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BACILLUS anthracis AND ANTHRAX

ABSTRACT-

Bacillus anthracis is the causative agent of the disease anthrax and occurs via the production of a plasmid encoded A-B type exotoxin. Edema factor is associated with Edema toxin and results in edema of affected areas, Lethal factor is associated with Lethal toxin and is known to inhibit intracellular signalling whilst disabling immunological cells, of which the latter is also performed by the adenylate cyclase Edema factor. Protective antigen is the third protein subcomponent of the toxin and serves to provide passage into target cells for EF or LF as a heptametrical complex via an acidified vesicle. As a naturally occurring soil bacterium it is found throughout the world mainly as dormant spores in soil. The bacterial cycle is reactivated in the presence of a suitable host, where germination, multiplication and subsequent production of toxins occur, generally leading to death. Due to the resistant nature of the spore, it has many military uses where it may readily be weaponised and disseminated via an aerosolised spray. However due to these properties terrorist organisations may use *B. anthracis* as a bioweapon, evoking death and psychological terror among civilian populations.

INTRODUCTION -

In the modern world the scientific study of micro-organisms has progressed rapidly, leading to the sequencing of emerging pathogens such as the SARS virus within months. Not to be forgotten are pioneers such as Pasteur, Koch and Petri, whom today's society owe a great debt. Before men like these the idea of disease causing pathogens was unheard of, rather more mystical explanations such as demons or curses were given to justify the onset of disease. In 1684 Leeuwenhoek became the first individual to observe '*wee animalcules*' and later Pasteur to disprove the theory of spontaneous generation[1]. However it was not until 1876 that the 'germ *theory of disease*' was created using '*Koch's postulates*'. These milestones in biological history led to the detection and classification of microorganisms which we are familiar with today.

MICROBIOLOGY OF *BACILLUS ANTHRACIS* -

Morphological structure was an area which had never been observed in great depth until the advent of powerful microscopes and staining techniques, eventually allowing three-dimensional digital images to be observed. Koch may have been able to postulate about the nature of bacteria, but would be amazed to view the aerobic, gram positive, rod-shaped, prokaryote *Bacillus anthracis (B. anthracis)*, with today's technology *(figure 1)*.

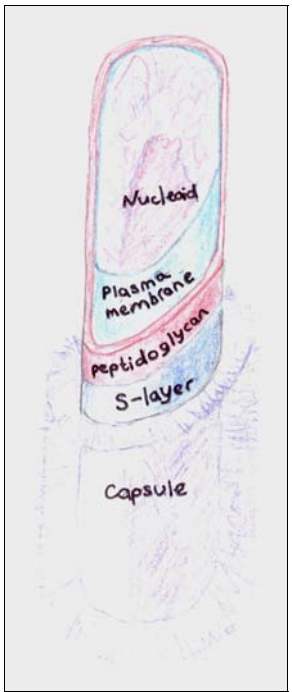


FIGURE 1– CUT AWAY SECTION OF *B. anthracis* IN VEGETATIVE FORM

As one of nearly 50 species comprising the *Bacillus* genus (*figure 2*) this organism varies between 3-5µm in length possessing a smooth, thick, peptidoglycan layer surrounding

the cell membrane. This unique bacterial layer serves to give shape and rigidity, having a similar role to the cellulose wall found in plant cells. Glycan tetrapeptide interconnected by crosslinked amino acids composes the biochemistry of peptidoglycan, whereby the extent of cross-linking confers its rigidity, allowing for over 100 variants.

Surrounding this layer is a patterned array of proteins called the paracrystalline surface layer, or S-layer. This two dimensional array comprises up to 10% of total cell protein and may function as a molecular sieve, preventing passage of large molecules whilst also providing rigidity in association with peptidoglycan. Detailed analysis of the S-layer reveals two 94-kDa proteins, Sap *(surface array protein)* encoded by the gene *sap* and EA1 *(extractable antigen 1)* by *eag* once *sap* expression has ended[2].

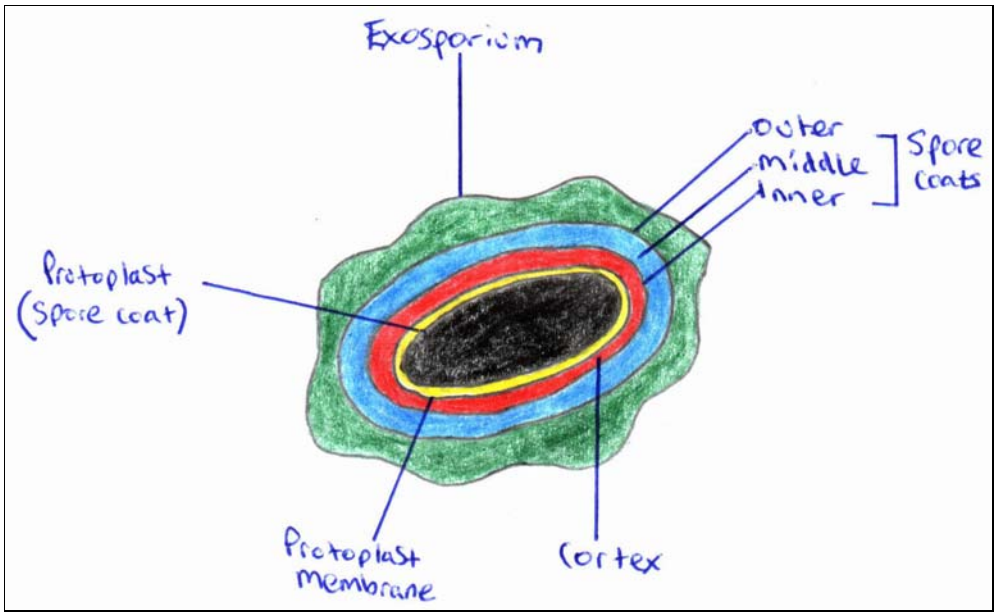
FIGURE 2 – *B. anthracis* IDENTIFICATION CHARACTERISTICS WITH ITS MOST CLOSELY RELATED MEMBER OF THE BACILLUS GENUS, *B. cereus*

SPECIES	Motility	Catalase Production	Parasporal Bodies	Lipid Globules In Protoplasm	Lecithovitellin Reaction	Citrate Utilisation	Anaerobic Growth	Voges Proskauer (V-P)	pH In V-P medium < 6.0	Growth At 50°C	Growth At 60°C	Growth In 7% NaCL	Acid From Ammonium Sulphate (AS) Glucose	Acid + Gas From AS Glucose	Nitrate Reduction	Casein Hydrolysis	Starch Hydrolysis	Propionate Utilisation
MORPHOLOGIC GROUP 1																		
B.anthracis	-	+	-	+	+	v	+	+	+	-	-	+	+	-	+	+	+	n/a
B. cereus	+	+	-	+	+	+	+	+	+	-	-	+	+	-	+	+	+	n/a

v = variable

Typical of this particular genus, *B. anthracis* is classified as an endospore (*figure 3)* forming bacterium containing dipicolinic acid. Produced endogenously these differentiated heat, radiation and chemical resistant cells are important in both the pathogenesis and ecology of the organism.

FIGURE 3 –ENDOSPORE STRUCTURE WITH NUMEROUS OUTER LAYERS



Most surprisingly is the ability to return to vegetative state within a short timeframe, mediated by the germination operon *gerX* found on plasmid pXO1. This re-growth is characterised by a period of activation (*in elevated temperatures*), germination (*in the presence of nutrients*) and outgrowth (*due to water uptake and protein synthesis*) conditions adequately provided within a mammalian body.

PATHOGENESIS -

As an encapsulated bacterium, *B. anthracis* is in this sense similar to *Salmonella* species, which possess this outermost capsule layer. Although non toxic itself, capsule presence contributes greatly to inhibition of phagocytosis, complement binding and antibody mediated targeting. Encoded by the pXO2 virulence plasmid (*figure 4)* genes *capB, capC and capA,* a slimy, adhesive, tight matrix layer comprised of polyglutamic acid (*poly-D-glutamyl)* is produced.

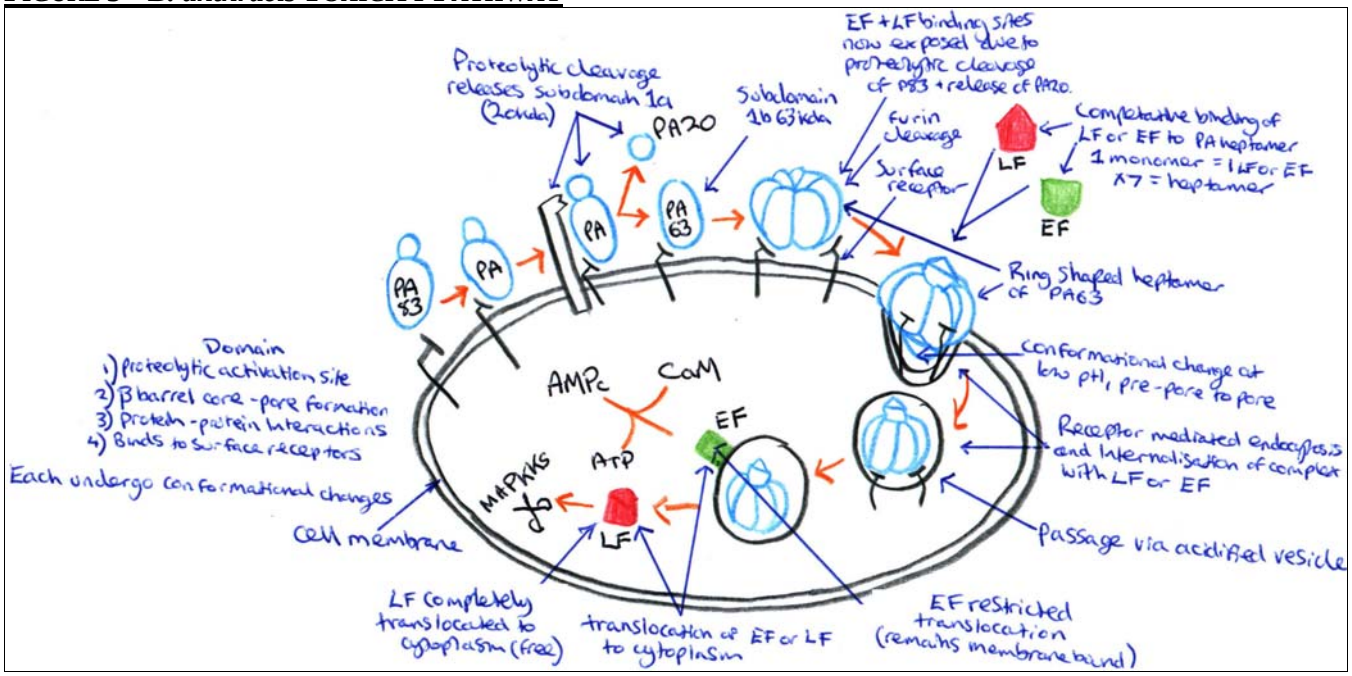
FIGURE 4 – PLASMID VIRULENCE PRODUCTION

PLASMID		VIRULENCE FACTORS	
pXO1	**pXO2**	**CAPSULE**	**TOXINS**
+	+	+	+
-	+	+	-
+	-	-	+
-	-	-	-

TOXINS -

However, most significantly is the production of an A-B type exotoxin encoded by the temperature sensitive plasmid, pXO1. Comprised of three protein components the toxin includes an adenylate cyclase the edema factor *(EF)* encoded by *cya*, a lethal factor *(LF)* by *lef* and protective antigen *(PA)* by *pagA*[3] *(antibodies to PA confer some degree of resistance)*. These components appear to be co rather than independent as singularly they do not cause anthrax, rather LF+PA causes death via a lethal toxin and EF+PA results in edema via edema toxin *(figure 5)*. Death occurs due to oxygen depletion, systemic shock, vascular permeability and failure of vital organs.

FIGURE 5 – *B. anthracis* TOXICITY PATHWAY



EDEMA FACTOR -

Slightly greater than PA, EF has 767 residues and in association with PA causes accumulation of fluids into tissue spaces *(edema)* by altering water and ion channel movements. EF is an adenylate cyclase converting adenosine triphosphate *(ATP)* into cyclic adenosine monophosphate *(cAMP)* dependant on the presence of calmodulin (*an important property, as elevated cAMP levels may increase membrane permeability whilst depleting ATP energy reserves concurrently).* After transportation to the cytosol, it interacts with host lipids and inhibits neutrophil function blinding the immune response.

LETHAL FACTOR -

LF is a zinc protease and binds to Zn^{2+}[4], in this way it resembles the botulinum toxin. The mode of LF serves to cleave mitogen-activated protein kinases *(MAPKKs)* thus inhibiting intracellular signalling. This negative effect also extends to disabling immunological cells like dendritic cells and macrophages, whilst stimulating high levels of tumour necrosis factor and interleukin-1 secretion due to elevated production of cAMP. However LF's ability to disable immune cells may have medicinal uses, it is now being researched as the basis of a drug to block unwanted immune responses such as in autoimmune diseases or transplant patients[5].

TOXIN COMMENTS -

Thus the bacterial strategy seems to attack the host in a variety of ways. It is largely protected from phagocytosis by its capsule, which also serves as an adhesive mechanism. As the bacterium is gram positive, its cell wall is essential harmless (*unlike toxic gram negative*), therefore attack must be mediated via an exotoxin containing a binding and active fragment. Components of this toxin seem to inhibit vital immune cells by catalytic activities, largely by energy depletion of ATP and concurrent attack of the host via unusually high cytokine production in response to elevated cAMP. When one obtains the common cold (*rhinovirus)* symptoms are due to immune responses like cytokine secretion causing inflammation. If these levels were excessively elevated during toxin attack, septic shock may occur. EF + LF are even assisted into the cell via host proteolytic cleavage of PA, revealing their binding sites! It is precisely this ability of the bacterium to hinder and inhibit vital immune cells which is so imperative in allowing its initial establishment and subsequent dissemination throughout the body.

***B. anthracis;* THE CAUSATIVE AGENT OF ANTHRAX -**

Causing up to 20,000 worldwide cases per year, anthrax may be acquired via three routes of entry; broken skin layer (*95% of cases),* inhalation (*infectious dose; 2500-55,000 spores*) and ingestion (*relatively rare)* (*figure 6*).

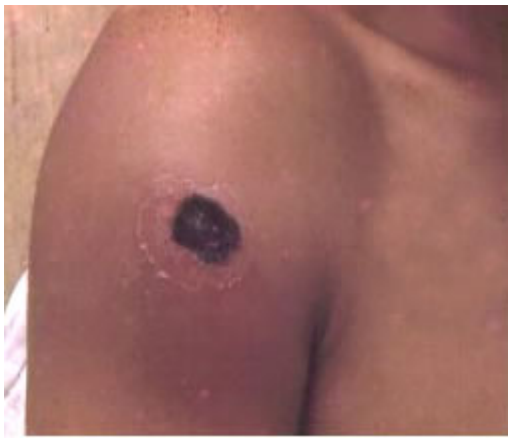
FIGURE 6 – POSSIBLE ROUTES OF INFECTION RESULTING IN ANTHRAX

TYPE OF INFECTION	ROUTE OF ENTRY	REASON FOR INFECTION	SYMPTOMS	% SURVIVORS	% MORTALITIES
CUTANEOUS	*Skin abrasion*	*Handling spore coated animal material (e.g. fur)*	*Small pimple within 2-3 days, progressing to painless black eschar*	*95%*	*20% (if left untreated)*
GASTROINTESTINAL	*Ingestion (mouth)*	*Ingestion of contaminated undercooked animal meat*	*Inflammation of intestine after 2-5days, nausea, vomiting, fever, abdominal pain*	*35-75%*	*25-65%*
PULMONARY*	*Inhalation (mouth)*	*Inhalation of spores*	*Begins resembling flu/upper respiratory infection, difficulty breathing, non contagious*	*~0%*	*~100%*

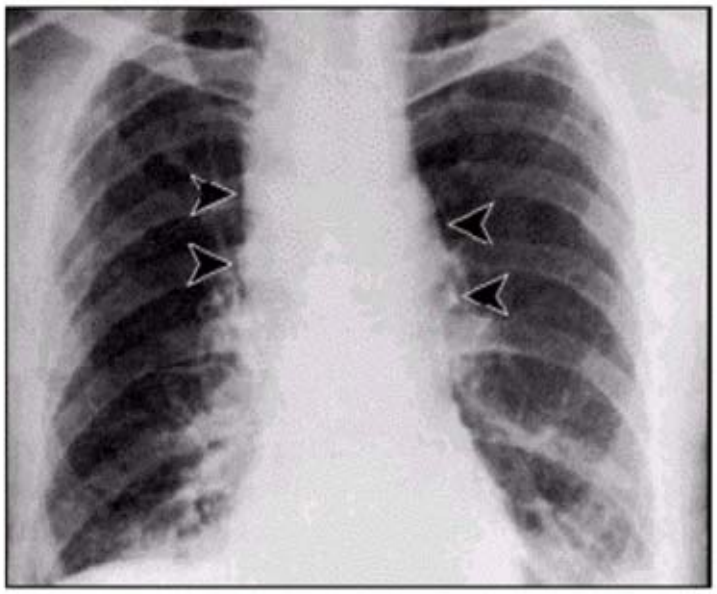
** The extent of this infection is largely determined by size of spores. Generally particles over 5µm will not penetrate deeply into the alveoli to cause severe symptoms (such as during attachment to other particles in air)*[6].

CUTANEOUS ANTHRAX-

This image displays a typical painless, black skin eschar surrounded by edema which has progressed from a red papule and vesicular ring. In this case, bacterial spores have germinated at the site of entry and multiplied, resulting in death of the surrounding tissue shown by the dark black colouration. Although edema toxin will be produced here, if left untreated a systemic infection may subsequently ensue. Death arises due to build-up of toxins, including lethal toxin, causing systemic shock.



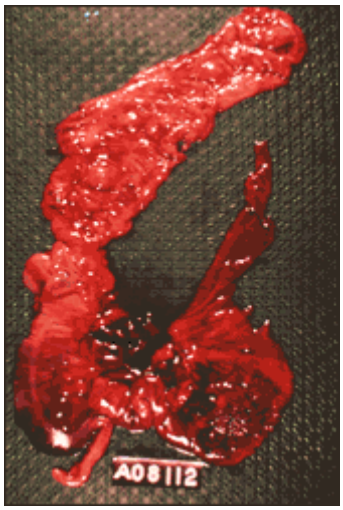
PULMONARY ANTHRAX –



Depicted in this chest x-ray[7] is the gradual widening of the mediastinal area, including the pleural sacs, heart and thoracic regions. Although at an early stage of infection, this will progress to a pleural effusion encompassing almost the entire chest region. Infection most likely occurred by the inhalation of a large number of spores[8], which were subsequently deposited in the terminal alveoli. Following ingestion by alveolar macrophages the bacteria germinated within them, whilst on-route to mediastinal lymph nodes via the pulmonary lymphatics. Vegetative cells will begin to multiply in lymph node regions, subsequently overwhelming the nodes and become competent of toxin production. Initially the mediastinal area and lymph nodes are targeted, causing edema and severe loss of blood to the surrounding tissues (*haemorrhage*) in the lungs. Ultimately a systemic infection will ensue via the thoracic duct, causing septicaemia then death[9]. Almost 100% of cases will be fatal due to a late diagnosis, fluid build-up in lungs and dissemination via the circulatory and lymphatic systems.

GASTROINTESTINAL ANTHRAX –

A similar infection pattern is found with cutaneous anthrax in the sense that bacteria are localised around and enter via a pre-existing wound, here within the mucosal lining of the intestines. Germination of spores or multiplication of bacteria occurs in the submucosal tissue, where toxin production will be initiated. As shown in this picture edema toxin produced, resulting in breakdown of endothelial cell linings causing severe internal bleeding. Dissemination occurs again via the lymphatic system[10], the extent of which determines severity of symptoms. Accumulated toxin production leads to septicaemia and death



DIAGNOSIS -

Diagnosis of anthrax accompanies decontamination *(hypochlorite)* procedures and varies according to the form acquired; black skin eschars are the most obvious external sign and chest x-rays the most obvious internal sign. Confirmatory assays (*figure 7)* occur by the culture of bodily fluids or tissues stained with polychrome methylene blue.

FIGURE 7 – LABORATORY ASSAYS USED IN CONFORMATION OF *B. Anthracis*

TYPE OF INFECTION	SOURCE OF SAMPLE	IDENTIFICATION PROCEDURES	CULTURE GROWTH**	COLONY CHARACTERISTICS	MOTILITY TEST
		Gram positive rods = Gram stain *Capsule = India ink stain* *Alternative methods involve use of fluorescent antibodies to identify capsule or PCR analysis to reveal toxin genes*	*Inoculate sample & streak on HBA. Incubate 3 days with CO^2, growth may appear after 8hrs, No growth on MacConkey agar*	*Well isolated colonies 2-5mm, possible 'medusa head' projections, grows rapidly, flat, irregularly round, tactile, ground glass appearance, may appear as chains under microscope*	*Non-motile, do not deviate from inoculum swab, observe under light microscope, 40X objective*
CUTANEOUS	*Vesicular fluid/ Swab beneath eschar surface*				
INTESTINAL	*Blood, stool, rectal swab*				
PULMONARY	*Blood, sputum*				

FACTORS INFLUENCING DIAGNOSIS -

Whilst all forms of anthrax are extremely serious, mortality rates often depend on how soon diagnoses and subsequent treatment *(figure 8)* occurs, spore dosage, toxin production and state of the host immune system. However diagnosis may often occur too late due to an incubation period and initial stages of infection which may not trigger the victim's immediate attention. Inhalation resembles the flu and may have a 6 week incubation period (*Sverdlovsk*[11]*)*, skin pustles begin resembling an insect bite and intestinal infections may be mistaken for food poisoning.

All these factors work in favour of the bacteria, allowing adequate time for establishment, multiplication, dissemination and production of toxins. To compound these problems, antiphagocytic mechanisms and germination within alveolar macrophages limit the effectiveness of immune cell defence. The disease itself also occurs in two stages, the first whereby bacteria germinate, become established and multiply may not as already discussed, cause serious attention grabbing symptoms. This incubation stage is also dealt with quite efficiently by the host system, where they are generally filtered out by the spleen. However the second stage, intense

multiplication, systemic dissemination and maturation to toxin production causes both rapid and serve onset of symptoms associated with organ failure.

FIGURE 8 – TREATMENTS FOR SUSPECTED ANTHRAX CASES[12]

DRUG	REASON FOR ADMINISTRATION	ROUTE	SIDE EFFECTS
****PENICILLIN (500MG)**	*Protection against possible exposure*	*Oral Tablet (as prescribed)*	*Stomach upsets, breathing difficulties, rash, facial swelling*
****DOXYCYCLINE (100MG)**	*Protection against possible exposure including inhalation*	*1 Oral Tablet twice daily / 12hrs intravenously for Inhalational cases*	*Breathing problems, nausea, sensitivity to sunlight*
*****CIPROFLOXACIN (500MG/400MG)**	*Protection against possible exposure including inhalation*	*1 Oral Tablet twice daily / 12hrs intravenously for Inhalational cases*	*Dizziness, headache, increased chance of sunburn, seizures*
AMOXICILLIN (250MG/5ML)	*Protection against possible exposure*	*Oral Tablet every 8hrs / Oral liquid*	*Breathing problems, swelling, itching*

All medication must be completed to prevent the onset of disease due to varying bacterial latency periods, effectiveness correlates to how soon medication is given after suspected infection

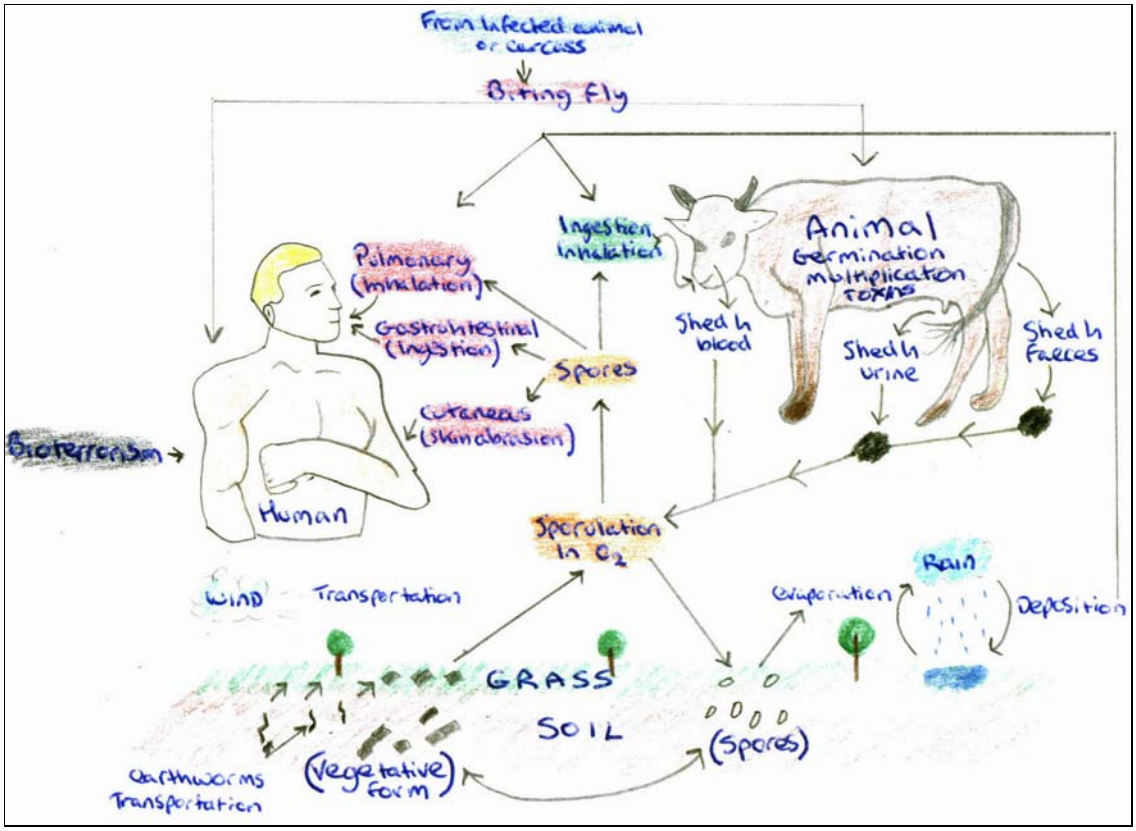
*** Seems to be most effective treatment when combined*

**** May be favoured during bioterrorist attack, due to new resistant strains*

ECOLOGY -

B. anthracis has a varied relationship with other organisms and its physical environment. Present as living bacteria, dormant spores and found in soil, water, air and vegetation, this organism has a wide yet constrained ecological niche (*figure 9).*

FIGURE 9 – ECOLOGICAL CYCLE OF *B. anthracis*



EDAPHIC INFLUENCE –

As a natural saprophyte it is most commonly found in moist, alkaline, calcium rich soils with abundant decaying organic material producing high nitrogen levels, using herbivores such as horses or cattle as its primary germination and reproduction vesicle.

In soil and water, *B. anthracis* spores[13] have been known to survive for decades, making land previously used for military testing unusable (*Gruinard Island, Scotland*[14]*)* unless decontamination with water and formaldehyde[15] occurs. However in the square ended vegetative state, specific nutrient and physiological conditions are required for survival.

Edaphic factors vary between geographical locations due to either abiotic factors such as land topography or biotic factors like anthropogenic interference, both of which ultimately produce varying environments either favouring or hindering bacterial germination. Therefore some soils such as in colder, dryer climates are likely to have more endospores present than warm, moist climates which will have a higher

percentage of bacteria in the vegetative state, although nutrient requirements such as calcium, alkalinity and organic material will also determine this. However these factors are largely theoretical and vegetative cells in the soil are rare, therefore the large majority of times they are found as spores. Soil samples may be tested for spore content through a variety of methods such as direct agar contact, vacuuming, swabs and wiping, before being taken for laboratory identification procedures.

ZOONOTIC INFECTIONS -

One constant in the ecological cycle of *B. anthracis* are the presence of mammalian hosts such as grazing herbivores, which provide suitable conditions for germination to occur. Typical signs of infected animals including becoming distressed, not eating food or producing less milk, difficulty in breathing may also occur due to fluid build up in lungs and bleeding from the nose due to increased vascular permeability. Many countries may vaccinate livestock or administer treatment. Should the animal not respond to treatment and die, in no case should it be opened for examination so as to avoid sporulation of vegetative cells in contact with air. Figure 10 summaries methods used for infected animal disposal[16].

FIGURE 10 – DISEASED ANIMAL DISPOSAL METHODS

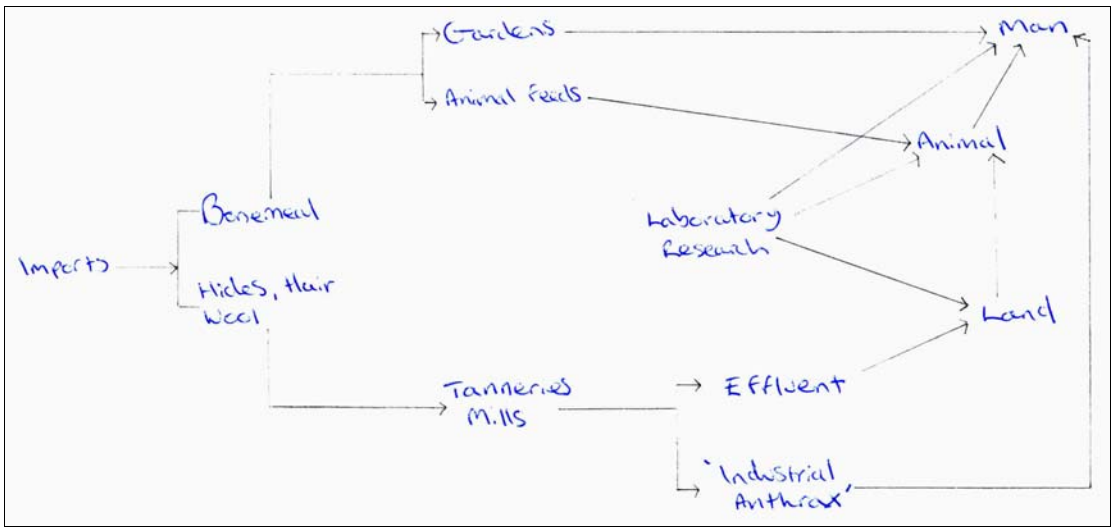
MEANS OF DISPOSAL	METHOD	ADVANTAGES	DISADVANTAGES
CARCASS UNMOVED	*Covered with leaves, sticks, fenced off*	*Where other means are unavailable, cheap, quick, bacteria will not sporulate within animal*	*Disturbance by scavenger may cause sporulation, anal leakage, bleeding via mouth / nose may also cause sporulation*
BURIAL	*Carcass buried 6ft below ground level with contaminated soil*	*Cheap, putrefactive process kill bacteria, when no fuel available*	*Ploughing or construction work may disturb site, earthworms may bring spores to surface*
INCINERATION (*SEE PHOTOS OF RAISED INCINERATION*)	*Soil & animal burnt, decontaminate nose/anus varying means of incineration, e.g. pit/raised*	*Vegetative cells vulnerable to heat, dilution in air minimises immediate spore risk*	*Spores may survive in inefficient incinerator, aerolised updraft of spores, requires specialised equipment*
RENDERING	*Decontamination, chopping into small pieces, passed through steam chamber 100-150°C*	*Parts of carcass may be reused for commercial purposes, most effective method of disposal*	*Time consuming, expensive equipment, waste water if untreated can contaminate environment.*

As the bacteria rarely germinate in soil and almost exclusively within mammals, this creates an interesting eco-genetic link. Whilst most bacteria replicate and generally live in the open environment, they are constantly exposed to factors which may alter their genetic makeup, i.e. become mutated. Having an almost exclusive replication within mammals avoids potential mutagenic factors such as UV radiation, chemicals or even bacteriophages, thus accounting for the lack of diversity between natural strains.

GLOBAL DISTRIBUTION -

Most people do not have to worry about contracting anthrax as it is primarily a zoonotic disease of herbivores and unless deliberately distributed, there is a very low natural risk of infection. Incidences of anthrax due exist and are directly related to the interaction with diseased animals. An example of which occurred during 1979-1985 where 10,000 people in Zimbabwe[17] contracted anthrax from handling and ingesting infected cattle. Thus those most at risk include agricultural workers, especially in the regions of Asia (S. *India, Vietnam)*, the Middle East (*SW Iran*[18]*)*, Southern parts of Europe (*Greece, Spain)* and North America (*Texas, Nebraska)*. However due to the resistant nature of spores, global dissemination has increased in correlation with improved exports and imports between countries (*figure 11*).

FIGURE 11 – POSSIBLE ROUTES LEADING TO ANTHRAX CASES BETWEEN TRADING NATIONS



Whilst these routes do provide possible means of exposure, examples do exist where people working with infected animal products do not all become infected. During

1899-1912 only 354 cases of anthrax were reported out of thousands of workers exposed to spores in Britain. In the USA mill workers were found to be inhaling 600-1300 spores over an eight hour shift, only 1.4% developed the disease. Workers in wildlife reserves also tend not to become infected. This data suggests; 1) the infective dose of spores is relatively high and individuals are unlikely to become exposed to thousands of spores unless artificially distributed 2) some individuals are more susceptible than others 3) different strains may have differing infective doses 4) decontamination of animal material such as goat hair[19] may prevent further cases 5) natural strains are not as lethal compared to '*military grade*' spores, when comparing incidences such as the 10,000 infected in Zimbabwe (*with a low fatality rate)* to the Sverdlovsk incidence from a military installation (*high fatality rate*[20]*).* Therefore one may be inclined to become less concerned with natural strains of *B. anthracis,* and more so with refined military strains, in particular their use as a bioterrorism agent.

USE AS BIOTERRORISM AGENT -

Historically, the use of biological weapons may be traced back to the 6th century BC, with the Assyrians using rye ergot *(containing a fatal mycotoxin)* to poison enemy wells. During World War II the Japanese stockpiled 400 kilograms of anthrax[21], using prisoners as research subjects. In 1979 an accidental aerosol release of anthrax spores occurred in Sverdlovsk causing 66 civilian fatalities. In 1995, four years after the first United Nations inspection of Iraq, 8,500 litres of concentrated anthrax were found, of which 6,500 litres was filled into munitions for offensive purposes[22]. September 11th 2001 saw the deliberate distribution of anthrax spores using postal services, each letter containing enough spores to kill 100,000 people. Examples such as these clearly illustrate the increasing potential threat to Western nations and their neighbours; deadly bacterial *(brucellosis)*, viral *(smallpox)*, toxin *(botulinum)*, nuclear and chemical *(cyanide)* agents may be assimilated and disseminated by hostile nations *(Halabja, 1988, Iraq*) or terrorist organisations *(Tokyo subway, 1995, sarin nerve gas attack, Japan)* with broad and horrific consequences[23].

In 1969 President Nixon cancelled all offensive biological and toxin weapon research leading to the destruction of stockpiles in 1971-1972; among the destroyed agents were *B. anthracis*. Since then over 140 countries including Russia and the United Kingdom signed a convention prohibiting the stockpiling of biological agents and toxins for offensive purposes[24]. However not all countries have followed this example, at least 10 hostile nations including Iraq, North Korea and Iran were later suspected of stockpiling offensive agents.

BIOLOGICAL AGENTS AND HEALTH AUTHORITIES -

Due to this threat in the modern world, the role health authorities have changed from identifying natural disease outbreaks to distinguishing between natural and intentional outbreaks[25]. Important factors include the examination of historical disease patterns within populations, the recognition of symptoms, routes of exposure and the subsequent laboratory identification of pathogens. Therefore the pattern of disease enables one to distinguish between a natural and intentional outbreak, such as a large number of unusual cases in a confined geographical location within a short timeframe, causing many unexplained diseases or deaths. Should an anthrax attack occur in a civilian population, it is estimated to cost health services $26.2 billion per 100,000 individuals exposed[26]. However the recognition of these factors may be compounded by the type of biological agent used (*figure 12*), it is therefore imperative that education of the public and preventative measures are untaken at times of greatest risk, although this must be done with caution to avoid widespread panic and overwhelming health services[27].

FIGURE 12 – VARYING EFFECTS OF BIOTERRORISM AGENTS

RESPIRATORY CASUALTIES	
RAPID ONSET	**DELAYED ONSET**
Nerve Agents	*Inhalation Anthrax*
Cyanide	*Pneumonic Plague*
Mustard Gas	*Q Fever*
SEB Inhalation	*Ricin Inhalation*
NEUROLOGICAL CASUALTIES	
RAPID ONSET	**DELAYED ONSET**
Nerve Agents	*Botulism-peripheral symptoms*
Cyanide	*VEE-CNS symptoms*

***B. anthracis* AND BIOTERRORISM -**

Using *B. anthracis* spores has advantages and disadvantages (*gigure 13*). However successful dissemination has never really occurred on mass by terrorist organisations and seems more suited to military applications where highly refined '*military grade*' powder is used. Failed attempts include the terrorist organisation which carried out the sarin nerve gas attack in Tokyo, reports suggested they had tried to release spores on many occasions but failed. Recently during the September 11th attacks spores were deliberately distributed by a government scientist in letters, infecting 22 people. However this latter example demonstrated the usefulness of PCR, allowing variable number tandem repeats (*VNTRs*)[28] to be identified in the variable region of the vvrA gene[29], revealing the strain and its origin. Where individuals are at risk whether in industrial, military or civilian professions, a vaccine derived from the supernatant of an attenuated strain is available for those aged 18-65. It is administered in 6 vaccinations over an 18 month period, followed by yearly boosters.

FIGURE 13 – FACTORS RELATING TO USE AS BIOTERRORISM AGENT

ADVANTAGES	DISADVANTAGES
• *Spores highly resistant, thus easy to transport + weaponise* • *Natural strains easy to cultivate* • *Incubation period* • *Aerosolised spray can infect large numbers* • *Cyclic infection due to dormant spores and sporulation* • *Psychological terror*[30]	• *Military grade, non clumping, dry powder is most effective form, but expensive + time-consuming to prepare* • *Environmental factors make dissemination patterns unpredictable* • *Dilution effect in air* • *High Infectious dose* • *Suspended spores most effective but difficult to achieve* • *Liquid anthrax falls to ground quickly, not very effective* • *Antibiotics effective if used early* • *Non contagious* • *Spores fall to ground rapidly* • *Vaccines*

CONCLUSION –

Figure 14 summaries findings presented in this report.

FIGURE 14 – REPORT SUMMARY

HISTORY	First isolated by Koch to prove bacteria cause disease
MAIN CHARACTERISTICS	Gram-negative, spore forming, Bacillus genus, rod-shaped, A-B exotoxin
PATHOGENICITY	Virulence plasmids pXO1 -> Toxins EF/Edema Toxin (*cya)* LF/Lethal Toxin (*lef)* PA/Protective antigen (*pagA)* pXO2 -> Capsule (poly-d-glutamyl) *capB, capC, capA*
DISEASES	Cutaneous anthrax Pulmonary anthrax Gastrointestinal anthrax
DIAGNOSIS	Horse blood agar / polychrome methylene blue
TREATMENT	Vaccine, Penicillin, Doxycycline, Ciprofloxacin, Amoxicillin
ECOLOGY	Zoonotic disease of herbivores, saprophyte, mainly found as spores
USE AS BIOTERRORISM AGENT	Most effect as military grade, non clumping dry powder, potential terrorist uses

Word Count – 2,935

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