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Review of Anthrax in Animals and its Public Health Importance

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Abstract: Anthrax is a zoonotic disease that threatens both human and animal health. It is an infectious disease caused by the spore-forming bacterium *B. anthracis*. The natural reservoir of Bacillus anthracis (*B. anthracis*) is soil. Anthrax is most commonly developed in domestic and wild herbivores. The outbreaks of the disease typically occur in the summer during the prolonged period of hot, dry weather that follows heavy rain and flooding. The dissemination of infection is by the activity of scavenging animals and birds and also by blowflies and biting flies. However, anthrax has a history of use as a biological agent in which it is a serious anti livestock agent. Anthrax in humans develops in three forms as inhalational, cutaneous and gastrointestinal anthrax. Humans can get the infection by the activity of bioterrorism, from the infected animal products by direct contact and consumption, as well as from animal byproduct such as hair, wool hide, etc and also from consumption of infected meat and bone meal. The control measures for anthrax in humans are primarily dependent on the control of the disease in other animals including prompt treatment of infected animals, isolation of suspected cases and animals exposed to suspected sources from the apparently unaffected animal, vaccination of affected herds, quarantine of affected premises, control marketing and slaughtering infected animals to prevent the introduction of infected meat or other products into the food chain, proper burials of the carcass of infected animals, decontamination of all items materials that become contaminated with *B. anthracis* spores. However, the control and prevention of anthrax in humans include; appropriate use of personnel protective methods, vaccination of persons in high-risk categories, antibiotic treatment of infected individuals and infection control. However, the control and prevention of human anthrax can be through the decontamination of contaminated materials and the environments. Furthermore, additional research for control measures should be enhanced by the Medical Community especially against the bioterrorist anthrax dissemination.

Key words: Anthrax · *B. anthracis* · Public health · Review

INTRODUCTION

Anthrax is an ancient zoonotic disease that continues to threaten human and animal health. It remains enzootic in many regions of the world and cases of anthrax among humans are frequently reported. Anthrax is the infection caused by the spore-forming bacterium *B. anthracis*. In Europe in the 19th century, anthrax outbreaks caused substantial loss of livestock and human life, which stimulating early study of the disease. According to these authors, the natural reservoir of anthrax is soil. Outbreaks in animals are often associated with low lying areas with soil that has high moisture and organic contents and alkaline PH. However, sporulation occurs when the infected carcasses are disrupted by scavenger activity. The spores' are concentrated by water run off into low lying areas and infective in soil for decades [1]. According to these authors, anthrax most commonly develops in domestic and wild herbivores, such as cattle, sheep, goats, bison and antelope and deer. However, outbreaks of the disease typically occur in the summer during prolonged periods of hot, dry weather that follow heavy rain and flooding. Additionally, outbreaks may be triggered by disruption of the soil in areas where anthrax affected carcasses have been buried or may develop as a result of animal consumption of food stuffs.

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Furthermore, Anthrax infection disseminated by the activity of scavenging animals and birds, blow flies and biting flies. Anthrax in humans, primarily develop following exposures to infected animals, tissues, products from infected animals or to spores of *B anthracis*. In humans, it has historically been grouped into either agricultural or industrial exposures [1]. According to CDC [2], the incidence of naturally occurring anthrax in humans decreased during the past century and it is now relatively infrequent in developed countries as a result of animal disease control; improvements in industrial hygiene; and a decrease in the use of imported, contaminated raw materials. In the United States, the incidence in humans declined from an estimated 130 cases annually in the early 1900s to no more than 2 cases by the end of the century. However, a more recent manifestation of industrial exposures has emerged with the occurrence of anthrax in workers who use contaminated animas hides for drum making [3] and cutaneous or inhalational anthrax among persons who have played contaminated goat skin drums has been reported [4].

Anthrax has a history of use as a biological agent against both human and animal's populations and is regarded as a serious ant livestock agent. It is considered to be an important biowarfare or bioterrorism threat because of the persistence of the *B. anthracis* spores, the ability of aerosolized spores to readily cause infection after inhalation and the high mortality rate among resultant anthrax cases [5]. The objective of this paper writing is therefore to have an over view of the condition of anthrax in animals and humans based on available literature.

Epidemiology and Occurrence of Anthrax: The natural reservoir of *B. anthracis* is soil. Outbreaks in animals are often associated with low lying areas with soil which has high moisture and organic contents and alkaline PH. Grazing animals are thought to be become infected when they ingest *B. anthracis* spores on vegetation in area where the soil or water sources are contaminated by the spores. The vegetative bacilli are shed in the blood and other discharges from infected animals that are dying or dead. Those bacilli then sporulate and contaminate the under lying and immediately surrounding soil and water sources. Sporulation also occurs when infected carcasses are disrupted by scavenger activity. The spores are concentrated by water run off into low lying areas and can remain viable and infective in soil for decades. The endospores of Bacillus which are the infectious particles of anthrax are dormant bacterial morphotypes [3], resistant to a variety of physical morphotypes [3], resistant to a variety of physical and oxidation. The ability to switch between this cell type and the rapidly dividing vegetative form provides the bacilli with a highly effective strategy for persistence in the environment. However, the toxicity of *B. anthracis* is by secretion of exotoxins encoded from plasmid pX01 into the host cell [1, 6]. Microbiological characteristics of *B. anthracis* is a large (1-1.5 wide x 3-10 μm long), aerobic, Gram positive, non-haemolytic on sheep-blood agar, spore forming, non-motile member of the Bacillus species with square and concave ends. It forms a spore of 1 m in diameter, which is resistant to drought, heat, ultraviolet light, gamma radiation and numerous disinfectants. The *B. anthracis* spore can remain viable and infective in the environment for decades. Growing readily on all ordinary laboratory media at 37°C, *B. anthracis* forms rough grey white colonies of 4-5 mm, with characteristic comma-shaped or comet-tail protrusions. The two principal virulence factors of *B. anthracis* (capsule and toxins) are encoded on two plasmids. The bacteria can evade the immune system by producing an anti-phagocytic capsule. The capsule material contains poly-D-glutamic acid, which helps protect the bacillus from ingestion by phagocytes. The virulence of *B. anthracis* is also determined by the production of three proteins (protective antigen: PA; lethal factor: LF and oedema factor: EF) that act in association to form two exotoxins described as lethal toxin (PA+LF) and oedema toxin (PA+EF). Both lethal and oedema toxin require participation of a common transport protein (PA). These toxins cause local necrosis and extensive oedema [7].

According to Shadomy and Smith [1], anthrax is most commonly developed in domestic and wild herbivores, such as cattle, sheep, goats, bison, antelope and deer. In North America, outbreak of the disease typically occur in the summer during prolonged periods of hot, dry weather that follow heavy rain and flooding. Additionally, outbreaks may be triggered by disruption of soil in areas where anthrax-affected carcasses have been buried or may develop as a result of animal consumption of contaminated food stuffs. The scavenging activity of animals and birds may help to disseminate the spores on the environment as well as the disruption of infected carcasses.

The incidence of anthrax in animal populations varies geographically, but the disease is detected globally. It is most common in agricultural regions, in south and central America, Sub-Saharan Africa, central and south Western Asia and southern and eastern Europe [1].

In humans, anthrax primarily develops following exposures to infected animals, tissues or products from infected animals or spores of *B anthracis* [8]. Anthrax in humans has historically been grouped into either agricultural or industrial exposures. Agricultural exposures occur among persons with direct contact with sick or dying *B. anthracis* infected animals or through handling of the carcasses or tissues of such animals [9]. On the other hand, industrial exposures result from cutaneous or inhalation of particles containing anthrax spores that are generated during the cleaning and industrial processing of contaminated hides, hairs or wools from infected animals Workers in wool and Mohair processing facilities were particularly at risk for disease [1].

The incidence of naturally occurring anthrax in humans decreased during the past century and it is now relatively infrequent in developed countries as a result of animas disease control; improvements in industrial hygiene and a decrease in the use of imported, contaminated raw materials. In the United States, the incidence in humans declined from an estimated 130 cases annually in the early 1900s to no more than 2 cases by the end of the century [2]. The disease in human also develops following domestic use of products derived from animals with anthrax such as persons working with anthrax-contaminated wool yarn or bone-meal fertilizers. An additional occupational risk exists for laboratory workers, who are at risk for infection when working with cultures of *B anthracis*, especially cultures that contain spores [10]. Anthrax has a history of use as a biological agent against both human and animal populations and is regarded as a serious anti livestock agent [1].

Pathogenesis and Clinical Manifestations

Inhalation Anthrax: Inhalation anthrax follows depositions of spores forming particles of 1-5µm into alveolar spaces. Macrophages ingest the spores, some of which under go lyses and destruction. Surviving spores are transported via lymphatics to mediastinal lymph nodes, where germination may occur up to 60 days later [11]. The process responsible for the delayed transmission of spores to vegetative cell is poorly understood but well documented. In Sverdlovsk, cases occurred from 2-43 days after exposures. However, once germination occurs, disease follows rapidly and replicating bacteria release toxin to leading to hemorrhage, edema and necrosis [1].

The clinical presentation of inhalation anthrax has been described as a two stages of illness. The primary stages of developed signs are non-specific symptoms including fever, dyspnoes, cough, head ache, vomiting, chills, weakness, abdominal pain and chest pain. However, this stage of illness lasted from hours to a few days. In this stage some patients may recover, but other may also progress directly to the 2nd fulmitant stage of illness [12]. This 2nd stage developed abruptly, with sudden fever, dyspnoea, diaphoresis and shock. Massive lymph adenopathy and expansion of the medistinum led to stridor on some cases. Consequently, this 2nd stage of illness recognized by rapid and progress cyanosis and hypotension, in which death will sometimes occur within hours [13].

In fatal cases, the interval between the onset of symptoms and death averaged 3 days. This is similar to the disease course and case fatality rate in untreated experimental monkeys, which have developed rapidly fatal disease even after a latency as long as 58 days [11].

According to Bossi *et al.* [7], aerosolized anthrax spores can be trapped in the upper airways, although spores of 2 to 3 µm can pass through the bronchi to the alveoli and be transported via the lymphatics to the hilar and mediastinal lymph nodes, where germination to the bacillary form may occur. Spores do not immediately germinate and may continue to vegetate in the host for several weeks after inhalation. Germination has been described to occur up to 98 days later in non-human primates. The very long incubation times described in the Sverdlovsk outbreak are also attributed to late germination. It has been suggested that antibiotics, which are not effective against the non-vegetative or spore form of *B. anthracis*, may prolong the incubation period. Spores germinate and begin replication only after having been taken up by alveolar macrophages. Replicating bacteria release several toxins leading to haemorrhagic thoracic lymphadenitis and mediastinitis, oedema and necrosis. Typical bronchopneumonia is not found on clinical or postmortem examination. Haemorrhagic meningitis frequently develops and can be observed in up to half of patients. The median period from exposure to the onset of symptoms is approximately 4 days (range 1-6 days) but cases that occurred from 2 to 43 days after exposure have been reported in humans. For the inhalation anthrax cases reported in the US in 2001, the median period was 7 days. The incubation period seems to be inversely related to the dose of *B. anthracis* spores. To cause inhalational anthrax, the estimated infectious dose by the respiratory route is 8000-50, 000 spores, although it may be significantly smaller for some individuals. Early diagnosis is very difficult or impossible, without a clinician's high index of suspicion. Initial non-

specific symptoms are indistinguishable from a host of other diseases. The classic clinical presentation is a biphasic illness. The initial symptoms are non-specific, including mild fever, nonproductive cough, myalgia, dyspnea, headache, vomiting, chills, weakness, abdominal pain and malaise and chest pain, similar to a viral upper respiratory tract infection. Physical examination is usually unremarkable, but chest examination can reveal bilateral decreased breath sounds, rhonchi and/or inspiratory rales.

Cutaneous Anthrax: The cutaneous anthrax comprises 95-99% of cases among humans world wide. It develops following inoculation of spores into sub cutaneous tissues, usually through contact with infected animal products. Cuts or abrasions on skins increase susceptibility to infection. However, cutaneous anthrax in humans with no history or evidence of preexisting skin lesions has been reported. In laboratory study, cutaneous anthrax was induced in mice via epicutaneous inoculation of spores on to unshaved, intact skin; infective foci were subsequently detected in hair follicles. In humans, the incubation period for cutaneous anthrax approximately 5-7 days [1].

According to Shadomy and Smith [1], in cutaneous anthrax, the areas of exposed skin, such as arms, hands, face and neck, are the most frequently affected. Although, after the spores germinates in skin tissues, toxin production results in local edema, due to edema factor. Then, an initially pruritic maculae or papule enlarges into a round ulcer by the second day, which in turn, 1-3mm vesicles may appear. However, the development of a painless, depressed, black schar follows, often associated with extensive local edema. The eschar dries loosens and falls off in the next 1-2 weeks, most often leaving no permanent scar.

According these authors, the edematous swelling of the surrounding tissue is present, often with regional lymphadenopathy and lymphangitis.the painless ulcer with blackened schar and surrounding area of edema is considered to be the hallmark appearance of cutaneous anthrax. Fever malaise and head ache can also develop. The case fatality among human with cutaneous anthrax can be as high as 20% with out appropriate treatment but is typically < 1%if antimicrobial is administered [8].

Ingestion Anthrax: According to World Health Organization [14], there are two clinical manifestations of anthrax that may result from ingestion of *B. anthracis* in contaminated food or drink which can lead to the occurrence of the oro-pharyngeal anthrax and gastrointestinal anthrax. The spectrum of disease ranges from asymptomatic to severe, including sepsis, septic shock and death. Untreated cases are associated with a mortality rate of 25-75%. The lesion of oro-pharyngeal anthrax is generally localized in the oral cavity, especially in the buccal mucosa, tongue, tonsils, or posterior pharynx wall. The main clinical features are sore throat, dysphagia and painful regional lymphadenopathy in the involved side of the neck. Oro-pharyngeal anthrax is identified less often than gastrointestinal disease. Oro-pharyngeal anthrax can lead to toxemia and acute respiratory distress syndrome followed by shock, coma and death. However, the lesion of gastrointestinal anthrax may occur anywhere within the gastrointestinal tract but is usually in the ileum and cecum. Lesions are usually ulcerative, multiple and superficial, with surrounding edema and may bleed. Symptoms of gastrointestinal anthrax are usually nonspecific and include nausea, vomiting, anorexia, fainting spells, asthenia, mild diarrhea, fever and headache. Intestinal lesions may cause hemorrhage, obstruction or perforation by themselves or in combination. The infection may become disseminated with sepsis and pulmonary or meningeal involvement [5, 15].

The gastro intestinal form of anthrax develops following consumption of contaminated meat from anthrax infected animals [16] and often identified in point source outbreaks following the slaughter or salvage but butchering of infected animals. It has incubation period ranges from 1-6 days. In humans, gastro intestinal anthrax has 2 clinical forms: oropharyngeal and intestinal disease. The orophryngeal form is associated with infection of the oropharyngeal epithelium. Edematous lesion develops and progress to necrotic ulcers that are covered with pseudo membranes. Edema and lesions develop in the oropharynx and neck, accompanied by cervical lymphadenopathy, pharyngitis and fever [1].

According to Shadomy and Smith [1], the intestinal form develops following infection of the gastro intestinal tract epithelium with *B anthracis* spores. Symptoms range from in apparent to severe, pain and include diarrhea, nausea, vomiting, fever, anorexia and abdominal pain. Hematemesis, bloody diarrhea and abdominal distension with hemorrhagic ascites may also be present. The disease may progress to septicemia and toxemia, cyanosis and shock and death with both the oro-phryngeal and intestinal forms have been reported.

Means of Acquiring Anthrax Infection in Humans

Bioterrorism: Anthrax has a history of use as a biological agent against both human and animal populations and is regarded as a serious ant livestock agent. It is currently considered as one of the most serious bioterrorism threats, in which this scenario has been beginning in the second half of the twentieth century. Anthrax was developed by several countries as part of a biological weapons programs [17].

According to Bossi *et al*. [7], Anthrax is seen as one of the most likely biological agents for use as a weapon. *B. anthracis* spores can be transmitted by aerosolisation. Inhalation anthrax has a high mortality rate and the organism's spores, compared with other potential biological warfare agents, are quite stable in the environment. The use of anthrax in warfare has been recorded throughout history. In December 1941 the British Government began testing the effect of anthrax on sheep on the Scottish island of Gruinard. By 1945 the Japanese programme had stockpiled 400 kg of anthrax spores to be used in bombs. It has been estimated that 50 kg of *B. anthracis* spores released over an urban population of 5 million would sicken 250 000 and kill 100 000. The United States (US) has weaponised anthrax spores, as did other countries in the 1950s and 1960s; this was evidenced, for example, by the accidental aerosol release of *B. anthracis* spores from a Soviet military microbiology facility in Sverdlovsk in the former Soviet Union in April 1979. This was the largest known outbreak of inhalational anthrax in the 20th century. Cases have been also reported in animals located more than 50 km from the site. During the first Gulf War, it was established that Iraq conducted research and development work on anthrax. In 1990 Iraq was in possession of 50 R400-bombs and 10 SCUD with anthrax. Iraq produced 8500 liters of concentrated anthrax. In 2001 22 cases of bioterrorism-related anthrax were reported in the US: 11 confirmed inhalational and 7 confirmed and 4 suspected cutaneous cases. In March 2002, a laboratory worker in Texas presented with cutaneous anthrax after exposure to a contaminated surface in a laboratory. No other bioterrorism-related or outbreak after deliberate release has been reported in the literature, though there are reports that the cult of Aum Shinrikyo in Japan tried on several occasions to disperse anthrax unsuccessfully in Tokyo before the sarin attack. Infection in humans most often involves the skin and more uncommonly the lungs and the gastrointestinal tract. Inhalation anthrax remains the most lethal form of the disease and is of particular interest for possible deliberate release. However cases of cutaneous anthrax have also been associated with the deliberate release of the organism, as occurred in 2001 in the US. Person-to-person transmission of inhalation anthrax has never been described.

Anthrax is considered to be an important biowarfare or bioterrorism threat because of the persistence of the *B. anthracis* spores, the ability of aerosolized spores to readily cause infection after inhalation and the high mortality rate among resultant anthrax cases [5]. In 2001, the threat that anthrax pose as a bioterrorism agent for groups of workers or entire populations not previously at risk was revealed. In October and November of 2001, 21 confirmed or suspected cases of anthrax were identified in the eastern United States after *B. anthracis* spores were sent through the mail in powder-containing envelops to news media companies and US Congressional Leaders [1].

The centers for disease control and prevention (CDC) considers *B. anthracis*, the causative organism of anthrax to be a category A potential bioterrorism agent [3]. However, the anthrax attack can be perpetrated via the mail through envelopes containing *B. anthracis* spores which have a potential to cause the cutaneous and inhalational anthrax [17].

According to Desai [17], a number of factors contributed to concern about the use of anthrax as a biological weapon include the availability of *B. anthracis* in laboratory, the evidence that techniques for mass production and aerosol dissemination of anthrax have been developed, the high fatality rate, the low infectious dose and the genetic manipulation so as to make anthrax resistant to antibiotics.

Animal Product and by Product Processing: Cutaneous anthrax develops following inoculation of spores into subcutaneous tissues, usually through contact with infected animal products. This skin infection is come directly or indirectly in humans in intact with infected tissues, blood and contaminated materials of animal products such as hair, wool, hides and also byproducts such as drums and etc [1]. On the other hand, human can get anthrax when consuming the contaminated food stuffs of animals' origin such as meat, bone meal and others [18].

According to Shadomy and Smith [1], humans can get anthrax infection from industrial exposures result from cutaneous inoculation or inhalation of particles containing anthrax spores that are generated during the industrial processing of contaminated hides, hair, or wool from infected animals. Workers in wool-and Mohair-processing facilities were particularly at risk for anthrax infection.

A more recent manifestation of industrial exposures has emerged with the occurrence of anthrax in workers who use contaminated animal hides for drum making [3] and cutaneous or inhalation anthrax among persons who have played contaminated goatskin drum has been reported [4]. The disease in humans also develops following domestic uses of products derived from animals with anthrax, such as persons working with anthrax-contaminated wool yarn or bone meal fertilizers [1].

Environmental Contamination of Anthrax: Anthrax outbreaks can occur where carcasses have previously been buried because *B. anthracis* spores may be brought to surface by soil disruption or erosion. However, the spores area concerned by water run off into low lying areas and can remain viable and infective in soil for decades. The outbreaks of the disease may also be triggered by disruption of the soil in areas where anthrax affected carcasses have been buried or may develop as a result of animal consumption of contaminated food stuffs, such as animal origin feed, or water contaminated by waste waters from industrial such as tanneries, that process anthrax contaminated animals materials. However, the activity of scavenging animals and birds may help disseminate the spores in the environment as well as disrupt infected carcasses. Blow flies may contaminate vegetation after feeding on infected carcasses and biting flies may act as mechanical vectors [1].

Anthrax Control and Prevention in Humans

Control Measures in Animals: The control of anthrax outbreaks among domestic animals is primarily dependent on rapid identification and treatment of affected animals; enhanced surveillance for additional cases; implementation of control measures including quarantine, prophylaxis and vaccination; prevention of animal access to suspected sources such as potentially contaminated feed or pastures; and appropriate disposal of infected carcasses and disinfection of affected premises [1].

According to Shadomy and Smith [1], prompted treatment of infected animals with antimicrobial agents is necessary because of the rapidly progressive and often fatal nature of the diseases. Although, affected animals appear to respond well to treatment even after clinical signs appear, treatment may not always prevent death. For this reason, the practitioners should refer to manufacturer label directions and current references for species-specific antimicrobial dosages and regimes, particularly with considerations of species-specific treatment concerns such as withdrawal times and potential drug hypersensitivity reactions. However, *B. anthracis* is susceptible invitro to several broad spectrum antimicrobial agents.

For effective treatment of anthrax infection in animals; the adequate dose of penicillin with sub inhibitory concentrations of flocloxacillin, administration of streptomycin in competition with penicillin {pen strep} and parental administration of ox tetracycline [19]. However, anti-microbial treatment of affected animals should be continued for a minimum of 5 days to prevent relapse disease [1].

The suspected cases and animal exposed to suspected source should be separated from apparently unaffected animals and monitored. In the face of an outbreak, vaccination of affected herds has reduced mortality rates beginning 8 days after vaccine administration. Prophylaxis of potentially exposed animals with one effective antimicrobial agent such as tetracycline or penicillin, following by vaccination 7-10 days later, may treat incubating infectious and reduce the number of deaths. However, antimicrobial agents should not be administered to anima with 7 days of vaccination with live-spore veterinary vaccines. The affected premises should be quarantined and any marketing and slaughtering of the infected animals must be prevented to eliminate introduction of infected meat or other product into the food chain. Additionally, surrounding premises should be quarantined and susceptible resident animals should be vaccinated; active case surveillance at those sites should be conducted. Releases from quarantine of affected and surrounding premises should be determined by appropriate animal health authorities [1].

Investigation of anthrax outbreaks in animals must identify the source of *B anthraces* to prevent additional exposures; such as contaminated pastures and the access of livestock to such areas should be restricted. Investigation may also identify other sources, such as contaminated bone meal or feed, which should be eliminated to prevent additional cases Incineration is the most effective method for disposal of carcasses of animals that dies as a result of *B anthracis* infection and contaminated material such as bedding or soil. If that is not feasible, an affected carcass should be buried depth having at least 6.25 feet with a covering of chloride of lime and soil [1].

According to Shadomy and Smith [1], the annual vaccination of livestock is the principal tool for the preventing of anthrax. This is particularly true in the region where an outbreak occurs in the wildlife population (example Deer) in which the disease cannot be controlled.

Outbreaks of anthrax among livestock may be attributable in part to a lapse in vaccination practices. Since, its introduction, the virulent stern strain vaccine has been proven effective and is the most commonly used animal vaccine [20].

Vaccination: Vaccination against anthrax is recommended for parsons in high-risk categories, such as laboratory personnel working with *B anthracis* cultures, persons engaged in initiatives with a high potential for production of or exposure to aerosolized *B anthraces* spores might occur. However, vaccination might be indicated for veterinarians and other persons handling potentially infected animals in areas with a high incidence of anthrax [3, 10].

The anthrax vaccine is an inactivated cell-free product which made from the cell-free filtrate of a non-capsulated attenuated strain of *B anthracis*. The principal antigen responsible for inducing immunity is the protective antigen. In study of experimental monkeys inoculation with vaccine at 0-2 weeks was completely protective against an aerosol challenge at 8 and 38 weeks and 88% effective at 100 weeks [21]. Anthrax vaccine adsorbed (AVA), which is made by Bioport (Lasing, Mich) under the name Biothrax, is the sole licensed anthrax vaccine in the United States and has been available since 1970. An inactivated vaccine derived from a cell-free filtrate, it is administered in a 6-dose series over 18 months and requires yearly boosters [22]. The clinical evidence for the efficacy of AVA comes form a 1950's industrial exposures study at 4 mills on a predecessor vaccine to AVA [13]. It is from studies on primates that the FDA has concluded that the vacations effective in protecting humans against inhalational anthrax [23].

According to Weiss *et al.* [23], the anthrax vaccine varies widely in efficacy among species, in which it provides no protection to Hamsters. However, the studies have shown the vaccine to be protective against aerosolized spores at amounts 900 times the LD_{50} in monkeys [22].

The efficacy may be affected by genetic engineering in which the insertion of gene for cereolysin AB from *Bacillus cereus* inhibit the protective effect of the ST-1 anthrax vaccine in Syrian gold Hamsters as reported by, in Russia. ST-1 is alive spore vaccine made from a Russian strain of *B .anthracis*. The US anthrax vaccine, an inactivated cell free product was licensed in 1970 and is produced by Bioport Corp; Lansing, Mich (formerly called the Michigan Biological Products Institute). The vaccine is licensed to be given in a 6- dose series and has recently been mandated for all US military active and reserve-duty personnel [23].

Therapy: The appropriate treatments possible after differentiating the case of naturally occurring cutaneous anthrax, from case that result from exposure to aerosolized *B. anthracic* spore. Early treatment of cutaneous anthrax will limit the size of the lesion; however, treatment with antimicrobial agents will not alter the pathological changes associated with the cutaneous lesion because edema and schar is likely toxin mediated. In humans with localized or uncomplicated naturally occurring cutaneous anthrax. Oral administration of ciprofloxacin or doxycycline for 7 to 10 days is recommended. If results of antimicrobial susceptibility testing are supportive, oral administration of penicillin or amoxicillin may be used to complete the course of treatment [21].

For severe naturally occurring cutaneous anthrax with systemic involvement, extensive edema, or lesion of the head and neck, or for cutaneous anthrax in children < 2 years of age, intravenous administration of ciprofloxacin or doxycycline for 7 to10 days is recommended for severely affected individuals, administration of 1or 2 additional antimicrobial agents with known efficacy against *B anthracic* is recommended [9]. The treatment of coetaneous anthrax generally prevents progression to systemic disease, although it does not prevent the formation and evolution of the schar. Tropical therapy is useful [21]. The treatments for individual with serious systemic anthrax, such as inhalation anthrax, gastrointestinal anthrax, meningitis or cutaneous anthrax with systemic involvement, multidrug antimicrobial treatment is recommended. How ever, radical and effective treatment with antimicrobial agent is essential to treat inhalational anthrax because disease may progress extensively between the time of exposure and clinical intervention and the condition of patients may rapidly define following initial signs [9]. Intravenous administration of ciprofloxacin is recommended as the primary antimicrobial treatment with the inclusion of 2 or more additional antimicrobial agent that has in vitro activity against the *B anthracis* strain isolated [9].

Other antibiotics effective against *B. anthracis* is invitro include chloramphenicol, erothromycin, chlindamycinhydrochloride, cefazolin and other first-generation cephalosporins. The antimicrobials such as sulfamethoxazole, trimethoprim, cefuroxime, cefotaximesodium, aztreonam and ceftazidimine, should not be used for the treatment or prophylaxis of anthrax

infection due to the existence of natural resistance of *B. anthracis* strains against them Joellenbeck *et al.* [22]. On the other hand, the use of immune globulin may limit or prevent the toxin in mediated morbidity and death associated with anthrax and hyper immune serum of animal origin has been used for years in the treatment of anthrax in human [1].

Post Exposure Prophylaxis: Guidelines regarding which population would repair post exposure prophylaxis following the release of anthraxes a biological weapon would need to be developed fickly by state and local health department in consultation with national experts. These decisions require estimates of the timing and lactation of the exposure and the relevant winter conditions in an outdoor release [21]. In the case of naturally occurring cutaneous exposure, post exposure prophylaxis is generally not recommended if not, the exposure is substantial or inhalation exposure occur, antimicrobial post exposure-prophylaxis for 7 to14 days may be considered [2]. According to Joellenbeck *et al.* [22], the post-exposure prophylaxis involving oral administration of an antimicrobial agent for 60 day combined with a 3-dose vaccination series provides optimal protection against inhalation anthrax. In the event of inhalation exposure to *B .anthracis* spore containing aerosols, antimicrobial prophylaxis should be ignited as soon as possible Ciprofloxacin and doxycycline are recommended as equivalent first line antimicrobial agents of choice [24].

Management of Special Groups: Specific recommendations for post-exposure prophylaxis, including regimes for special populations such as pediatric patients, a nursing mother and pregnant women are available [24]. However, it has been recorded that ciprofloxacin and other fluoroquinolones should not be used in children less than 16 to 18 years old because of a link to permanent arthropathy in small and transient recommended to use in pediatric population. But ciprofloxacin recommended using in pediatric population for initial therapy or post exposure prophylaxis following an anthrax attack. In addition penicillin and doxycycline could be used in which the doxycycline can cause retarded skeletal growth in the infant and discolored teeth both in infants and children as recommended by the American Academy of pediatrics [21].

According to Inglesby *et al.* [21], US vaccine is licensed for use only in persons aged 18 to 65 years which was not recommended for children less than age of 18 years old. Like in children, flouroquinolones are not generally recommended during pregnancy due to their complication associated with arthropathy in adolescent animals and small numbers of children. However, the ciprofloxacin is recommended for pregnant women against risk concerning of anthrax due to engineered antibiotic resistant strain for therapy and post exposure prophylaxis following anthraxes attack. The working group recommends that pregnant women receive flouroquinolones in the usual adult dosages. If susceptibility testing allows, intravenous administration of penicillin in the usual adult dosage should be substituted flouroquinolones. On the other hand, intravenous administration of doxycyline could be used as alternative drug. The tetracycline class of antibiotics has been associated with both toxic effect in the liver in pregnant woman and fetal toxic effects, including retarded skeletal growth [21]. Ciprofloxacin (and other flouroquinolones), penicillin and, doxycycline (and other tetracycline's) are each excreted in breast milk. Therefore, a breast feeding woman should be treated or given prophylaxis the same antibiotics as her infant based on what is most safe and effective for the infant to minimize risk to the infant [21].

Infection Control: There are no data to suggest patient to-patient transmission of anthrax occurs [5]. Thus, standard barrier isolation precautions are recommended for hospitalized patients with all forms of anthrax infection, but the use of high-efficiency particulate on filter masks or other measures for airborne portion are not indicated [21]. In addition to immediate notification of the hospital epidemiologist and state health department, the local hospital micro-biology laboratories should be notified at the first indication of anthrax so that safe specimen proceeding under biosafety level 2 condition can be undertaken. A number of disinfectants used for standard hospital in faction control such as hypochlorite, are effective in cleaning environmental surfaces contaminated with infected body fluids [21].

According to Inglesby *et al.* [21], proper burial or cremation of humans and animal that have died because of anthrax infection is important in preventing further transmission of the disease. Embalming of bodies could be associated with special risks. If autopsies are performed, all related instruments and materials should be autoclaved or incinerated.

Decontamination: Recommendations regarding decontamination in the event of an intentional aerosolization of anthrax spores are based on evidence concerning aerosolization, anthrax spore survival and

environmental exposures at Sverdlovsk and among goat hair mill workers. The greatest risk to human health following an intentional aerosolization of anthrax spores occurs during the period in which anthrax spores remain airborne, called *primary erosolization*. The duration for which spores remains airborne and the distance spores travel before they become non infectious or fall to the ground is dependent on meteorological conditions and aerobiological properties of the dispersed aerosol [21].

The risk that the anthrax spores might pose to public health after the period of primacy aerosolization can be inferred from the Sverdlovsk experience, investigation in animal hair processing plants and modeling analysis by the US Army. At Sverdlovsk, new cases of inhalational anthrax developed as late as 43 days after presumed date of release, but none occurred during the months and year after ward [21]. Some have questioned whether any of those cases with onset of disease beyond 7 days might have represented illness following resuspension of spores from the ground or other surfaces, a process that has been called *secondary aerosolization*. While it is impossible to state with certainty that secondary aerosolization did not occur, it appears unlikely. It should be noted that fewer efforts were made to decontaminate the environment after the accident and only 47,000 of the city's 1 million inhabitants were vaccinated [1].

Although, persons working with animal hair and hides are known to be at increased risk of developing inhalational or cutaneous anthrax. However, during the first half of this century, a significant number of goat hair-mill worker were likely exposed to aerosolized spores. Thus, mandatory vaccination became required for working in goat hair mill only in the 1960s, Brachman [25]. However, the environmental contamination with anthrax spore could be decontaminated by high dose and frequent use of formaldehyde and seawater until the test concludes the full decontamination of the area suspected. The use of 5% formaldehyde is effective in decontamination of soil that contains *B anthraces* and can prevent disruption of the carcass by scavengers. How ever, it also will provide superficial decontamination at the carcass site and immediate surrounding environs [1].

All items or materials that become contaminated with *B anthraces* should under go decontamination. Spores can be eliminated via steam sterilization under pressure (autoclaving), at 121°C for 30 minutes or via ethylene oxide gas sterilization with a contact time of at least 18 hours. Soaking articles in 10% formaldehyde or 4% glutaraldehyde for at least 2 hours is also effective. A 10% hypochlorite bleach solution may also be used for decontaminating items and surfaces. However, chlorine is unstable and susceptible to in activation by organic material and free chlorine concentration should be verified. Fumigation with chlorine dioxide or vaporized hydrogen peroxide (H_2 O_2) and exposure to gamma-radiation are also effective means of decontamination**.** Boiling of items expected to having spores in 10-minutes should effectively kill spores [3, 12].

Additional Research: Develop a maximally effective response to a bioterrorist in incident involving anthrax; the Medical Community will require new knowledge of the organism, its genetics and pathogenesis, improved rapid diagnostic techniques, improved prophylactic and therapeutic regimens and improved second-generation vaccine [22].

CONCLUSION AND RECOMMENDATION

Anthrax is a major and serious zoonotic disease among the other zoonotic diseases. However, it is the most important disease that is devastating to the health of domestic animals and humans. Thus, it has a major economic importance. The elimination of this disease or pathogen is very difficult due to the persistence of the *B .anthracis* in the soil by forming spores and its high resistance against disinfectants and desiccation. Therefore, the disease must be controlled by giving high attention, thus the following should be recognized for future:

- Educating the public about the major zoonotic importance of the disease
- Reducing the major way of its transmission and dissemination
- Developing a maximally effective response to a bioterrorist incident involving anthrax dissemination.
- Seeking an improved way of controlling the disease such as:
  - An improved second-generation vaccine
  - Developing new knowledge of the organism, it's genetic and pathogens, then try to treat it.
  - Improved rapid diagnostic technique
  - Improved Prophylactic and therapeutic regimens.

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