a peptidoglycan layer called the cortex. The core benefits from being comparatively dry (Setlow, 2003). The thick protein shells known as coats envelop the cortex. It has a very thin, darkly pigmented coat (Driks, 2002). The exosporium, a protein shell, is the spore's outermost component (Driks, 2009).

The contents of the interspace, which separates the exosporium and coat in many species, remain unknown (Fox et al., 2003). The *B. anthracis* spore's core, cortex, coat, interspace, and exosporium are all depicted in the illustration (Driks, 2009).

Gastrointestinal Anthrax

There are three clinically recognised types of anthrax: gastrointestinal, inhalational, and cutaneous. This classification depends on the spores' mode of entry into the host (McKendrick, 1980). The pathophysiology of gastrointestinal and cutaneous anthrax is considerably more comparable. In the mechanism of infection, the host consumes the spores, and the gastrointestinal tract's epithelium becomes the major site of infection, ultimately resulting in ulceration. However, the vegetative form of *B. anthracis* can also function as a major site of infection in both cutaneous and gastrointestinal anthrax (Fox et al., 1973). The swallowing anthrax spores can result in lesions from the mouth cavity to the cecum. It appears that this type of anthrax is deficient, which makes diagnosis challenging due to inadequate facilities. The breadth of diseases that cause host death in subclinical infections is not entirely understood. In many regions, the number of gastrointestinal anthrax cases exceeded that of cutaneous anthrax cases (Sirisanthana & Brown, 2002b).

Cutaneous Anthrax

Most of the time, humans can contract anthrax directly or indirectly from sick animals. Inhalation or contact with *B. anthracis* spores is necessary for its primary mode of transmission. According to Doganay et al. (2010), humans can become infected intentionally or through the industrial and agricultural environments that transmit disease. The majority of cutaneous anthrax is self-limiting, and 80–90% of patients have lesions that go away with little care and no sequelae. Rarely, toxic shock and widespread oedema are seen, which can result in potentially fatal consequences for cutaneous anthrax (Turnbull, 2008). The cutaneous form is brought on by natural environmental exposure; spores enter through any cut, abrasion, or lesion and create non-suppurative vassiculation, ulceration, and finally a black eschar, which gives the illness its name, anthracis, which means "coal like." Typically, it self-limits (Chensue, 2003).

Inhalational Anthrax

The notion that a single *B. anthracis* spore can be lethal is widely accepted, but this is because the scientific foundation for evaluating microbial risk—specifically, dose-response assessment—is still lacking (Coleman et al., 2008). Its symptoms were chills, lethargy, low-grade fever, and cough, according to reports. However, additional symptoms such as chills, nausea, a strong headache, and night sweats have been noted in patients (Mayer et al., 2001). The mostdeadly type of anthrax is inhaled, which results in 100% death in situations that go untreated. In clinical settings, this kind first manifests as flu-like symptoms, which are followed by fever, nausea, and dyspnoea. Later, treatment is no longer effective (Quintiliani Jr & Quintiliani, 2003).

Injectional Anthrax

In 2001, a heroin user in Norway had an infection around the site of a subcutaneous injection. Despite therapy, infection results in septic shock and death. Because it differed from the cutaneous type, this illness was called injectional anthrax (Ringertz et al., 2000). It is thought

that spores germinate more quickly at the injection site, which leads to the vegetative form spreading quickly throughout the soft tissues. Additionally, in certain situations, thrombocytopenia and coagulopathy develop, which causes the patients to go into shock (Booth et al., 2014).

Toxins of *B. anthracis*

Two plasmids called pX01 and pX02 encode the capsule and are linked to toxins in *B. anthracis* (Koehler, 2009). Three proteins secreted by *B. anthracis* give rise to two different kinds of toxins: deadly factor, protective antigen, and oedema factor. There are two types of toxins: oedema toxin, which causes oedema, and lethal toxin, which causes death in animals and contains protective antigen and fatal factor protein. Lethal and oedema factors enter eukaryotic target cells through protective antigens. pX01 encodes all of these poisons. Adenylate cyclase and metalloprotease, which are calmoduline-dependent channels, are used by oedema factor and fatal factor. As they develop further, these three proteins' roles in pathogenesis, regulation, and immunoprotection become clear (Brossier & Mock 2001). Its plasmid, pX02, is responsible for the capsule development of *B. anthracis*. All capsules contain pX02, regardless of whether they are virulent or not (Green et al., 1985).

Due to its adenylyl cyclase, *B. anthracis* toxin, also known as oedema toxin, plays a significant role in the pathogenicity of anthrax. Pathology investigations showed that there was an accumulation of intraluminal fluid, followed by ileal and adrenal gland haemorrhage (Firoved et al., 2005). The lethal factor is another important component of toxins. This toxin kills lab animals by cytolyzing macrophages and their cell lines. Its zinc binding motif for metalloproteases gives LF a distinct characteristic, and there is evidence that its hydrolysis activity contributes to its cytotoxicity (Vitale et al., 1998). It is considered that these two plasmids are only linked with *B. anthracis* but there are some reports of rare *B. cereus* harboring similar plasmids (Hoffmaster et al., 2004; Avashia et al., 2007).

Vaccine

The founding fathers of microbiology started researching disease prevention in the 1980s, when Jenner was one of the people who invented vaccination, published the variole vaccine, and investigated its causes and effects. Pasteur gave evidence of protective vaccination against anthrax in 1881 and fowl cholera in 1880 at that time. In 1939, Sterne created a live-attenuated spore vaccine derived from the avirulent non-capsulated strain of *B. anthracis* (Nicol & Sterne, 1942). The virulent bovine isolate that gave rise to the toxic, non-capsulated *B. anthracis* strain 34F2 is currently in use all over the world (Sterne, 1939). Vaccines of the pasture type have been abandoned globally. The 34F2 animal vaccines are used in their original formulation, which contained about 107 spores per millilitre (Sterne, 1939). It has been proposed that only animals that can be isolated from sick animals should receive vaccinations. The ring vaccination strategy should be employed if it is difficult to separate those animals. Whereby the herds or animals that are in the vicinity of the diseased farm receive vaccinations (Turnbull, 2008). The current vaccine for anthrax produces an immune response against its toxins, particularly the protective antigen (Cybulski Jr et al., 2009).

Additionally, it has been noted that vaccination rates are low globally, with particularly low rates of disease reporting and vaccination in developing nations. This map displayed the average vaccination rate for livestock, which may indicate that farmers used to kill and sell tainted meat without understanding the risk of infection in humans because they didn't want to lose money (Carlson et al., 2019).

Conclusion

The anthrax continues to pose a serious threat to biosecurity and public health, connecting historical pandemics with contemporary dangers. Its significance in the development of microbiology and medicine is highlighted by its historical role as a catalyst for scientific discovery, ranging from germ theory to vaccine development. Anthrax remains a problem because of its zoonotic nature, environmental resilience, and potential for weaponization, even though improvements in diagnosis, treatment, and prevention have lessened its effects in many areas. Emerging issues like global bioterrorism and antibiotic resistance highlight the necessity of strong research, surveillance, and readiness plans. We can address the persistent threat of anthrax and protect public health in a world that is becoming more interconnected and vulnerable by drawing on historical knowledge and modern scientific discoveries.

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