

# An overview of anthrax: a neglected zoonosis of the tropical region

## Abstract

Anthrax is a neglected bacterial zoonosis that can be highly contagious and potentially lethal. The disease, which mainly affects herbivorous ungulate animals, is caused by *Bacillus anthracis*, a rod-shaped, gram-positive bacterium. The pathogenicity depends on the production of toxins by *Bacillus anthracis* and the sensitivity of the host. The infection is transmitted to humans when they come in to contact with infected animals or their products. It is an important occupational risk to the abattoir workers. Clinical manifestations of disease in humans include different forms, including cutaneous, pulmonary and intestinal. The disease is widespread in African and Asian countries with frequent reports of cases. Lack of appropriate and effective control programs in these countries has led to increase in the number of human cases. *Bacillus anthracis* spores are extremely resistant to environmental conditions, and can persist for several decades in nature and, thus making the control or eradication of the disease difficult. Disease control involves managing contaminated animal products, avoiding contact with infected animals, livestock vaccination in endemic regions and routine surveillance of animals. The most effective and dependable way to control zoonotic diseases like anthrax is through collaborative monitoring programs including the "One Health" approach.

**Keywords:** animal, anthrax, *Bacillus anthracis*, human, one health approach, zoonosis

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## Introduction

Zoonotic diseases have substantial impact on both animal health and public health in addition to their economic implications. These diseases can occur in sporadic and epidemic form affecting both sexes, and all age groups.<sup>1</sup> Zoonotic diseases are recognized as a major concern in developing nations and need a resolution.<sup>2</sup> It is commonly agreed that detecting, managing, and eliminating zoonotic diseases requires joint efforts from the animal and human health sectors.<sup>3</sup> Joint monitoring systems such as the "One Health" strategy are the most efficient and reliable means of addressing zoonotic diseases, such as anthrax in low-income countries.<sup>4</sup> The majority of nations lack an integrated control system that would allow them to solve gaps with little collaborative effort in the food, environmental, animal, and human health sectors. Because of the absence of particular investigative techniques, a lack of expertise, and poor coordination among all parties involved, the elimination of zoonotic diseases continues to be an unfulfilled aim.<sup>5</sup>

Many zoonoses, including brucellosis, anthrax, rabies, leptospirosis, plague, echinococcosis, leishmaniasis, taeniasis/cysticercosis, and schistosomiasis, are often ignored. The majority of neglected diseases arise in impoverished countries because of their poor environmental cleanliness and insufficient medical facilities. Among these, anthrax is a neglected bacterial zoonosis that can be highly contagious and potentially lethal. It has been reported in numerous countries around the world including India.<sup>6</sup>

Anthrax, also known as carbon, malignant pustule or wool sorter's disease, is a widespread zoonosis that mainly affects herbivorous animals, and is caused by a rod-shaped, Gram-positive bacterium known as *Bacillus anthracis*.<sup>1,7</sup> Anthrax most often occurs in warm-blooded wild or domesticated livestock such as sheep, cattle, and goats but can cause disease in humans, inducing three forms of lung (pulmonary), digestive (intestinal), or skin (cutaneous) infections.<sup>1</sup> Ultimately, all forms of anthrax may spread across the body and

cause death if not properly treated with antibiotics at the right time. A systematic review on human anthrax in India mentioned handling or consuming dead or sick animals as a major risk factor for human infection.<sup>8</sup>

The increasing prevalence of emerging infectious diseases suggests that it is imperative to integrate animal, human, and environmental health through the "One Health" concept. With their extensive knowledge of biological systems, understanding of disease processes and epidemiology, expertise in diagnosing and treating illnesses in large animal populations, and track record of successfully curing and preventing infectious diseases, veterinarians are best suited to provide this bridge.<sup>9</sup> Management and effective control of anthrax through one health concept is described as a highly demanding approach, although it needs robust implementation globally.<sup>10</sup> The objective of this communication is to delineate information on neglected tropical bacterial zoonosis anthrax from a One Health perspective.

## Anthrax

The bacterium that causes the zoonotic illness anthrax is called *Bacillus anthracis*.<sup>11</sup> The organism is a capsulated aerobic or facultative anaerobic bacteria that produces spores that enable prolonged survival when exposed to the environment through the bodily fluids of a deceased person.<sup>12</sup> The vegetative cells cannot endure very long outside the host body without sporulation. According to,<sup>13</sup> when a body is closed for more than 72 hours, vegetative cells experience sporulation inhibition and eventually end their life cycle. After they have sporulated, they are resistant to changes in pH, humidity, desiccation, radiation, chemical disinfection, salting, and temperature.<sup>14</sup>

## Etiology

*Bacillus anthracis*, a spore-forming rod-shaped, Gram-positive, immobile, capsulated, aerobic, or facultatively anaerobic bacterium that belongs to the *Bacillaceae* order and genus *Bacillus*, is the causative

agent of anthrax.<sup>12</sup> Compared to the bacterium's vegetative form, the spores are more active.<sup>15</sup> This *Bacillus* sporulates more readily in an environment that is between 53 and 107°F (12°C–42°C), but it does not sporulate at temperatures lower than 48–53°F (9°C–12°C.<sup>16</sup> The spores cause disease outbreaks when the right circumstances are present,<sup>15</sup> and they revert to the vegetative state once the host animal-a human-becomes infected.<sup>16</sup>

## Epidemiological triad

### Host

All herbivorous ungulate animals are susceptible to anthrax infection, but cattle followed by sheep are more often infected due to their feeding habits.<sup>17</sup> Goats and horses are less frequently infected. Another interesting fact is that among ungulates, adults are more susceptible to anthrax infection, while young ones are relatively resistant.<sup>18</sup> Humans occupy an intermediate position between this group and the relatively resistant pigs, dogs and cats. In farm animals, the disease is almost invariably fatal, except in pig and even in this species the case fatality rate is high. Cold-blooded vertebrates are apparently resistant to anthrax infection and perusal of the literature revealed no confirmed cases in them.<sup>19</sup>

### Agent

The virulence of pathogenic strains originates from two plasmids, including *pxO1* on which genes code for LF (lethal factor), EF (edema factor) and protective antigen, while *pxO2* genes code for capsule biosynthesis.<sup>12</sup> The protective antigen comprises toxins and a spore-forming component. The main components of *Bacillus anthracis* virulence are the toxin and capsule. The three protein components that make up the complex bacillus anthrax are components I, II, and III in order of complexity. The protection factor (PF) is component number two, the EF is component number one, and the LF is component number three. Every element is a different, moveable protein. By competitively interacting with PF, which has a membrane translocation function, EF and LF can enter the target cells.<sup>20</sup> Together, these three elements work to cause the toxic impact observed in anthrax infection. There is maximum lethality when component three is added, whereas components one and two induce low mortality. The only pathogenic strains are those that are encapsulated and toxic.<sup>21</sup>

When anthrax-bacilli-containing material is exposed to the air, spores are formed that prolong the environment's infectiousness for extended periods of time. These spores are resistant to the majority of external factors, such as salting, typical environmental temperatures, and common disinfectants. Anthrax bacilli have been shown to survive for 60 years when kept in a rubber-stopper bottle. Field observations suggest that they can also survive for a comparable amount of time when exposed to soil, especially when there is organic matter present, the soil is undrained and alkaline, and the environment is warm. *Bacillus anthracis* had a lower chance of surviving in acidic soils.<sup>22</sup>

### Environment

Since the spores survive in the soil, in tropical and subtropical regions with substantial yearly rainfall, severe and frequent anthrax outbreaks are recorded. Anthrax is known to be a hot-season disease, and outbreaks occur frequently in hot-dry climates with occasional rainfall.<sup>23</sup>

In temperate, cool climates, only sporadic outbreaks result from soil-borne infections. The anthrax outbreaks have been associated with heavy rain after a prolonged drought, dry summer months after prolonged rain and always warm weather when the environmental temperature is 15°C. The hypothesis that these climatic conditions

lead to sporulation and vegetative proliferation with the production of incubator areas for anthrax in the soil appears improbable, but spores have a high buoyant density, and in wet soil they could become concentrated and remain suspended in standing water with further concentration on the soil surface as the water evaporates. This relationship to climate has made it possible to predict anthrax life expectancy in the soil.<sup>24</sup>

### Transmission

The pathogen can enter the body through the skin, ingestion, or inhalation.<sup>1</sup> Streams, insects, dogs, and other carnivores, as well as wild birds and animal feces, can all contribute to the organism's spread within a region. Usually, contaminated animal products, such as bone meal, fertilizers, skins, and wool or contaminated concentrates or fodder spread the infection into a new area. Animal inhalation infections are generally seen as being of little consequence, although it is always important to take contaminated dust contamination into account. Humans who work in the wool and hair industries can contract wool sorter's disease by breathing in anthrax spores; however, even in this sector, cutaneous anthrax is far more common.<sup>25</sup>

The disease in animals occurs in three forms, namely peracute, acute, and sub-acute.<sup>1</sup> In humans, three forms are described, cutaneous, gastrointestinal (oropharyngeal, intestinal), and pulmonary (inhalation) based on the mode of transmission. The cutaneous form (malignant pustule) is the most common clinical manifestation of human anthrax, accounting for over 95% of cases. A pulmonary form known as wool sorter's disease carries a very high mortality rate and is observed in people working in the animal product processing industry. Mortality rates in untreated patients in cutaneous, gastrointestinal, and pulmonary forms may be 20%, 25–75%, and 95–100%, respectively. Anthrax is considered an occupational zoonosis of abattoir workers, hide and wool industry workers, livestock keepers, veterinarians, tanners, skimmers, shearers, agricultural farmers, renderers, and shepherds.<sup>6,26</sup>

### Pathogenesis

*Bacillus anthracis* spores may enter the body through ingestion, skin abrasion or inhalation, although ingestion is most common route of infection.<sup>12</sup> Following entry, the spores may have commenced germination and are carried to the lymphatic system, where they multiply. Initially, during the incubation period, the bacteria are filtered out by the spleen and other parts of the reticulo endothelial system. However, the system finally breaks down due to toxin action during the last few hours of life. The action of a toxin breaks the endothelial cell lining of the blood vessels, resulting in internal bleeding.<sup>27</sup> The anthrax toxin is believed to play a role in two stages of infection. Early during infection, they target the immune response to allow survival in the host and facilitate dissemination. In systemic disease, they target tissues and induce lethality.<sup>28</sup>

On ingestion of the spores, infection may occur through the intact mucus membrane, through defects in the epithelium around erupting teeth, or through scratches from tough, fibrous food materials. The organism is resistant to phagocytosis, in part due to the presence of the body-D-glutamic acid capsule, and proliferates in regional draining lymph nodes, subsequently passing via the lymphatic vessels into the bloodstream; septicemia, with a massive invasion of all body tissues, follows. *Bacillus anthracis* produces a lethal toxin that causes edema and tissue damage, death resulting from shock, acute renal failure, and terminal anoxia.<sup>29</sup> The virulence level depends on the amounts of toxins produced, the quality of the capsular coat and the sensitivity of the host.<sup>12</sup>

## Clinical findings

### In animal

*Bacillus anthracis* is an obligate pathogen, having an incubation period of 3–7 days or ranging from 1–14 days. In herbivores, the clinical course ranges from acute to chronic.<sup>30</sup> The per-acute form is characterized by sudden and rapid onset, staggering, dyspnea, trembling, collapse, and convulsive movements that may occur in cattle, sheep, or goats without any previous evidence of illness.<sup>21</sup> Rigor mortis is absent or incomplete. Dark, tarry-like blood that does not clot is evident at the mouth, anus, nostrils, and vulva.<sup>31</sup>

An acute form is characterized by a sudden increase in body temperature, a period of excitation, depression, respiratory trouble, convulsions, and death. Rumination stops, the body temperature might increase to 41.5°C, and animals may abort. The average duration of blood discharge from the body's natural orifice is 48 hours.<sup>30</sup> Fever, anorexia, listlessness, and edema of the throat, face, neck, and belly, together with petechial bleeding on the skin, are observed in pigs and horses. Bloody froth in the nostrils may indicate dysentery.<sup>31</sup> Localized subcutaneous edematous swelling, most commonly in the ventral neck, shoulders, and thorax, is the hallmark of the chronic form.<sup>32</sup>

### In humans

More than 95% of cases of anthrax are of the cutaneous form. Most lesions appear on exposed skin, and they frequently start itching. There are multiple stages that they go through papular, vesicular, and eschar. The eschar stage appears two to six days after the hemorrhagic vesicle dries and turns into a depressed black scab (malignant pustule). It may also have extensive edema (swelling) and surrounding redness. Although anthrax lesions often don't hurt, the surrounding edema may cause pain. Untreated lesions have the potential to spread and affect local lymph nodes. Severe cases may result in overwhelming septicemia. It is mentioned by<sup>33</sup> that untreated cutaneous anthrax has a case fatality rate of 5–20%, but death is uncommon when prompt, effective treatment is received. The pulmonary (inhalational) form of anthrax is extremely uncommon and typically manifests as fever, malaise, mild coughing, or chest pain (upper respiratory tract symptoms are uncommon).

Early signs can be mistaken for a flu-like sickness. After three to six days, there is a rapid development of dyspnea, hypoxia, and fever, along with radiographic indications of mediastinal expansion. Meningitis happens rather often. With postponed or nonexistent therapy, the death rate gets close to 100%. According to,<sup>31</sup> the mortality rate is considerably reduced when the right antibiotics are started during the prodrome. Although it is extremely uncommon in industrialized nations, the intestinal/oro-pharyngeal form of anthrax can arise in huge epidemics in developing nations as a result of eating meat from infected animals. Gastrointestinal symptoms in intestinal anthrax may be followed by fever, septicemia, and even death. Case fatality rates of 25–75% have been reported. In oropharyngeal anthrax, fever, neck swelling due to lymphadenopathy, throat pain, oral ulcers, and dysphagia may be followed by severe local ulcers and swelling, septicemia, and death. Case fatality rates are similar to the intestinal form.<sup>31</sup>

## Diagnosis

The presumptive diagnosis is based on symptoms and epidemiological data, while laboratory diagnosis is required for further confirmation. To confirm the diagnosis of an unopened carcass, peripheral blood or local edema fluid should be collected by

needle puncture. Blood can also be carefully collected from an ear vein to avoid unnecessary contamination and sporulation. The smears should be prepared and interpreted by an experienced and qualified microbiologist. Note that the zoonotic potential of this organism is high when handling carcasses and submitting specimens.<sup>25</sup> In direct microscopy, *Bacillus anthracis* produces a capsule in vivo, and either Giemsa or polychrome methylene blue stains are used to demonstrate the capsule, which is of diagnostic importance. The capsule material is more abundant if the blood smear has been taken from recently dead animals. Polychrome methylene blue-stained smears reveal square-ended, blue rods in short chains surrounded by pink capsular materials. In the case of Giemsa-stained smears, the capsule is reddish.<sup>34</sup>

*Bacillus anthracis* can be isolated and grown aerobically at 37°C for 24 to 48 hours on sheep or ox blood agar. Hair, bone meal, and other contaminated materials should be finely crushed, steeped in saline solution, and then heated to 65°C for ten minutes. After the suspension cools, it is centrifuged and dyed using gauze. According to,<sup>35</sup> the deposit can be used for animal inoculation or culture. In a day, colonies of virulent strains that are cultivated in conditions containing either serum, bicarbonate, or both form capsules. They are typically smooth to mucoid, non-hemolytic, and have a gray, flat appearance. Bacteria cannot form capsules without serum or bicarbonate, resulting in rough colonies.<sup>36</sup> *Bacillus anthracis* and the majority of *Bacillus* species do not normally produce capsules in or on laboratory media, and the colonies have a dry appearance. However, *Bacillus anthracis* can be induced to produce a capsule by growing it on nutrient agar containing 0.7% sodium bicarbonate under 10% CO<sub>2</sub>. The colonies are quite mucoid.<sup>34</sup> *Bacillus anthracis* produces an inverted fir tree type of liquefaction with side shoots radiating from the stab line, while the other species rapidly liquefy nutrient gelatin.

An animal test is used for confirmation of the diagnosis. *Bacillus anthracis* is much more pathogenic for guinea pigs and mice than other bacillus species, causing death within 24 hours. Large encapsulated rods are demonstrated in smears of the spleen and blood of infected animals. The polymerase chain reaction (PCR) assay holds importance in the diagnosis of anthrax, especially for the identification of virulent strains.<sup>21</sup>

## Treatment

Penicillin, chloramphenicol, streptomycin, tetracycline, and erythromycin can all be effective against *Bacillus anthracis*. At least five days should pass while receiving treatment. However, antibiotic therapy is frequently ineffective in treating acute anthrax.<sup>37</sup> The animals were protected against anthrax throughout therapy, which was started 24 hours after infection; however, many of them perished from anthrax after treatment was terminated, with antibiotics protecting varying degrees (10–90 percent). All animals were completely protected even after treatment ended when antibiotics and a protective antigen vaccination were administered together. Different degrees of bacteremia and toxemia were formed in animals whose treatment was postponed for more than 24 hours after infection.<sup>38</sup>

## Control and Prevention

When an outbreak or a case of anthrax occurs, animal health authorities must be notified to supervise control measures for carcass disposal, which involves incineration or deep burial; to treat and isolate sick animals; to vaccinate susceptible stocks; and to quarantine the premises for 3 weeks after the last established case. Milk from infected animals must be discarded under appropriate precautions. Disinfecting barns and fences with 10% sodium hydroxide is mandatory. Boiling utensils for 30 minutes will kill spores, and

surface soil spores can be killed by treating them with a 3% acetic acid solution at the rate of eight liters per square meter.<sup>37</sup>

The vaccination of animals has great value in the control of disease in several parts of the world. Sterne vaccine, a live attenuated spore vaccine has been effectively used in anthrax control programs for several years. Sterne attenuated live vaccine that has proved to be useful is derived from a virulent encapsulated strain of *Bacillus anthracis*. The vaccine gives protection for one year. The vaccines prepared from non-living antigens do not give adequate immunity.<sup>39</sup> A new wave of research on vaccines against the capsule has also introduced new candidates for development.<sup>28</sup>

The prevention of spillover of infection from meat- and milk-producing animals to the human population must be an important component of the Control program. When an outbreak occurs, the placing of the farm in quarantine, the proper disposal of discharge and cadavers, and the vaccination of survivors are parts of the animal disease control program and indirectly reduce human exposure. Prohibition of the movement of milk and meat from the farm during the quarantine period should prevent the entry of the infection into the human food chain. Discontinuation of the infection source is an essential first step in breaking the cycle of infection. Moving other animals away from the affected area is an important early action. If flies are suspected of being important vectors, fly control should be considered. Prevention of *Bacillus anthracis* exposure through animal products imported from certain areas requires disinfection of such materials as hair and wool with formaldehyde. Bio-endemic meals sterilized by dry heat (150°C per 3 hours) or steam at 115°C for 15 minutes are very important.<sup>37</sup>

## Conclusion

Anthrax is an infectious disease caused by the bacteria *Bacillus anthracis*, and it affects both animals and humans. Generally, the disease causes huge economic losses by causing the death of animals, reducing animal products, and the complete condemnation of carcasses and by-products, as well as the closure of abattoirs. It also results in pulmonary, intestinal, or cutaneous forms of anthrax in humans. The prevention of spillover of infection from meat- and milk-producing animals to the human population must be an important component of the control program. When an outbreak occurs, the placing of the farm in quarantine, the proper disposal of discharge and cadavers, and the vaccination of survivors are parts of the animal disease control program and indirectly reduce human exposure.

**Generally, to reduce the incidence of this disease, the following recommendations based on ‘One Health Approach’ are forwarded:**

- a) Livestock vaccination in endemic areas is advised.
- b) Routine surveillance of animals should be conducted.
- c) Proper carcass disposal for infected animals is imperative.
- d) Eating raw meat should be prohibited.
- e) Rapid diagnosis and treatment of sick animals with effective antibiotics are important.
- f) Health education for farmers, butchers, tanners, and other industrial workers should be imparted.
- g) Environmental and personal hygiene, medical care, and disinfection of wool and soil with formaldehyde should be practiced.

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## Contribution of authors

All the authors contributed equally.

## Conflicts of interest

The authors declare that there are no conflicts of interest.

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