SYSTEMATIC REVIEW OF ANTHRAX, A ZOONOTIC BACTERIAL INFECTION IN AFRICA

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ABSTRACT

On the 13th of June 2023, the Federal government of Nigeria announced the outbreak of anthrax disease in some neighbouring countries within the West African sub-region. It was specifically stated that the disease caused by a bacteria known as Bacillus anthracis has begun to be widespread specifically in northern Ghana, bordering Burkina Faso and Togo and has resulted into loss of lives. Border States in Nigeria such as Sokoto, Kebbi, Niger, Kwara, Oyo, Ogun and Lagos states because of their proximity to Burkina Faso, Togo and Ghana are at higher risk and could affect other parts of the country. Anthrax caused by B. anthracis is a zoonotic disease that affects both human and animals. The spores are naturally found in the soil and commonly affect domestic and wild animals but it can spread to human when they come in contact with affected animals or through contaminated animal products. Although, anthrax is not a contagious disease and so, one cannot get it by coming in close contact with an infected person but it could be dangerous when contacted. Signs and symptoms of anthrax include cough, fever, muscle aches and if not diagnosed and treated early, leads to pneumonia, severe lung problems, difficulty in breathing, shock and death. A quick intervention as well as appropriate information and knowledge about this zoonosis is very important. Anthrax remains a global public health concern, especially in resource-limited, rural agricultural areas, including Africa.

Keywords: Anthrax, *Bacillus anthracis,* Zoonosis, Bacteria

INTRODUCTION

Anthrax is a serious infectious disease caused by gram-positive, rod-shaped bacteria known as *Bacillus anthracis* Cohn 1872 (Bacillales: Bacillaceae). It occurs naturally in soil and commonly affects domestic and wild animals around the world. People can get infected with anthrax if they come in contact with infected animals or contaminated animal products. Domestic and wild animals can become infected when they breathe in or ingest spores in contaminated soil, plants, or water (NCDC, 2023). The carrier animals can include cattle, sheep, goats, antelope and deer. In areas where domestic animals have had anthrax in the past, routine vaccination can help prevent outbreaks (CDC, 2018). *B. anthracis* contain endospores which are the infectious particles of anthrax. The pores are dormant bacterial morphotypes that are able to withstand harsh environments for decades therefore contributes to their ability to be formulated and dispersed as a biological weapon (Liu *et al.*, 2004). There are two large

plasmids essential for toxicity of *B. anthracis;* they are pXO1 that contains the toxin genes and pXO2, which encodes a capsule. *B. anthracis* forms a highly monomorphic lineage within the *Bacillus cereus* Frankland and Frankland 1887 (Bacillales: Bacillaceae), but strains of *Bacillus thuringiensis* Berliner 1915 (Bacillales: Bacillaceae) and *B. cereus* exist that are genetically closely related to the *B. anthracis* cluster (Kolstø *et al.,* 2009).

The National Institute of Allergy and Infectious Diseases (NIAID) classifies *B. anthracis* among the agents that cause plague, botulism, smallpox and viral hemorrhagic fevers as a "category A" pathogen, which is known to pose the highest threat to national health security. Typically, the bacteria reside in the soil as persistent, dormant spores that can infect grazing animals with the disease (Ndolo *et al.,* 2022). Direct or indirect contact with infected animals or work-related exposure to infected animal products is the main causes of naturally acquired human anthrax infection. The degree of exposure to infected animals determines the occurrence of the natural disease in people. Africa and central and southern Asia have the greatest rates of anthrax cases among humans. In sub-Saharan Africa, the economic significance of the meat from an animal that has unexpectedly passed away outweighs the perceived dangers of the illness that could arise from eating it, which may be the cause of this (Espinosa *et al.*, 2020).

Although findings of researches suggest that humans are generally immune to anthrax, outbreaks and epidemics sometimes happen in humans, and can occasionally be quite large. The Zimbabwean epidemic, which started in 1979 and raged in 1984 – 1985, was one of the most famous. Despite the modest (1 – 2%) case-fatality rate, more than 10,000 people suffered from the disease (Kobuch *et al.*, 1990; Pugh and Davies, 1990). Only 12 deaths were documented out of the 448 human cutaneous anthrax cases diagnosed during the pandemic in the Gambia (Heyworth *et al.*, 1975). Furthermore, in year 2000, Ethiopia was reportedly affected by anthrax infection involving several people, many of whom had oral and gastroenteric illnesses. These incidents all involved skinning and slaughtering sick and dead animals, handling tainted meat and eating undercooked or raw meat (WHO, 2000).

The widespread usage of penicillin might have lowered mortality rates in these outbreaks, but case-fatality rates can be extremely high, as in the Sverdlovsk incident in the former Soviet Union, where 66 people (Abramova *et al.*, 1993; Meselson *et al.*, 1994) and possibly many more died (Guillemin, 2002). Exposure rates in the 2001 bioterrorist anthrax letter occurrences in the United States are unknown, although it appears likely that the 22 clinical cases (11 inhalational [5 deaths] and 11 cutaneous) constituted a small fraction of those exposed. The extensive use of antibiotics for prophylaxis is also likely to have played an influence on the final case rate (Jernigan *et al.*, 2001; Inglesby *et al.*, 2002). This review focused on the pathogenesis, etiology and possible preventive intervention to mitigate the reemergence of anthrax.

MATERIALS AND METHODS

The literature search for this article was done on PubMed Central, Google Scholar and Medline using keywords: pathogenesis, clinical features of *B. anthracis*, anthrax, human, animal and zoonosis. Articles search was conducted between June and August 2023 and articles that met the aim of this study were reviewed. Such articles were in form of clinical reports, cohort studies, reviews, case studies and editorials.

RESULTS AND DISCUSSION

Epidemiology of Anthrax in Africa: Anthrax is widely distributed in Africa. The geographical distribution of *B. anthracis* in African is as shown in Figure 1. Confirmed records of *B. anthracis* are as denoted in color blue.

Prevalence: The first known case of anthrax in sub-Saharan Africa was reported at the turn of the 20th century, with cases appearing in nations like South Africa, Zimbabwe and Kenya. In Africa, anthrax is spread through humans, animals, wildlife and the environment.

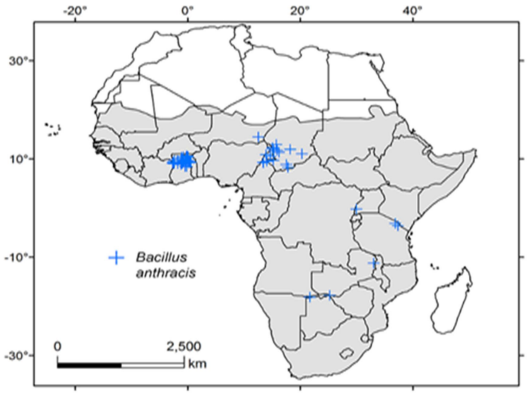

Figure 1: Occurrence points and calibration areas of *Bacillus anthracis* in Africa, blue indicates the endemic regions (Romero-Alvarez *et al.,* 2020)

As a result, the One Health Concept had been used to the fight against anthrax. Anthrax is a disease with endemic distribution in Africa and Asia, but it only manifests itself internationally in sporadic, low-incidence episodes in affluent countries, according to the World Health Organization (Badri *et al.*, 2022).

Ghana has been reported to have high rate of human anthrax associated with high case-fatality rate (CFR). One study reported that nearly 1,000 persons died from anthrax in Ghana between 1980 – 2000. Furthermore, severe cases of human anthrax and resulting deaths have been reported across northern Ghana from 2005 – 2016 (Blackburn *et al.*, 2021).

Anthrax outbreaks recently occurred in the Upper East Regions of Talensi and Binduri in June 2023. In May 20, 2023, four cattle and twenty sheep died according to government officials. It was anticipated that 100 people would consume meat from diseased animals, and 11 people had cutaneous sores on their hands or faces. This outbreak has a direct correlation to mortality. Because these animals act as disease reservoirs, anyone who came into touch with livestock, including cattle, sheep, and goats, or the products they produce, ran the risk of contracting anthrax. The disease can spread via the skin, gastrointestinal tract and respiratory system, to name a few routes (Osei, 2023; Welsing**,** 2023).

The Federal Ministry of Agriculture and Rural Development (FMARD) of Nigeria reported a case of the anthrax disease in a mixed livestock farm in the Niger State. This was the first animal case to be reported in Nigeria since the West Africa outbreak started in Ghana in June 2023. In this farm, there were eight recorded sudden livestock deaths on July 13, 2023. Furthermore, it was noted that the dead animals had been bleeding from exterior orifices without blood clotting (NCDC, 2023)

The Arusha region in Tanzania was reported to have the highest incidence of anthrax in human and the next is Kilimanjaro region from the result of a 4-year studies. Again, from the period of 2006 -2016, there was a record of 330 human anthrax cases in the two regions. Also, a great percentage of both wildlife and animal samples from the regions were found to harbour anthrax (Mwakapeje *et al.*, 2018).

Lesotho recorded three outbreaks of anthrax in Maseru area in 2019, about 106 cow and 24 other livestock were affected. This also resulted to a number of locals been affected after the consumption of beef that has been affected by *B. anthrax*. The quick intervention of the government of Lesotho which include quarantine and restriction of movement of cattle, disinfection of affected areas, vaccination of animals and the properly disposal of affected animals were rapidly embarked on which led to the curb of the spread (NICD, 2019).

The investigation of Hang'ombe and others during a suspected outbreak of anthrax in Zambia in the year 2011 showed that humans, hippopotamus and soil samples screened by culture and PCR methods indicated that 30.4% of the samples were culture-positive. Also, the isolates were resistant to vancomycin they showed 100% susceptibility to the penicillin (Hang'ombe *et al.*, 2012).

Kenya reported a sharp increase in livestock anthrax cases from 2005 to 2020 with only 12% of the sub-counties (decentralised administrative units used by Kenyan county governments to facilitate service provision) accounting for almost a third of the livestock cases (Ndolo *et al.*, 2022).

Mode of transmission: The vegetative forms of *B. anthracis* start to produce spores when the environment is unfavourable for their growth

and multiplication. *B. anthracis* only exists in the vegetative form inside the host, which grow and finally kill the host (WHO, 2008). Availability of free oxygen is necessary for sporulation of this organism, under natural environment; the infected host's has low oxygen therefore the vegetative cycles take place. After leaving the host, sporulation starts when exposed to air and the spore forms are practically the only phase present in the environment (Figure 2).

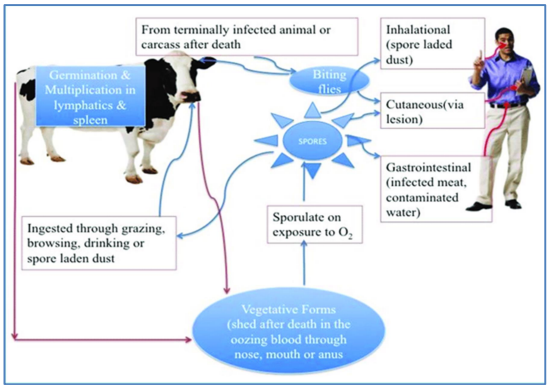

Figure 2: Transmission of anthrax infection (Mwakapeje, 2019)

Anthrax is mostly acquired through the inhalation of spores from the environment. A percentage of the bacteria that the dying or dead animal released into the environment are located typically on the soil beneath the carcass, they sporulate and are prepared to be ingested by other animals (Mwakapeje, 2019). Any time between a few minutes and many decades could pass before they are transmitted into a new host (Figure 2).

Spores Formation by *Bacillus anthracis*: Two gram-positive bacteria that produce endospores are *Clostridium* and *Bacillus*. In reaction to food deficiency, the endospores are created using a different developmental cascade.

Vegetative metabolism is reduced during sporulation and a number of alternative sigma factors are successively produced and activated to regulate the production of mRNAs involved in spore formation. Mature spores have a highly organized structure and are not metabolically active (Liu *et al.*, 2004). Even in extreme environmental circumstances, its structure offers the protection needed for long-term survival. Small molecules, frequently nutrients and/or ions, are sensed in the context of watery environments, which triggers spore germination, outgrowth and the start of a vegetative cycle. When connected with the host cells that engulf them, *B. anthracis* spores recognize certain signals offered by the local environment of a mammalian host and quickly germinate.

Routes of Exposure to Anthrax

Inhalation: Anthrax can be contracted by breathing in anthrax spores, people who work in wool mills — as well as slaughterhouse and tannery workers — may inhale spores from infected animals that lead to several respiratory issues. Inhalation anthrax is called woolsorter's disease (CDC, 2020).

Injection: Injection anthrax can infect heroin users. Anthrax injections can infect muscles or tissues deep beneath the epidermis (CDC, 2020).

Cutaneous (skin): The most typical and non-lethal type of anthrax is cutaneous. This occurs through penetration of microorganisms to the body through skin wound. Veterinarians and others who work with animal wool, hides, or hair are the most vulnerable (CDC, 2020).

Gastrointestinal: Gastrointestinal anthrax can affect people who consume raw or undercooked meat from infected animals. In developing countries where low or no emphasis are laid on medical examination and immunization of animals before slaughtering of livestock, infected animals could be slaughtered and consumed by people who consume raw or undercooked meat. The bacteria affect the oesophagus, throat, stomach and intestines of the infected animal (CDC, 2020). Because farmers in developed nations regularly immunize their cattle against anthrax and spot sick animals before butchering them, this is a rare occurrence.

Economic Impacts: Anthrax outbreak has a significant economic impact on the farmers. They are devastated by the death of cattle due to anthrax and it reduces their productivity. Control of the outbreak which include disinfection and formal destruction and disposal of corpses and byproducts were economically unsustainable. Purchase of new stock of animals after the outbreak and adherence to strict observer of quarantine protocols to curb the spread of the disease to the new cattle is highly costly. Farmers' and slaughterhouse workers' health is in severe jeopardy. A result of recent analysis of human anthrax cases in Ghana suggested that up to 35% of cases might result in fatalities (Al-Mustapha *et al*., 2023). This impact on the food security due to drastic reduction in the population of the cattle and other products due to death and poor reproduction.

Pattering to the Federal Government of Nigeria, the cost of carrying out surveillance, public health, and control measures contribute to the anthrax epidemic's financial burden. The Nigerian Veterinary Research Institute, the national reference laboratory, made an official determination of anthrax (bacterial culture) in Nigeria by July 2023 which has a lot of cost implication (Al-Mustapha *et al*., 2023).

Also, when examining a one health concept, the environment (air, water and soil) and other members of the human population are also put at danger if the disease is not quickly and adequately attended to and curb as a matter of urgency.

Clinical Diagnosis of Anthrax

Basic check: Diagnosis of anthrax requires a history of exposure to infected animals or materials, occupational exposure and residing in an endemic location. An inconspicuous, pruritic papule with vesicles and oedema, commonly on an exposed portion of the body is cause for concern. Gram-positive encapsulated bacilli from the lesion and/or positive culture for *B. anthracis* from the lesion and/or positive specialized tests confirms the clinical diagnosis (Doganay *et al*., 2023).

Differential diagnosis: The differential diagnosis of anthrax irritation includes a broad range of infectious and non-infectious diseases, such as vaccinia, orf, rickettsial infections, cowpox, ulceroglandular tularaemia, syphilitic chancre, plague, glanders, erysipelas, ulcer (especially tropical), arachnid bites and boil (early lesion), ecthyma gangrenosum or herpes, rat-bite fever, and leishmaniasis (Lewis-Jones *et al.,* 1993; WHO, 2008). The diagnosis may be assisted by the patient's activity, pain and the general lack of pus and typical anthrax oedema in these medical conditions (WHO, 2008). Once assumed to be anthrax in animals, the Rift Valley Fever outbreak actually affected a significant number of people. The differential diagnosis should include vision cellulitis, dacryocystitis, and deep tissue infection of the neck in cases of severe anthrax lesions including the neck, anterior chest wall, and face (Gibson, 2020). In the differential diagnosis of severe types of cutaneous anthrax, necrotizing soft tissue infections, notably Group A streptococcal infections and gas gangrene, as well as severe staphylococcal cellulitis, should be evaluated (Doganay *et al*., 2023). Gas and abscess formation are not seen in cutaneous anthrax patients. Only when the lesion is contaminated with other germs, such as streptococci or staphylococci, does an abscess occur.

Clinical tests: The rapid hand-held, on-site, immunochromatographic detection and diagnostic devices that have been developed can be used in the diagnosis of anthrax (Muller *et al*., 2015). In the case of a retrospective diagnosis of anthrax, serology can be supportive. Purified protective antigens and lethal factors are available commercially to aid the diagnosis.

WHO (2008) discovered seroconversion in 17 of 38(44.7%) patients with bacteriologically proven cutaneous anthrax, as well as five patients in whose bacteriological verification failed. The proportion of seroconverters (71%) was substantially higher among 14 14 people who had their matched sera tested than in the other 24(29%) people (Yagupsky *et al*., 2019). Likewise, seroconversion was identified in only 5 of 21(24%) individuals whose blood

was drawn 7 days after the first appearance of lesions, compared to 15(83%) of the 18 people whose blood was drawn 8 days after the first appearance of lesions (Yagupsky *et al.*, 2019). The 21 cases of bacteriologically confirmed anthrax and the 19 additional cases of anthrax that were clinically diagnosed were not able to seroconvert, which was taken to mean that treatment given early on in the course of the infection prevented the production of enough antigen to trigger a detectable antibody response (Jefferson *et al.*, 1998). Early antibiotic treatment following a known challenge with *B. anthracis* spores eliminated a detectable antibody response, according to studies in non-human primates (Friedlander *et al.*, 1993). Negative results should be carefully evaluated in light of the entire patient's history.

As a result of the 2001 anthrax letter mailings in the USA, 16 people with confirmed or suspected cutaneous or inhalation anthrax as well as one laboratory worker with laboratory-acquired cutaneous anthrax were all subjected to sera analysis (Quinn *et al.*, 2004). Anti-PA (anti-protective antigen) IgG was found 11 – 22 days (15 – 28 days) after the beginning of symptoms (15 – 28 days) in 6 individuals who survived inhalation anthrax (WHO, 2008). One patient with a laboratory-acquired illness and 10 of the 11 patients with cutaneous anthrax connected with bioterrorism had anti-PA IgG detected in their blood. Anti-PA IgG was found in these cutaneous instances 12 days after the start of symptoms (approximately 24 days after exposure). On day 18 following the beginning of symptoms, one patient with cutaneous anthrax was seronegative; nevertheless, on day 34, measurable anti-PA IgG was present. Anti-PA IgG was not found in one cutaneous anthrax patient 4, 5, 47, or 253 days after the beginning of symptoms. All 6 inhalation anthrax survivors and 7 out of 11 people with cutaneous anthrax had anti-PA IgG detectable 8–16 months after the onset of symptoms. Serum toxin-neutralizing activity and anti-PA IgG levels were positively correlated (WHO, 2008).

With the particular advantage over other diagnostic tests of being able to detect anthrax-specific antigens in tissues regardless of treatment, immunohistochemistry, noted by Fritz *et al.* (1995) in experimental inhalation of anthrax in rhesus monkeys, proved to be an invaluable aid to confirmation of the diagnosis in the anthrax letter events in the USA in 2001. This method had to be used on a skin biopsy collected up to 9 days after therapy had started in order to make a conclusive diagnosis retrospectively in one patient. The procedure is now restricted to specialized labs having access to the right particular antibodies.

In the Russian Federation, a skin test using AnthraxinT, which was initially approved in the former Soviet Union in 1962, is frequently used for the assessment of vaccines as well as the retrospective diagnosis of human and animal anthrax (WHO, 2008). This is a synthetic, heat-stable protein, polysaccharide and nucleic acid complex made from the oedematous fluid of animals given the STI-1 vaccination or the Zenkowsky strains of *B. anthracis* (WHO, 2008). It contains neither capsular nor toxigenic components. It's sterilized using an autoclave. The test requires injecting 0.1 ml of AnthraxinT intradermal and it is still used in the Russian Federation (WHO, 2008). Erythema of less than 8 mm and induration that lasts for at least 48 hours are considered positive test results (Shlyakhov *et al.*, 1997).

Up to 72% of instances with this delayed-type hypersensitivity were apparently able to be diagnosed with anthrax retrospectively, 31 years after the main infection (Shlyakhov *et al.*, 1997). This delayed-type hypersensitivity is thought to reflect anthrax cell-mediated immunity. It was successfully applied in a backward study of a number of incidents that took place in a Swiss spinning factory where synthetic fibres were mixed with Pakistani goat hair (Pfisterer, 1990). Similar to the Ascoli test antigen, the nature of the anthrax determines the diagnostic accuracy of AnthraxinT, not the specificity of the implicated antigens. In clinical samples, PCR is currently recognised as a sensitive technique for locating anthrax-specific DNA (Ellerbrok *et al.*, 2002; Shieh *et al.*, 2003).

Prevention of Anthrax: It is imperative that livestock be vaccinated against anthrax every year. Methods for disinfecting the farm location's, transportation vehicles, other belongings, and premises should be prescribed by the state veterinarian. Animals suspected of contracting anthrax should be buried, and people should stay away from the carcasses. Reporting suspected instances to the state veterinarian or animal health technician closest to you is the first step in handling them (NCDC, 2023).

To avoid contaminating humans, animals that animal that died from unidentified causes should never be eaten nor have any of their parts – such as skin or horns removed for any purpose. The corpses should be avoided and they should be buried according to the proper protocol. Avoid coming into close touch with an animal carcass that appears to have perished from anthrax. Even if they are not sick, farmers and slaughterhouse employees in the affected area should be sent to the closest medical facility for assessment and treatment (NCDC, 2023).

Conclusion: Anthrax, a bacterial disease caused by *B. anthracis*, a soil-borne bacterium infects predominantly grazing animals which could prose serious threat to animal, environmental and human health. Medical examination and certification of animals before slaughter as well as routine immunization and proper disposal of dead animals will go a long way in preventing outbreaks among animals and protect public health.

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