

Review Article

Study on status, Zoonoses, Biowarfare, Economic and public health importance of anthrax: Review

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Abstract

Anthrax is a serious infectious disease caused by a bacterium called *Bacillus anthracis*. It can affect humans and animals, especially grazing livestock such as cattle, sheep, and goats. Anthrax spores are very resistant and can survive in the environment for a long time. People can get anthrax from direct contact with infected animals or animal products, or from inhaling or ingesting anthrax spores. There are four types of anthrax infection in humans: cutaneous, gastrointestinal, inhalation, and injection. Anthrax is also a potential bioterrorism agent, as it can be easily produced and dispersed as a powder or a liquid. Anthrax is still a neglected global health challenge that requires constant vigilance and collaboration among various stakeholders. As new technologies and strategies emerge, the current status and trends in the prophylaxis and management of anthrax disease need to be updated and evaluated regularly. The disease poses a significant public health and economic burden in the countries, especially in rural areas where livestock is the main source of livelihood. Since the disease is endemic to Ethiopia awareness of its status, economic, zoonoses, and public health significance must be addressed. Anthrax is a disease that requires constant vigilance and preparedness, as it poses a threat to both natural and deliberate outbreaks, enhancing surveillance, outbreak response, and diagnostics can help prevent and control anthrax cases in animals and humans, and reduce the social and economic consequences of this disease. Therefore, the objectives of this paper are to review the status, zoonoses, biowarfare, and economic and public health importance of anthrax.

Abbreviations

BW: Body Weight; CDC: Centers of Disease Control and Prevention; CSF: Cerebrospinal Fluid; DACA: Drug Administration and Control Authority of Ethiopia; EF: Edema Factor; GP: Gram-Positive; KAP: Knowledge, Attitude and Practice; LD50: Lethal Dose; PA: Protective Antigen; PH: Power of Hydrogen; Sc: Subcutaneous; RT-PCR: Real-Time Polymerase Chain Reaction

Introduction

Anthrax is an infectious disease that affects both animals and humans [1]. It is caused by a bacterium called *Bacillus anthracis*, which can form spores that survive in the soil for a long time [2]. Anthrax can infect people who come in contact

with sick animals or their products, such as meat, wool or hide. Anthrax can also be used as a biological weapon by releasing spores into the air or contaminating food or water [3]. There are four types of anthrax infection in humans: cutaneous, gastrointestinal, inhalation, and injection. Cutaneous anthrax occurs when spores enter the skin through a cut or wound [4]. It causes a sore with a black center, fever, and swollen lymph nodes. Gastrointestinal anthrax occurs when spores are swallowed with contaminated food or water [5]. It causes nausea, vomiting, abdominal pain, diarrhea, and bleeding. Inhalation anthrax occurs when spores are breathed in [6]. It causes flu-like symptoms, chest pain, shortness of breath, and coughing up blood [7]. Injection anthrax occurs when spores are injected into the body with illegal drugs [8]. It causes redness at the injection site, organ failure, and meningitis [9].

Anthrax can be diagnosed by testing blood, skin, stool, or spinal fluid samples for the presence of the bacteria or its toxins [10]. Anthrax can be treated with antibiotics and antitoxins if started early enough. Anthrax can be prevented by vaccinating animals and people at risk of exposure, avoiding contact with infected animals or their products, and cooking meat thoroughly [11]. Anthrax is a serious infectious disease that affects both humans and animals. It is caused by a type of bacteria called *Bacillus anthracis*, which can form spores that can survive in harsh conditions for a long time. Anthrax spores can enter the body through the skin, lungs, or digestive system, and cause different types of infections depending on the route of exposure. Anthrax is not contagious, which means it cannot spread from person to person like a cold or flu. Anthrax is most common in agricultural regions where animals graze on contaminated soil or plants. People who work with animals or animal products, such as farmers, veterinarians, or wool workers, are at higher risk of getting anthrax [12]. Anthrax can also be used as a biological weapon by terrorists who may release anthrax spores into the air or contaminate food or water supplies [13]. Anthrax can be prevented by vaccinating animals and people who are at high risk of exposure [14]. Anthrax can be treated with antibiotics if it is diagnosed early. However, anthrax can be fatal if left untreated, especially in inhalation and gastrointestinal forms [15]. Therefore, it is important to seek medical attention immediately if you suspect you have been exposed to anthrax or have symptoms of anthrax infection. It is also endemic in Ethiopia [16]. The natural reservoir for *B. anthracis* is soil, and the predominant hosts are herbivores (cattle, sheep, goats, horses, pigs, and others) that acquire infection from consuming contaminated soil or feed. Anthrax spores can persist in soil for years and are resistant to unfavorable (harsh) environments and some disinfectants [17]. Anthrax *bacillus* produces high levels of two toxins: Edema toxin and lethal toxin. The severity of anthrax disease depends on the route of infection and the presence of complications, with case fatality ranging from 5% to 95% if untreated [18]. Depending on the site of infection, anthrax can occur in a cutaneous, gastrointestinal, or inhalational form [19]. Anthrax is generally a zoonotic disease. Humans become infected through contact with infected animals and animal products through several mechanisms, such as: contact with infected animal tissues, ingestion of contaminated, undercooked meat from infected animals, and inhalation of infectious aerosols [20]. Anthrax has a long history of being used as a bioweapon, dating back to ancient times [3]. Person-to-person transmission of *B. anthracis* does not occur with Gastrointestinal (GI) or inhalational anthrax but has been reported rarely with cutaneous anthrax [18]. Since the disease is endemic to Ethiopia awareness of its economic, zoonoses and public health significance must be addressed. Therefore, the objectives of this paper are to review the status, zoonoses, biowarfare, economic and public health importance of anthrax.

Literature review

Etiology and form of anthrax

Anthrax is a serious infectious disease caused by bacteria called *Bacillus anthracis*. These bacteria can form spores, which

are dormant and resistant forms that can survive in harsh conditions for long periods of time. When the spores enter the body of a susceptible host, such as a human or an animal, they can germinate and multiply, producing toxins that damage the tissues and organs [21]. *Bacillus anthracis* is a gram-positive, rod-shaped bacterium, vegetative bacilli, and spore-forming bacteria. The vegetative bacilli and the spore are the two forms that *B. anthracis* may exhibit. They are each 1-1.2 μ m wide and 3-5 μ m long. Anthrax that found all over the world, and has 1,200 different strains [22].

Spore and vegetative form

Anthrax is a serious infectious disease caused by the bacterium *Bacillus anthracis*. This bacterium can exist in two forms: vegetative and spore [23]. The vegetative form is the active form that grows and reproduces inside the host animal or human, releasing toxins that cause the symptoms of anthrax. The spore form is the dormant form that forms when the vegetative form is exposed to oxygen, such as when an infected animal dies and its body fluids dry up [24]. The spores are very resistant to harsh environmental conditions and can survive for years in the soil or other materials. The spores can infect new hosts when they are inhaled, ingested, or come into contact with a break in the skin. The vegetative bacilli and the spore form of *B. anthracis* are its two forms [25]. When conditions are unfavorable for bacilli development and multiplication, they frequently produce spores. The spore forms are noticeably resilient to biological extremes of heat, cold, pH, desiccation, chemicals, irradiation, and other similar unfavorable circumstances [26]. The spores germinate to generate vegetative forms inside the infected host. The evidence suggests that although *B. anthracis*' vegetative forms readily grow and multiply on or in typical laboratory nutrient agars or broths, they are more "fragile" than the vegetative forms of other *Bacillus* species, dying more suddenly in simple environments like water or milk, and being more dependent on sporulation for species survival [27]. And that proliferates, ultimately destroying the host. Some of the bacilli that the dying or dead animal discharged into the environment (often the soil beneath the body) sporulate [28].

The environmental variables that they are exposed to have a complicated impact on the rate and extent of sporulation by vegetative cells shed from sick and deceased animals. The main affecting factors include temperature, pH, oxygen availability, and the presence of certain cat ions like Mn^{++} . If the right circumstances are met, such as a temperature range of approximately 80 °C to 45 °C, a pH range of about 5 to 9, relative humidity of more than 95%, and the existence of sufficient nutrients, spores will begin to grow outside of an animal. How many further rounds of germination, multiplication, and re-sporulation are present and available for other animals to consume [29]?

Forms of the disease in humans: Depending on how the spores entered the system [30]. One of the following four manifestations of the illness occurs: cutaneous, injection, inhalational, or gastrointestinal. The latter two types, gastrointestinal and inhalational anthrax, are the most

dangerous and uncommon. Up to 95% of anthrax infections worldwide are cutaneous, and occupational exposure is the predominant cause of these infections [17]. Skin-like form: Cuts or abrasions in the epidermal layer of the skin cause sores that allow immediate endospores to enter the host body and cause cutaneous anthrax. Initial symptoms of cutaneous anthrax include the development of papules on the skin. Eventually, a black eschar covers their vesicles, which burst and produce a depressed ulcerated region [31]. Gastrointestinal form: Similar to cutaneous anthrax, gastrointestinal anthrax can spread to people through the consumption of raw or undercooked food. The most common symptoms of gastrointestinal anthrax include nausea, stomach discomfort, bloody diarrhea, and ulcerative lesions in the GI tract [32]. Inhalational pulmonary anthrax is arguably the most deadly kind. For those who have inhalational pulmonary anthrax, inhalation is how endospores initially enter the body from the lung. Without prompt care, a patient who has had a septic shock for two or three days might pass away within 24 to 36 hours. In fact, people who have been diagnosed with anthrax inhalation have fatality rates that are almost 100%. [17]. Injection anthrax: This is a recently identified route of anthrax infection and has been reported only in Europe. Infection develops through injecting illegal drugs. Signs and symptoms include redness at the area of injection, multiple organ failure, and meningitis. There are three main forms of anthrax: cutaneous, inhalational, and gastrointestinal. Each form has different symptoms and requires different treatment. *Cutaneous anthrax* is the most common and least dangerous form of anthrax [15]. It occurs when the bacteria enter a cut or wound on the skin. The infection causes a painless, black sore that may be surrounded by swelling. Cutaneous anthrax can be treated with antibiotics if diagnosed early [33]. *Inhalational anthrax* is the most deadly form of anthrax and it occurs when the bacteria are inhaled into the lungs. The infection causes flu-like symptoms at first, followed by severe breathing problems and shock [34]. Inhalational anthrax can be fatal even with treatment [35]. *Gastrointestinal anthrax* is the rarest form of anthrax and it occurs when the bacteria are ingested through contaminated food or water. The infection causes nausea, vomiting, diarrhea, and abdominal pain [36]. Gastrointestinal anthrax can also be treated with antibiotics if diagnosed early.

Pathogenesis

Pathogenesis of the disease related to the lethal anthrax toxins. Anthrax spores germinate at the site of entry into tissue (mucosa of the throat, gastrointestinal tract, lung, and skin) and the growth of the vegetative organisms results in the formulation of gelatinous and congestion [37]. If the strain of organisms is highly virulent, a capsule will be formed and protects the organisms from phagocytosis and lysis [38]. The bacteria moved to the local lymph node by motile phagocytosis. After proliferation in this site, the bacilli pass via the lymphatic system into the bloodstream and septicemia with a massive invasion of all lethal toxins, namely edema, tissue damage death resulting from shock and renal failure, and terminal anorexia mediated by the central nervous system [39]. Anthrax one time it was held that death from anthrax was due to

capillary blockage, hypoxia, and depletion of nutrients by the exceedingly large numbers of bacilli [40]. Anthrax toxin is a mixture of three protein components: -These Protective Antigen (PA), Edema Factor (EF), and Lethal Factor (LF) [41]. At one time it was held that death from anthrax was due to capillary blockage, hypoxia, and depletion of nutrients by the exceedingly large numbers of bacilli. Subsequently, it was shown that death is attributable to a toxin [42]. The main virulence factors of *B. anthracis* are the anthrax toxins and the capsule. The anthrax toxins consist of three proteins: Protective Antigen (PA), Lethal Factor (LF), and Edema Factor (EF). PA binds to specific receptors on host cells and facilitates the entry of LF and EF into the cytoplasm. LF is a zinc-dependent metalloprotease that cleaves and inactivates Mitogen-Activated Protein Kinase Kinases (MAPKKs), disrupting cell signaling and causing apoptosis [43,44]. EF is a calmodulin-dependent adenylate cyclase that elevates intracellular cyclic AMP levels, leading to edema, impaired phagocytosis, and immunosuppression. The capsule is composed of poly-D-glutamic acid and protects the bacterium from phagocytosis by host macrophages. The genes encoding the anthrax toxins and the capsule are located on two plasmids, pXO1, and pXO2, respectively [45,46]. The clinical manifestations of anthrax depend on the route of exposure and the host's immune response [47].

Risk factors

Environment and Other Influencing factor: There is little dispute that anthrax is a seasonal disease; its incidence in any one place is related to temperature, rains, or drought; however, examination of the literature shows that the conditions which predispose to outbreaks differ widely from location to location [48]. Climate probably acts directly or indirectly by influencing the way in which an animal comes into contact with the spores (for example, grazing closer to the soil in dry periods when the grass is short or sparse, or movement of herds to restricted sites when water becomes scarce), or by affecting the general state of health of the hosts and thereby affecting their level of resistance to infection [49].

Host range and susceptibility: Anthrax is primarily a disease of herbivores. However, reports of its occurrence in dogs scavenging anthrax carcasses and in carnivorous animals in zoological gardens and wildlife sanctuaries or parks are not entirely uncommon, though outbreaks affecting large numbers of carnivorous animals are very rare [50]. Animals generally acquire anthrax by ingestion of spores, and some sort of lesion is necessary for the establishment of infection many factors influencing infectivity, such as the strain of *B.anthraxis*, the route of infection, the species, breed or strain, and status of health of the animal [24].

The virulence factor of *B.anthraxis*: The lethality of the anthrax disease is due to the bacterium's two principal virulence factors: the poly-D-glutamic acid capsule, which protects the bacterium from phagocytosis by host neutrophils, and the tripartite protein toxin, called anthrax toxin [51]. Anthrax toxin is a mixture of three protein components: Protective Antigen (PA), Edema Factor (EF), and Lethal Factor (LF). PA plus LF produces a lethal toxin, and PA plus EF produces an edema



toxin. These toxins cause death and tissue swelling (edema), respectively [6,52]. According to the currently accepted model, PA binds to receptors on the host's cells and is activated by a host protease which cleaves off a 20 kDa piece, thereby exposing a secondary receptor site for which LF and EF compete to bind. The PA+LF or PA+EF are then internalized and the LF and EF are released into the host cell cytosol LF appears to be a Calcium and Zinc dependent metalloenzyme endopeptidase [6,53]. The endothelial cell linings of the capillary network may also be susceptible to lethal toxin and the resulting histologically visible necrosis of lymphatic elements and blood vessel walls is presumably responsible for systemic release of the bacilli and for the characteristic terminal hemorrhage from the nose, mouth and anus of the victim [54].

Some of the risk factors for human anthrax include: Working with animals or animal products that may be infected with anthrax, such as wool, hides, or hair [17]. Traveling to areas where anthrax is endemic or where outbreaks have occurred, such as parts of Africa, Asia, and South America, and handling or receiving mail or packages that may contain anthrax spores, such as letters or parcels that have been tampered with or sent by terrorists [55]. Eating undercooked meat from animals that may have been infected with anthrax. Having a weakened immune system due to diseases such as HIV/AIDS or cancer, or taking medications that suppress the immune system [56]. Anthrax can be prevented by avoiding contact with potential sources of infection, wearing protective clothing and equipment when handling animals or animal products, and getting vaccinated if you are at high risk of exposure [57].

Humans have an increased risk of getting anthrax if they:

- Work with anthrax in a laboratory
- Work with livestock as a veterinarian (less likely in the United States)
- Handle animal skins from areas where anthrax is common
- Travel to areas where anthrax is common
- Inject illegal drugs- Injection anthrax: This is a recently identified route of anthrax infection and has been reported only in Europe. Infection develops through injecting illegal drugs [58].

Epidemiology and transmission

The epidemiology of anthrax varies by region and animal reservoir [59]. Anthrax is more common in areas where livestock are not vaccinated and where animal products are not properly handled or disposed of [60]. Anthrax outbreaks can occur sporadically or seasonally, depending on environmental factors that affect spore survival and exposure [35]. Anthrax is rare in developed countries but still occurs in parts of Africa, Asia, and South America. Anthrax spores can be found on all continents, even Antarctica [61]. The disease outbreak is endemic in Ethiopia as though it has sporadic nature as

well as seasonal. Disease outbreak occurs irregularly and is commonly associated with neutral or alkaline, calcareous soils where the spores revert to the vegetative form and multiply to infectious levels if environmental conditions of soil, moisture, temperature, and nutrition are optimal [16,62]. The disease has also killed 15 Cattle, during the first outbreak in the Fentale district of Oromia region, some 200km from the capital Addis Ababa [10,63]. There is an outbreak in the Afar region of Ethiopia [64]. Transmission of anthrax is the process of transferring anthrax spores from one source to another, either intentionally or unintentionally [65]. Anthrax is a serious infectious disease caused by the bacterium *Bacillus anthracis*, which can form spores that are resistant to harsh environmental conditions and can survive for long periods of time [2]. Anthrax commonly infects wild and domesticated herbivorous mammals that ingest or inhale the spores while grazing, especially grazing livestock such as cattle, sheep, and goats. Ingestion is thought to be the most common route by which herbivores contract anthrax. Carnivores living in the same environment may become infected by consuming infected animals [66]. Diseased animals can spread anthrax to humans, either by direct contact (e.g., inoculation of infected blood to broken skin) or by consumption of a diseased animal's flesh [50].

Anthrax spores can enter the body through inhalation, ingestion, or skin contact, causing different types of anthrax infections: cutaneous (skin), inhalation (lung), gastrointestinal (digestive), or injection (bloodstream) [5]. Anthrax is not contagious from person to person, except in rare cases of cutaneous anthrax where the skin lesions may be infectious. Anthrax spores can be found naturally in soil and animal products, such as wool, hair, hides, and bones [67]. People who work with these materials are at risk of exposure to anthrax spores. Anthrax spores can also be used as a biological weapon, as they can be easily dispersed in the air or contaminated food or water sources [67,68]. It can affect humans and animals, especially livestock and Anthrax can be transmitted through contact with infected animals or their products, such as wool, hide, or meat and it can also be used as a bioterrorism weapon by releasing spores into the air [15]. There are three main forms of anthrax in humans, depending on the route of infection: cutaneous (skin), inhalation, and gastrointestinal [5]. Cutaneous anthrax occurs when spores enter a cut or abrasion on the skin and cause a painless black sore that can be treated with antibiotics. Inhalation anthrax occurs when spores are breathed in and it causes flu-like symptoms that progress to severe breathing problems and shock. It is often fatal if not treated early [69]. Gastrointestinal anthrax occurs when spores are ingested with contaminated food and it causes nausea, vomiting, diarrhea, and abdominal pain [6].

The current status of anthrax in Ethiopia

Anthrax is a neglected tropical disease that affects humans, livestock, and wildlife worldwide. It is caused by a soil-borne spore-forming bacterium called *Bacillus anthracis* [14]. According to a recent review article, anthrax disease is mostly found in the developing world, where it causes significant mortality and



morbidity in humans and livestock. However, anthrax can also pose a threat to developed countries, as demonstrated by the 2001 anthrax attacks in the United States that killed five people and infected 17 others [70]. Therefore, effective surveillance, prevention, and treatment of anthrax are essential for public health and national security. The Centers for Disease Control and Prevention (CDC) maintains anthrax surveillance data that are published weekly and annually, and Anthrax is a reportable disease in all 56 U.S. states and territories and a nationally notifiable condition that requires immediate notification to CDC in certain circumstances [71]. CDC also provides guidance and resources for healthcare providers and public health practitioners on how to diagnose, treat, and prevent anthrax infections [72].

Anthrax is still a global health challenge that requires constant vigilance and collaboration among various stakeholders. As new technologies and strategies emerge, the current status and trends in the prophylaxis and management of anthrax disease need to be updated and evaluated regularly [73]. In Ethiopia, anthrax is a reportable disease and is assumed to be endemic, although laboratory confirmation has not been routinely performed until recently. The disease poses a significant public health and economic burden in the country, especially in rural areas where livestock is the main source of livelihood [74,75]. The prevalence of anthrax in Ethiopia is not well documented, but several outbreaks have been reported in different regions over the years. For example, between 2018 and 2019, two outbreaks were confirmed by real-time polymerase chain reaction (qPCR) in the Amhara region, involving 49 cattle and 40 human cases (two fatal) in Wag Hamra zone, and two livestock and 18 human cases (one fatal) in South Gondar zone. Another study used a machine learning algorithm to develop a predictive map of anthrax suitability in the Amhara region, based on 128 georeferenced confirmed outbreak reports of anthrax in livestock and 22 environmental variables. The study found that the central and southern parts of the region were more suitable for *Bacillus anthracis* than the northern parts and that variables such as annual precipitation, precipitation of warmest quarter, precipitation of wettest month, cattle density, sheep density, annual maximum temperature, altitude/elevation, and sand content were the most important predictors [76].

The Knowledge, Attitude, and Practice (KAP) of the community towards anthrax is also an important factor that influences the transmission and control of the disease. A cross-sectional survey conducted in 2019 among 422 households in four districts of the Amhara region revealed that only 38.6% of the respondents had heard about anthrax, and only 18.7% knew how it was transmitted. The majority (82.5%) of the respondents did not seek medical care when they had cutaneous lesions suspected to be anthrax, and 41.5% reported consuming meat from animals that died of unknown causes [75,77]. The survey also found that respondents who had formal education, owned livestock, and had previous exposure to anthrax had better KAP scores than those who did not [75].

These findings suggest that anthrax is a serious but under-recognized health problem in Ethiopia, especially

in the Amhara region [78]. There is a need for improved surveillance, laboratory diagnosis, carcass management, ring vaccination of livestock, training of health professionals, and outreach with livestock owners to prevent and control anthrax outbreaks. Moreover, there is a need for more research on the epidemiology, ecology, and socio-economic impact of anthrax in Ethiopia to inform evidence-based interventions [79].

Vaccination of anthrax

The most widely used vaccine for the prevention of anthrax in animals was developed by Sterne (1937) and he derived a rough variant of virulent *B.anthraxis* from culture on serum agar in an elevated CO₂ atmosphere. This variant, named 34F2, was incapable of forming a capsule and was subsequently found to have lost the pXO₂ plasmid, which codes for capsule formation and also it has become the most widely used strain worldwide for animal anthrax vaccine production [80]. In Central and Eastern Europe, an equivalent pXO₂ derivative, Strain 55, is the active ingredient of the current livestock vaccine [81]. Anthrax is a zoonotic disease that affects both humans and animals [60]. It is caused by a bacterium called *Bacillus anthracis* which can form spores that survive in the environment for long periods. Anthrax can be transmitted through contact with infected animals or their products, such as meat, wool, or hides [39]. Anthrax can cause severe skin lesions, gastrointestinal symptoms, or respiratory failure, depending on the route of exposure [82]. In Ethiopia, anthrax is a reportable disease and is assumed to be endemic, especially in rural areas where livestock farming is common. According to a study by Wassie, et al. 2022, Ethiopia reported the first PCR-confirmed outbreaks of anthrax in the Amhara region in 2018–2019. The outbreaks affected 49 cows and 40 humans, resulting in three human deaths. The study highlighted the need for improved surveillance, laboratory diagnosis, and carcass management to prevent further spread of the disease. One of the most effective ways to prevent anthrax is vaccination of animals and humans at risk. Ethiopia has been using the One Health approach to develop national control and prevention strategies for anthrax and other zoonotic diseases [75,83]. The One Health approach recognizes that human health, animal health, and environmental health are interconnected and require collaboration across sectors and disciplines. Ethiopia aims to improve surveillance, laboratory diagnostic capacity, and vaccine distribution for anthrax as part of its One Health strategy [84]. The vaccination schedule for Ethiopia recommends that livestock animals be vaccinated against anthrax annually. The vaccine is produced by the National Veterinary Institute and distributed by regional livestock agencies. The vaccine is administered subcutaneously or intramuscularly to cattle, sheep, goats, camels, horses, and donkeys. The vaccine provides protection for one year and should be given before the onset of the rainy season when anthrax outbreaks are more likely to occur [85].

The vaccination schedule for Ethiopia also recommends that humans who are at high risk of exposure to anthrax be vaccinated with three doses of Anthrax Vaccine Adsorbed (AVA) [55]. The vaccine is available at designated health facilities and requires a prescription from a physician [86]. The vaccine is

administered intramuscularly in the deltoid muscle of the arm. The first dose is given at any time, followed by a second dose four weeks later, and a third dose six months after the first dose. A booster dose is recommended every year for continued protection [87]. Vaccination of anthrax in Ethiopia is an important public health intervention that can reduce morbidity and mortality from this deadly disease [88]. By implementing a One Health approach that involves coordination and cooperation among human and animal health sectors, Ethiopia can enhance its preparedness and response to anthrax outbreaks and other zoonotic diseases [84].

Zoonotic and public health importance of anthrax

Anthrax is a serious infectious disease caused by the bacterium *Bacillus anthracis*. It can affect humans and animals and can be transmitted from animals to humans through direct contact, inhalation, or ingestion of contaminated animal products [89]. Anthrax is considered a zoonotic disease, meaning that it can spread between animals and humans [90]. The zoonotic importance of anthrax lies in its potential to cause outbreaks of human and animal disease, as well as its potential use as a bioterrorism agent. Anthrax can cause severe and often fatal illness in humans, especially if left untreated. Therefore, it is important to monitor and control anthrax in animal populations, and to prevent human exposure to infected animals or their products. It can also be used as a weapon by deliberately releasing spores into the air or contaminating food or water sources [91].

This could result in widespread infection and death among humans and animals, as well as environmental contamination and economic losses. Therefore, it is important to enhance the preparedness and response capabilities of public health and veterinary authorities and to develop effective vaccines and treatments for anthrax. Anthrax is a serious and deadly infectious disease caused by the gram-positive, rod-shaped bacterium *Bacillus anthracis* [92]. It occurs naturally in soil and affects domestic and wild animals, especially herbivores, around the world. Anthrax is a zoonotic disease, which means it can be transmitted from animals to humans and vice versa [93,94]. Humans usually become infected when butchering and eating contaminated carcasses and come into contact with infected animals or their products and it is primarily an occupational hazard for handlers of processed hides, goat hair, bone products wool, infected wildlife, and abattoir workers by contact with infected meat when contracted [16,94]. Anthrax spores most likely spread as an aerosol and can also be used as a bio-warfare or bio-terrorism agent, therefore; any new case can be assessed with this possibility in mind, particularly but not exclusively in cases of pulmonary anthrax [16]. *B. anthracis* also has a unique capsule which is considered to be a major contributor to its virulence [39]. The capsule enhances the bacterium's ability to evade host defenses, as well as inducing septicemia. New areas of infection in livestock may develop through introducing animal feed containing bone meal. Anthrax is still a significant risk in some countries and outbreaks occasionally occur in humans. In Africa, estimates suggest that each cow with anthrax can result in up to ten human cases

[95]. However, the incidence of anthrax has declined sharply in developed nations [39].

In many countries, cases of anthrax occur infrequently and sporadically, mainly as an occupational hazard among veterinarians, agricultural workers, and workers who process hides, hair and wool, and bone products. Or by inhaling, ingesting, or getting spores in their skin [96]. Anthrax can cause severe illness and death in both humans and animals if left untreated and the bacteria produce powerful toxins that damage the body's tissues and organs [44]. Anthrax is rare in the United States, but more common in some agricultural regions of the world where animals are not routinely vaccinated against it and humans can get anthrax by coming in contact with infected animals or contaminated animal products, such as meat, wool, or hides [91]. There are different types of anthrax depending on how the spores enter the body: cutaneous (through the skin), inhalation (through the lungs), or ingestion (through the mouth) and the symptoms vary according to the type of anthrax, but they usually include fever, chills, swelling, sores, and difficulty breathing. Anthrax is a serious public health threat because it can be used as a bioterrorism weapon and spores can be deliberately released into the air, water, or food supply to cause widespread infection and panic. Anthrax can also affect livestock production and trade, as well as wildlife conservation [97].

However, anthrax is still a major challenge in some parts of the world where animal vaccination programs are not available or effective. Anthrax is a zoonotic disease, which means it can be transmitted from animals to humans and vice versa. It is found naturally in soil and can infect domestic and wild animals, especially herbivores [98]. Anthrax can cause severe illness and death in both animals and humans, depending on the route of exposure, and produce powerful toxins that damage the tissues and organs of the infected host [99]. Anthrax is a global problem that affects agricultural regions of Central and South America, sub-Saharan Africa, central and southwestern Asia, southern and Eastern Europe, and the Caribbean [91]. It is rare in the United States, but sporadic outbreaks do occur in grazing animals such as cattle and deer and it can be prevented by vaccinating animals in areas where the disease is endemic or has occurred in the past [100].

Economic importance

Anthrax is a serious disease that affects both animals and humans. It is caused by a bacterium called *Bacillus anthracis*, which can form spores that survive in harsh conditions for long periods of time [101]. Anthrax can be transmitted through contact with infected animals or their products, such as meat, wool, hides, or bones and anthrax can also be used as a biological weapon by deliberately releasing spores into the air or contaminating food or water sources [13,89]. Anthrax has a significant impact on public health and the economy in many parts of the world, especially in Africa, Asia, and some regions of Europe and America [102]. Anthrax can cause high mortality and morbidity among livestock, resulting in losses of income and food security for farmers and communities, and also can cause severe illness and death in humans, especially if left



untreated or if exposed to large doses of spores [103]. Anthrax is a disease that requires constant vigilance and preparedness, as it poses a threat to both natural and deliberate outbreaks, enhancing surveillance, outbreak response, and diagnostics can help prevent and control anthrax cases in animals and humans, and reduce the social and economic consequences of this disease [104]. Anthrax is a serious infectious disease caused by bacteria that form spores and these spores can survive in harsh conditions for long periods of time and can be used as biological weapons [23]. Anthrax can affect humans and animals, causing severe illness and death. The economic importance of anthrax lies in its impact on public health, agriculture, trade, and security [105].

Public health: Anthrax can be transmitted from animals to humans through contact with infected animals or animal products, inhalation of spores, or ingestion of contaminated food or water [89]. Anthrax can cause skin lesions, respiratory failure, septic shock, and death if not treated promptly with antibiotics. Anthrax outbreaks can also overwhelm health systems and create panic among the population [106].

Agriculture: Anthrax can affect livestock such as cattle, sheep, goats, horses, and pigs. Anthrax can cause high mortality rates among infected animals and reduce their productivity and quality. Anthrax can also contaminate animal products such as meat, milk, wool, and hides. Anthrax outbreaks can result in significant economic losses for farmers and rural communities [107].

Trade: Anthrax can disrupt the trade of animals and animal products across regions and countries. Anthrax can impose trade restrictions and bans on affected areas and products. Anthrax can also damage the reputation and competitiveness of exporters and importers [108]. Anthrax outbreaks can affect the global market and supply chain of animal products.

Security: Anthrax can be used as a weapon of mass destruction by terrorists or rogue states and anthrax can be easily dispersed in the air, water, or food supply and cause widespread casualties and fear [109]. Anthrax can also pose a threat to military personnel and facilities and its attacks can undermine national and international security and stability. Anthrax is a serious disease that affects both animals and humans. It is caused by a bacterium called *Bacillus anthracis*, which can form spores that survive in harsh conditions for long periods of time.

Anthrax has a significant impact on public health and the economy of affected countries. According to the World Health Organization (WHO), anthrax is still endemic in most countries of Africa and Asia, and some parts of Europe and America. Anthrax can cause high mortality rates among livestock, especially cattle, sheep, goats, horses, and pigs. This can result in losses of income and food for farmers and communities. Anthrax can also affect wildlife populations and biodiversity. Anthrax can be prevented and treated with vaccines and antibiotics. However, these measures are not always available or accessible in developing countries, where anthrax outbreaks are more common. Therefore, enhancing surveillance, outbreak

response, and diagnostics is essential to prevent anthrax cases in both animals and humans, and to reduce death, illness, and economic losses associated with anthrax [110].

Biowar fairness of anthrax

Biowarfare is the use of biological agents such as bacteria, viruses, fungi, or toxins as weapons to harm or kill humans, animals, or plants [111]. Anthrax is one of the most likely agents to be used in biowarfare because it is highly lethal, easy to produce and disperse, and can survive for a long time in the environment [112]. Anthrax is caused by the bacterium *Bacillus anthracis*, which forms spores that can infect humans through inhalation, ingestion, or skin contact. The symptoms of anthrax vary depending on the route of exposure, but they usually include fever, chills, headache, cough, chest pain, nausea, vomiting, diarrhea, and skin lesions [113]. Anthrax can be transmitted through contact with infected animals or their products, such as wool, meat, or hides. Anthrax can also be used as a biological weapon, as it was in 2001 in the USA, when letters containing anthrax spores were mailed to several people, causing five deaths and 17 infections. Anthrax can be treated with antibiotics if diagnosed early, but it can be fatal if left untreated [114]. The recent status of biowarfare readiness for anthrax is uncertain. There is no reliable way to detect or verify the presence of anthrax spores in the environment or in potential targets and there is also no effective vaccine or prophylaxis for anthrax that can protect against all strains and routes of exposure. Moreover, there is a risk of accidental or intentional release of anthrax spores from laboratories or stockpiles that could cause outbreaks or epidemics [115]. Therefore, the threat of biowarfare using anthrax remains high and requires constant vigilance and preparedness from the international community [116].

Diagnosis in humans and animals

In 2001, the US Center for Disease Control (CDC) developed interim case definitions for anthrax [117]. A confirmed case was defined as a clinically compatible one that was laboratory confirmed by the isolation of *B. anthracis* from the patient, or by laboratory evidence based on at least two supportive tests employing non-culture detection methods [118]. Symptoms prior to the onset of the final hyperacute phase are nonspecific and suspicion of anthrax depends on the knowledge of the patient's history [119]. The illnesses began insidiously with mild fever, fatigue, headache, chills and fever dyspnoea, coma, and death. The diagnosis of anthrax requires a high index of suspicion because the disease often presents with nonspecific symptoms [120]. Initial identification and diagnosis of the organism rely on the evaluation of infected tissue (blood, sputum, CSF fluid collected from an unroofed vesicle, ulcer, eschar, skin lesion scraping, or stool). The gold standard for anthrax diagnosis is a direct culture of clinical specimens onto blood agar with a demonstration of typical Gram stain, motility, and biochemical features. Blood cultures, which are positive nearly 100% of the time in inhalational anthrax, should be obtained prior to antibiotic administration because there is rapid sterilization of blood after a single dose of antibiotics [121]. Because laboratories may view gram-positive bacilli as



contaminants and because *B.anthraxis* may be a risk to laboratory personnel, clinicians should notify the laboratory when anthrax is suspected [122]. Other tests available through the public health laboratory system include culture, polymerase chain reaction (PCR), serologic tests, and immunohistochemistry [123]. History and clinical manifestation are important for the diagnosis of animals [10]. *Ruminants*:–Sudden death, bleeding from orifices, subcutaneous hemorrhage. *Equines*:–fever, restlessness, dyspnoea. *Pigs, carnivores*:–local edema and swelling of the face and neck or lymph node. A blood smear should be obtained with a swab from a small incision in the ear or from an ear clipping (the ear usually recommended as being accessible, supplied with an extensive capillary network, or by means of a syringe from an appropriately accessible vein a smear is made and dried ,fixed and stained with polychrome methylene blue so that through the sequence procedure the bacteria can be seen as fine threads of varying length under the low power (10x, objective), under oil immersion(100x, objective) the capsule is seen clearly (pink) surrounding the blue-black often square ended bacilli [124].

Treatment anthrax

The standard treatment for anthrax is a course of an antibiotic. However, the type and duration of antibiotic therapy may vary depending on the route of infection and the severity of symptoms [89]. Anthrax can be prevented by getting vaccinated if you are at high risk of exposure, avoiding undercooked meat from animals that may be infected, and getting treatment with antibiotics in case of exposure to spores before symptoms develop [125]. Anthrax can cause skin, lung, or intestinal infections, and can be fatal if not treated promptly and the treatment of anthrax depends on the type and severity of the infection [6]. There are four types of anthrax: cutaneous (affecting the skin), inhalational (affecting the lungs), gastrointestinal (affecting the digestive system), and injectional (affecting the muscles) [32]. The most common and least serious type is cutaneous anthrax, which can be treated with antibiotics such as ciprofloxacin or doxycycline for 7 to 10 days. The most rare and deadly type is inhalational anthrax, which requires immediate hospitalization and intensive care. Inhalational anthrax can be treated with a combination of antibiotics, antitoxins, and supportive therapies such as fluids, oxygen, and ventilation [126]. The best way to prevent anthrax is to avoid exposure to spores or infected animals or products. People who work with animals or animal products should wear protective clothing and gloves and wash their hands frequently [71]. People who may be exposed to anthrax as a biological weapon should receive a vaccine that can protect against the infection for up to a year. The vaccine is given in five doses over 18 months, followed by annual boosters. The vaccine is not recommended for the general public because of its possible side effects and limited availability [127]. Anthrax is a serious bacterial infection caused by *Bacillus anthracis*. It can affect the skin, lungs, digestive system, or blood. Anthrax can be fatal if not treated promptly. Anthrax can be transmitted by contact with infected animals or their products, such as meat or hide, or by inhaling or ingesting anthrax spores. Anthrax can also be used as a bioterrorism weapon. The main treatment is antibiotics, which can kill the bacteria and prevent them

from multiplying. Antibiotics can be given orally, by injection, or intravenously. Some common antibiotics used for anthrax are ciprofloxacin, doxycycline and meropenem . Antibiotics are usually prescribed for 60 days to ensure complete eradication of the bacteria.

In addition to antibiotics, some patients may need antitoxin therapy and antitoxins are substances that neutralize the toxins produced by the bacteria. Antitoxins can help reduce the damage caused by anthrax toxins to the organs and tissues. Antitoxins are usually given intravenously and must be used together with antibiotics [36]. Some examples of antitoxins are raxibacumab and obiltoxaximab [128]. In some cases, surgery may be needed to remove infected tissues or drain fluid from the lungs or abdomen. Surgery can help prevent complications such as organ failure or meningitis. Surgery is usually performed after antibiotics and antitoxins have been given. Anthrax is a preventable disease. People who are at high risk of exposure to anthrax, such as veterinarians, farmers, laboratory workers, or military personnel, can receive anthrax vaccination. The vaccine consists of several doses given over a period of time [89]. The vaccine can protect against cutaneous and inhalation anthrax, but not gastrointestinal or injection anthrax. People who have been exposed to anthrax spores but do not have symptoms can also take antibiotics as a preventive measure. Anthrax is a serious but treatable infection. With early diagnosis and appropriate treatment, most people can recover from anthrax. However, some people may develop long-term complications or die from anthrax, especially if they have inhalation anthrax or do not receive treatment in time. Therefore, it is important to seek medical attention as soon as possible if you suspect you have been exposed to anthrax or have symptoms of anthrax [129].

Prevention and control

The control of meat-and milk-producing animals in infected herds in such a way as to avoid any risk to the human population is a special aspect of the control of anthrax [130]. It is necessary at the same time to avoid unnecessary waste and the imposition of unnecessarily harsh prohibitions on the farmer. When an outbreak occurs, the placing of the farm in quarantine, the destruction of discharges and cadavers, and the vaccination of Survivors are part 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. Vaccination of animals, although the vaccine is a live one, does not present a hazard to humans, although there is a withholding period for meat and milk after its use [131].

Disposal of infected material is most important and hygiene is the biggest single factor in the prevention of the spread of the disease. Infected carcasses should not be opened but immediately burned in situ or buried, together with bedding and soil contaminated by discharges. If this cannot be done immediately, a liberal application of 5% formaldehyde on the carcass and its immediate surroundings will discourage scavengers [130].



Burning is the preferred method of disposal. Approximately one cord of wood is required to effectively incinerate the carcass of a mature cow. Bags of charcoal briquettes have also been used (Hugh-Jones, 20021). Burial should be at least 2 mm deep with an ample supply of quicklime added. All suspected cases and in-contact animals must be segregated until cases cease and for 2 weeks thereafter the affected farm must be kept in quarantine to prevent the movement of livestock. The administration of hyper-immune serum to in-contact animals may prevent further losses during the quarantine period, but prophylactic administration of a single dose of long-acting tetracycline or penicillin is a much more commoner tactic [132].

Disinfection of premises, hides, bone meal, fertilizer, wool, and hair requires special care. When disinfection can be carried out immediately before spore formation can occur, ordinary disinfectants or heat (60 °C (140 °F) for a few minutes) are sufficient to kill vegetative forms. This is satisfactory when the necropsy room or abattoir floor is contaminated. When spore formation occurs (i.e. within a few hours of exposure to the air), disinfection is almost impossible by ordinary means. Strong disinfectants such as 5% Lysol require to be in contact with spores for at least 2 days. Strong solutions of formalin or sodium hydroxide (5% - 10%) are probably the most effective. Peracetic acid (3% solution) is an effective sporicide and, if applied to the soil in appropriate amounts (8 L/m²), is an effective sterilant. Infected clothing should be sterilized by soaking in 10% formaldehyde. Shoes may present a difficulty and sterilization is most efficiently achieved by placing them in a plastic bag and introducing ethylene oxide. Contaminated materials should be damp and left in contact with the gas for 18 hours. Hides, wool, and mohair are sterilized commercially by gamma-irradiation, usually from a radioactive cobalt source. Special care must be taken to avoid human contact with infected material and, if such contact does occur, the contaminated skin must be thoroughly disinfected [133].

Conclusion and recommendation

Anthrax is a serious infectious disease caused by the bacterium *Bacillus anthracis*. It can affect humans and animals and can be transmitted through contact with infected animals or animal products, inhalation of spores, or ingestion of contaminated food or water. Anthrax can cause severe illness and death if not treated promptly and appropriately. Anthrax has been used as a biological weapon since the early 20th century and has been involved in several incidents of biowarfare and bioterrorism. The World Health Organization (WHO), the Food and Agriculture Organization of the United Nations (FAO), and the World Organisation for Animal Health (OIE) have published guidelines for the prevention, diagnosis, treatment, and control of anthrax in humans and animals. The etiology of anthrax depends on how the spores enter the body. There are four main types of anthrax: cutaneous, inhalational, gastrointestinal, and injectional. Cutaneous anthrax occurs when the spores enter through a break in the skin, such as a cut or an insect bite. This is the most common and least deadly form of anthrax, accounting for about 95% of cases. Inhalational anthrax occurs when the spores are inhaled into the lungs, where they

can cause severe pneumonia and septicemia. This is the rarest but most fatal form of anthrax, with a mortality rate of up to 75%. Gastrointestinal anthrax occurs when the spores are ingested with contaminated food or water, where they can cause inflammation and ulceration of the digestive tract. This form of anthrax has a mortality rate of up to 60%. Injectional anthrax occurs when the spores are injected into the body with contaminated drugs or needles, where they can cause abscesses and septicemia. This is a relatively new form of anthrax, associated with heroin users in Europe. Anthrax is more common in areas where livestock are not vaccinated and where animal products are not properly handled or disposed of. Anthrax outbreaks can occur sporadically or seasonally, depending on environmental factors that affect spore survival and exposure. In Ethiopia, anthrax is a reportable disease and is assumed to be endemic, especially in rural areas where livestock farming is common. Some findings suggest that anthrax is a serious but under-recognized health problem in developing countries including Ethiopia. Based on the above conclusion the following recommendations are forwarded: Anthrax vaccination is recommended for certain groups of people who are at risk of occupational exposure to anthrax, such as laboratory workers, veterinarians, and military personnel. The vaccine is given as a series of injections before exposure, and may also be given after exposure in combination with antibiotics.

- Anthrax diagnosis is based on clinical signs and symptoms, epidemiological history, and laboratory confirmation. Laboratory tests including culture, polymerase chain reaction (PCR), immunological assays, and microscopy must be performed as soon as possible.
- Anthrax treatment consists of appropriate antibiotics, such as ciprofloxacin, doxycycline, or penicillin, for at least 60 days. Antitoxin therapy may also be considered for severe cases of inhalational anthrax.
- Anthrax control measures include surveillance, outbreak investigation, disinfection and decontamination, quarantine and movement restrictions, carcass disposal, and vaccination of animals must be applied.
- Occupational safety and health measures include personal protective equipment (PPE), engineering controls, administrative controls, and medical surveillance.
- It is important to raise awareness and preparedness among health professionals and the general public about anthrax and its prevention and control strategies.
- Animals and humans must be kept separately in developing countries.

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