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Anthrax as a Zoonotic Infection: A "One Health" Perspective and Achieving Sustainable Development Goals

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ABSTRACT

Anthrax is one of the most lethal zoonotic diseases with its ability to persist in the environment for decades and its high mortality rates in humans and animals caused by Bacillus anthracis. This article reviews the pathogen's life cycle and virulence factors such as the triple toxin complex and the capsid, which is resistant to phagocytosis, and is encoded by the plasmid pXO2 and pXO1, respectively. It also serves as an indicator of establishment and dispersion from soil reservoirs and grazing animals, human infection patterns and security implications due to its designation as a biological weapon. The results of the review confirms the importance of the two-fold approach: veterinary and environmental (annual livestock vaccination, prohibit autopsies, safe disposal of carcasses) and human medical (medical and treatment) interventions. As conclusion, this approach is directly linked to the achievement of the United Nations Sustainable Development Goals, namely Goal 3 (Good Health and Well-being), Goal 2 (Zero Hunger) and Goal 15 (Life on Land).

KEYWORDS: Anthrax , zoonotic infections, Bacillus anthracis, One Health.

INTRODUCTION

Zoonotic infections are a major nexus of human, animal and environmental health and include those infections that naturally cross from vertebrate animals to people [1,2]. Zoonoses make up a significant proportion of emerging and re-emerging infectious diseases worldwide [3], partly due to intricate ecological mechanisms, farming practices and environmental encroachment [4,5]. In this paradigm zoonotic bacterial pathogens are especially threatening [6]. They have different routes of transmission from direct contact to vectors to ingestion or inhalation of contaminated environmental reservoirs and are frequently able to survive in the environment [7]. An example of a very virulent zoonotic bacterial pathogen is the anthrax pathogen [8].

Anthrax is an enzootic disease of domestic and wild herbivorous mammals, and can spill over into human populations through occupational exposure to infected animals, contaminated animal products (e.g. wool, hides, meat) or by exposure to spore-contaminated soil [9]. Its zoonotic nature combined with its remarkable environmental survival makes anthrax a focal topic of bacterial zoonoses and public health [10].

It is one of the most lethal zoonotic diseases known to man, tackling the animals and humans with speed, and able to remain active in the environment for decades[11]. This reference article will aim to provide a comprehensive analysis of the disease life cycle, the transmission routes and security perspective in the context of the "One Health" approach.This approach highlights the close connection between human, animal and ecosystem health and the importance of integrated approaches to the management of this biological threat [12], going beyond medical response to environmental and veterinary management and undertaken within a global development framework [13].

ANTHRAX BACTERIUM

Anthrax is caused by the bacterium, *Bacillus anthracis*, which is a large, non-motile, facultative anaerobic, Gram-positive, rod-shaped bacterium [14]. An ecological and epidemiological property of *B. anthracis* is its ability to produce very durable endospores in environments devoid of nutrients. These spores are metabolically inactive and can survive in soil for many years and are extremely resistant to extreme temperatures, desiccation, ultra-violet light and strong chemical disinfectants [15]. When the spores get into a favorable host environment (usually via inhalation, ingestion or dermal abrasion), they germinate to vegetative bacilli that multiply rapidly and cause potential fatal toxemia and septicemia [16].

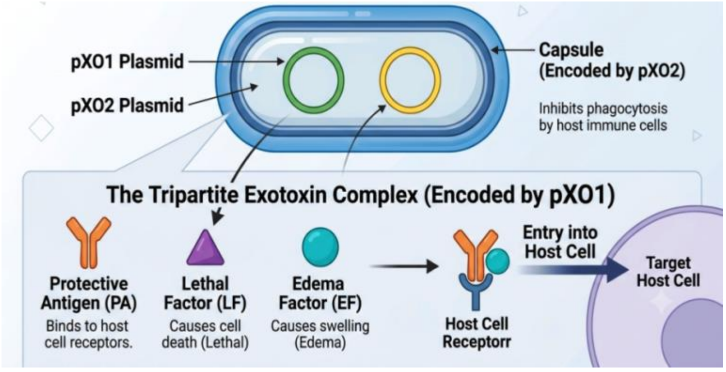

Figure 1: Key virulence determinants of Bacillus anthracis.

The pathogenicity of this bacterium is tightly associated with two major structural and secretory components each encoded by separate virulence plasmids (pXO1 and pXO2) as shown in Figure (1):

1- **The Capsule (pXO2)**
The vegetative cell is surrounded by an unusual high cross linked capsule, made of poly-γ-D-glutamic acid. This proteinaceous capsule is totally anti-phagocytic while the polysaccharide capsule of most other bacterial pathogens is not. It makes the bacterium more difficult for the host to detect and eliminates the need to kill the bacterium to prevent multiplication [17].

2- **The Tripartite Exotoxin (pXO1)**
The bacterium produces three non-toxic polypeptides that from the host cell surface to create highly lethal toxin complexes:

- Protective Antigen (PA): Binding component that binds receptor on host cell and helps with entry of the other two components into the cell [18].
- Lethal Factor (LF): A zinc-dependent metalloprotease that can disrupt the cell signaling cascades, causing the death of macrophages and severe systemic shock.
- Edema Factor (EF): An adenylate cyclase that can significantly increase the concentration of cAMP in the cell, which results in the massive outflow of fluid (edema) and prevents the innate immune response of the host [19].

TAXONOMIC CLASSIFICATION

Bacillus anthracis belongs to the group of bacteria (Figure 2) known as Bacillus cereus sensu lato, which is genetically closely related, yet shows broad differences in phenotypes and pathogenicity [20].

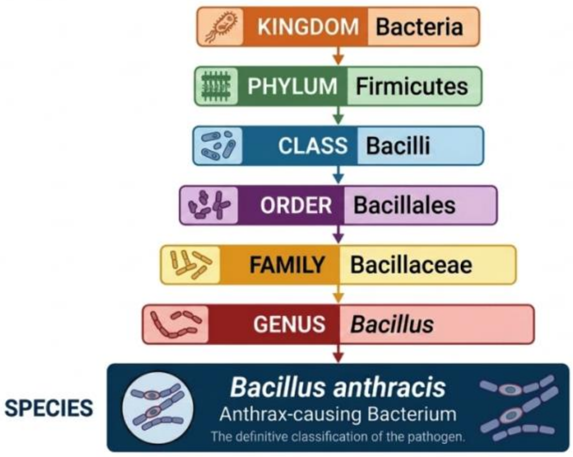

Figure 2: Taxonomic classification of Bacillus anthracis

RESERVOIRS OF ANTHRAX

Anthrax bacteria have a very complex, dual survival and dissemination strategy in which they alternate between dormant and active phases of the environment (Figure 3) . This ongoing transfer between soil and animals is what makes it a big environmental and veterinary problem to eradicate this disease [21].

1- SOIL AS AN ENVIRONMENTAL RESERVOIR

Soil is not just a carrier of bacteria, but the main incubator that allows the bacteria to survive for astounding periods of up to 50-100 years.

- **Survival Mechanism (Sporulation)**

Bacteria change into spores when the nutrients are exhausted and they come into contact with air (oxygen). The spores have hard protein shells and are virtually metabolically inert, which is like a time capsule [22].

- **Exceptional Resistance**

Due to its structure, anthrax spores have the ability to survive in the arid environment, in high temperatures (including incomplete burning), in extreme cold, from ultraviolet radiation and many standard chemical disinfectants. The spores are not all soil persistent. Alkaline soils (pH above 6.0) that have high levels of calcium and organic matter are ideal environments, called "anthrax fields. The spore characteristics protect decomposition and ensure their longevity [23].

- **Environmental Transport**

Water is a secondary transport agent, carrying the spores about in the environment to rest in the soil and so begins the cycle again [24].

2- ANIMALS RESERVOIRS (HERBIVORES)

The bacterial reproduction cycle is driven by herbaceous animals (ruminants and wild animals) which cause a huge increase in the number of bacteria.

- **Primary Victims and Reservoirs**

These include domestic ruminants (cows, sheep and goats) and wild animals (deer, elephants, hippos). This type of grazing occurs naturally, in some instances, disrupting plant growth and thus raising the risk of these animals consuming soil that has spores [25].

- **Reproductive Cycle (Germination)**

When the spores are ingested (either through the gastrointestinal tract or inhalation of dust) or introduced by a skin wound, they have the perfect habitat: warmth, humidity and abundant nutrients (including amino acids in the blood stream). The spores here lose their shells and transform back into the vegetative (active) cell. Active cells reproduce rapidly in the animal's bloodstream causing the release of toxins which cause shock and acute septicemia. Often a sudden death occurs without a long warning period [26].

- **Environmental Recontamination (Amplification and Persistence)**

Once the animal is dead, dark, heavily contaminated fluid is expelled from the natural openings of the animal's body (mouth, nose, and anus) and is known as the "milk of the white death. The fluid that oozes from the mouth, nose, and anus becomes dark and highly contaminated once the animal dies and is referred to as the "milk of the white death" due to the high concentration of bacteria. When this blood and fluid comes in contact with oxygen in the open air, the active bacteria spore, and immediately fall into the surrounding soil. That is what is so important about the strict prohibition against dissection of animals suspected of having anthrax: the bacteria need oxygen to be able to spore [27].

The knowledge of such a closed cycle (soil-animal-soil) is crucial for developing disease control programs. Human intervention can be done in two ways: either by vaccination to interrupt the biological cycle or by safe carcass disposal (burning or deep burial and liming) to interrupt the environmental cycle [28].

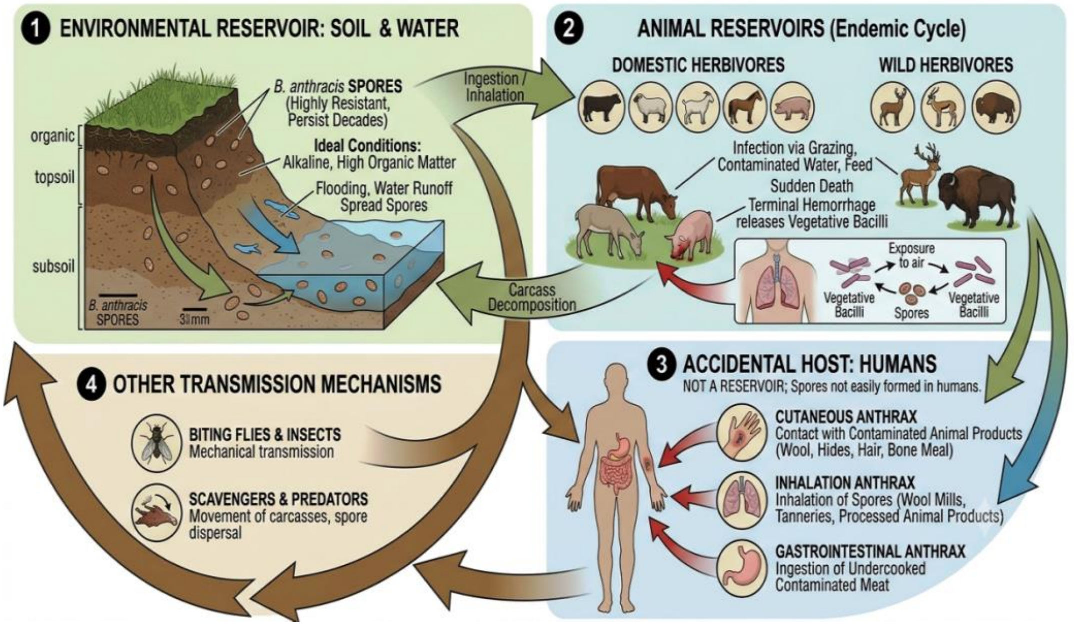

Figure 3: Reservoirs and transmission of Anthrax.

TRANSMISSION METHODS

There are several ways that anthrax can be transmitted, and humans can become infected with anthrax by contact with infected animals or their products. The infection doesn't spread from person to person [29]. Type and severity of infection depends on how the spores enter the body and classified into three main clinical routes:

1- Cutaneous Transmission

If human skin is open, an abrasion or scratch, is exposed to anthrax spores, this takes place. It is typically linked to direct contact with dead animals infected with the disease or when handling contaminated animal products like wool, hides bones and hair. The infection starts with an insect-bite like itchy or bumpy rash and progresses into a painless vesicle and then into a central black, necrotic crust (black lesion). Over 95% of the cases of humans worldwide are on this route. It's not very pleasant to watch, but it's the least bad, and very responsive and quick to respond to antibiotics and almost never deadly when treated in a timely fashion [30].

2- Gastrointestinal Transmission

Infection is by eating raw or undercooked meat from infected animals. The spores are not affected by stomach acid and invade the mucous membranes of the digestive system from the mouth and throat to the intestines. These start with symptoms of severe food poisoning – severe throat inflammation, difficulties in swallowing, nausea, bloody vomit, excruciating abdominal pain, severe bloody diarrhea caused by intestinal ulceration and mesenteric lymphadenitis. This route is not as commonly used, but is extremely dangerous because of the stricter veterinary control measures. It's a medical emergency that can be fatal if left undiagnosed and untreated because of bleeding and extreme septicemia in the body [31].

3- Inhalation Transmission

It is by inhalation of contaminated aerosols, dust, that settle directly in the alveoli of the lungs. In the past, this route was called "Wool Sorters' Disease" because it was thought that textile factory workers were the most vulnerable to it, but if wool factory workers were to be used as a biological weapon; this would be the most likely route [32].

There are two stages in the disease. The initial symptoms are subtle and easily mistaken for the common flu (low fever, tiredness, and a dry cough) and last several days. This is followed suddenly by a severe second phase characterized by extreme difficulty breathing, meningitis (in some cases), and acute hypoxia culminating in hemorrhagic shock. This is the most deadly way, and even with intensive care and potent anti-bacterial medications, the mortality rate is very high as the characteristic symptoms only occur when the bacteria have migrated to the chest's lymph nodes and released toxins into the bloodstream [33].

ANTHRAX BACTERIUM AS A WEAPON OF BIOTERRORISM

It is known to be one of the most dangerous biological agents (Category A) by global health and security agencies because of the serious threat it poses to the national security and public health (Figure 4). This classification is based on its distinctive biological features and on a number of historical events proving that it is very effective in causing destruction [34]. Spores are an ideal biological weapon because they have the following characteristics:

1- Exceptional environmental stability

Spores are capable of surviving harsh conditions, high heat, drought and even the pressure from munition explosions, allowing them to be easily integrated into weapons systems without being killed off [35].

2-Aerosolization

In the laboratory spores may be finely ground to form very small particles (1-5 microns) which can float through the air for long distances and enter the lungs directly through inhalation and settle in the alveolar cells [36].

3- The ease of production and deceptive identification

Anthrax is relatively easy and inexpensive to grow and mass produce. Moreover, the onset of the respiratory pattern is not distinctive until the infection culminates in life-threatening septicemia, which is challenging to treat, and the incubation period and earliest symptoms resemble those of the common flu [37].

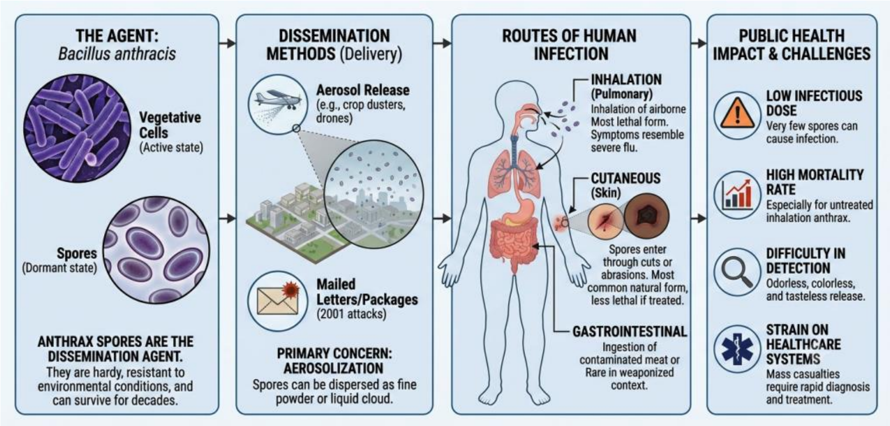

Figure 4: Anthrax as a biological weapon.

CONTROL AND PREVENTION

Two-step approach is necessary to control anthrax – break the cycle of the transmission in the animal environment, and at the same time directly protects human beings (Figure 5). There are different prevention strategies along two axes:

1- VETERINARY AND ENVIRONMENTAL INTERVENTIONS

- **Routine Livestock Vaccination**

Vaccinating at-risk animals (ruminants) at the time of the annual vaccination is the most important preventive measure in endemic areas. Usually a live attenuated vaccine (e.g. Sterne strain) is used, which gives effective immunity and prevents outbreaks [38].

- **Quarantine and Movement Restrictions**

Immediate isolation of herds showing signs of infection and prohibiting movement of animals and animal products (including meat, hides and wool) to/from the outbreak areas are critical for keeping the disease contained [39].

- **Safe handling of carcasses (Strict Prohibition of Dissection)**

Culling or dissection of any animal suspected of having died from the disease is forbidden. When the carcass is opened, the active bacteria in the blood of the animal are exposed to oxygen and converted to extremely resistant spores that can persist in the soil for decades [40].

- **Final Disposal (Environmental Disposal)**

Carcasses are either totally burned on the spot or buried with a thick layer of quicklime (calcium oxide) to stop scavenging animals from digging up and killing bacteria [41].

2- HUMAN MEDICAL INTERVENTIONS

- **Human Vaccines**

The vaccine is not available for general use but only given to high risk individuals (veterinarians, tannery and slaughterhouse workers, biological laboratory workers, military servicemen and women). Cell-free purified proteins are the basis for approved vaccines (for example, BioThrax) and vaccine doses are multiple [42].

- **Antibiotic Treatment**

If treatment is started early, anthrax bacteria are sensitive to antibiotics. First line antibiotics in clinical cases are ciprofloxacin or doxycycline.

- **Post-exposure prophylaxis**

If spore exposure is suspected (particularly in a laboratory accident or biological attack), then 60 days of a course of prophylactic antibiotics should be given ,spores can be dormant for long periods in the lungs before they are active[43].

- **Personal Protective Equipment (PPE)**

Ensure biosafety protocols are adhered to and use gloves, advanced respirators (N95 or above), and protective clothing when working with potentially contaminated materials or animals [44].

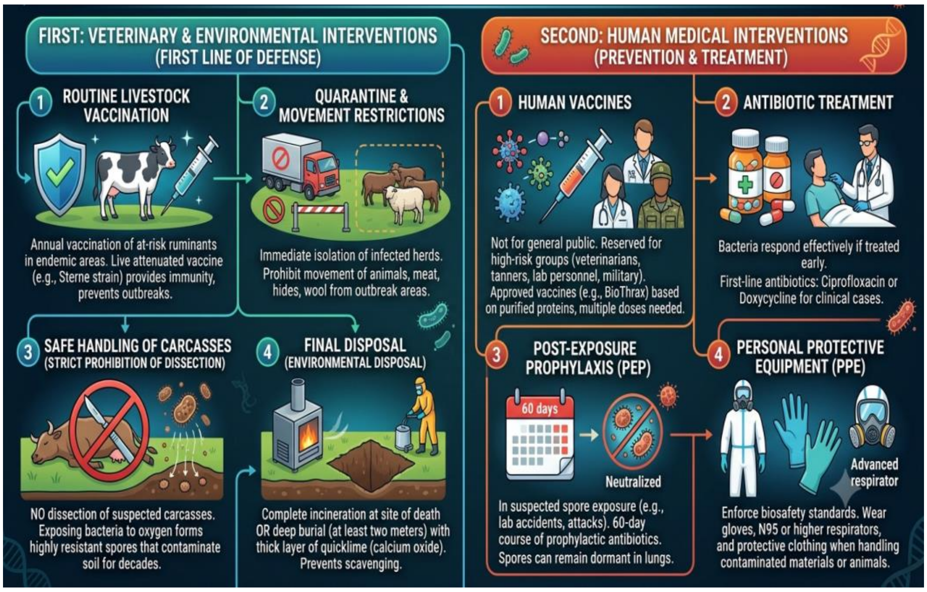

Figure 5: Effective Anthrax control :A two-pronged approach.

ONE HEALTH AND SUSTAINABLE DEVELOPMENT GOALS

Moving towards a broader, more preventative approach of the "One Health" concept by integrating anthrax control strategies in the context of the United Nations Sustainable Development Goals (SDGs) is a change from the mere response to a health crisis [45]. There are three major development targets which intersect with treatment of this disease (Figure 6):

Goal 3: Good Health and Well-being

Early intervention of animal outbreaks is the best way to control and avoid human transmission of zoonotic diseases to reduce morbidity and mortality. Improving epidemiological surveillance networks and the formulation of vaccines and treatment plan will help to build capacity to deal with health crises and increase international health security from biological threats both natural and man-made [46].

Goal 2: Zero Hunger

Anthrax is an economically devastating disease of animals which are the livelihood of large farming and pastoral communities. Sustainable immunization programs help to protect livestock herds, enable smallholder farmers to have stable livelihoods, safeguard secure food supply chains and prevent animal protein losses and contamination [47].

Goal 1: Life on Land

The best approach to controlling the disease is to manage soil in an environmentally conscious way to not create a decade’s long epidemic hotspot (the primary reservoir of spores). Carrying out these interventions properly with regard to carcass disposal will not lead to soil or ground water contamination, protected ecosystems and reduced cross-transmission among domestic and wild species, which will contribute to the conservation of biodiversity [48].

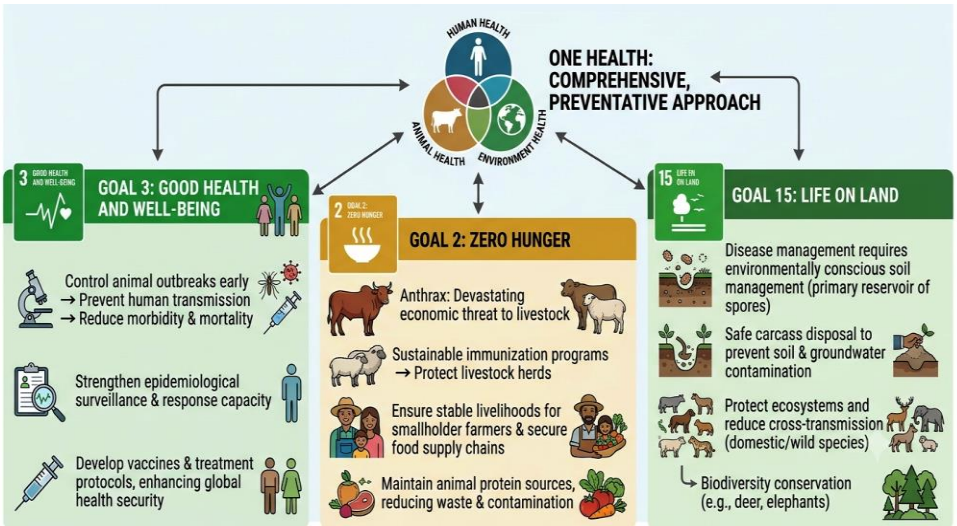

Figure 6: Combating anthrax and One Health relate to Development goals

CONCLUSION

Bacillus anthracis has a multidimensional impact not just in the realm of medicine, but also of public health and food security, and biosecurity at the global level. One of the main key factors in combating this threat is to break the biological and environmental cycle of the disease by not dissecting any carcass to avoid sporulation, disposal of carcasses safely by incineration or deep burial, and regular vaccination of livestock. Moreover, the collaboration between human medicine, veterinary medicine and environmental science within the "One health" concept is necessary. This integration will help secure livestock systems and farmers' livelihoods, help preserve ecosystems and biodiversity, and will increase the global capacity to predict and effectively manage health and biological crises.

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