Rev. sci. tech. Off. int. Epiz., 2014, **33** (2), 593-604

Anthrax as an example of the One Health concept

R.G. Bengis [1] & J. Frean [2]

(1) World Organisation for Animal Health, Working Group on Wildlife, P.O. Box 2851, Port Alfred, 6170, South Africa
(2) National Institute for Communicable Diseases, and University of the Witwatersrand, P/Bag X4, Sandringham 2131, Johannesburg, South Africa
*Corresponding author: roybengis@mweb.co.za

Summary
Anthrax is a peracute, acute or subacute multispecies bacterial infection that occurs on many continents. It is one of the oldest infectious diseases known; the biblical fifth and sixth plagues (*Exodus* chapters 7 to 9) that affected first livestock and then humans were probably anthrax. From the earliest historical records until development of an effective vaccine midway through the 20th Century, anthrax was one of the foremost causes of uncontrolled mortality in cattle, sheep, goats, horses and pigs, with 'spill over' into humans, worldwide. With the development of the Sterne spore vaccine, a sharp decline in anthrax outbreaks in livestock occurred during the 1930–1980 era. There were successful national vaccination programmes in many countries during this period, complemented by the liberal use of antibiotics and the implementation of quarantine regulations and carcass disposal. However, a resurgence of this disease in livestock has been reported recently in some regions, where complacency and a false sense of security have hindered vaccination programmes. The epidemiology of anthrax involves an environmental component, as well as livestock, wildlife and human components. This makes anthrax an ideal example for discussion in the One Health context. Many outbreaks of anthrax in wildlife are undetected or unreported, owing to surveillance inadequacies and difficulties. Human disease is generally acquired accidentally during outbreaks of anthrax in domestic livestock and wildlife. The exception is deliberate targeting of humans with anthrax in the course of biowarfare or bioterrorism.

Keywords
Anthrax – Environmental persistence – Host susceptibility – One Health – Transmission – Zoonosis.

Eco-epidemiological considerations

The organism and its environment

The life history of *Bacillus anthracis* differs markedly from those of most other pathogenic bacteria in that its replication and persistence appear to depend on extreme virulence and on the acute death of the host, after which it survives for prolonged periods outside the host (1). It is one of the few pathogens that must kill its host in order to propagate. Between outbreaks, the anthrax bacterium survives in the environment as a highly resistant spore (2). Anthrax spores survive best in alkaline soils that are rich in calcium and have a relatively high moisture and organic content (3). The characteristics of dormancy and resistance to environmental factors displayed by these spores are a function of their structure, especially their hydrophobic exosporium and spore coat, which may also restrict their dispersal (4). The low water content of the spore confers resistance to heat and ultraviolet light (5). Calcium cations appear to participate in maintaining dormancy, as well as in the germination process. Spores can survive for years in the environment and, under optimal conditions, some may survive for decades or even centuries (6, 7). Although *B. anthracis* appears to be a relatively monomorphic species, recent progress using molecular techniques to determine phylogenetic relationships of isolates from various global locations has enabled a broad separation of isolates into two major clonal groups, referred to as A and B. The A and B2 branch isolates are distributed worldwide, while the B1 branch is found only in southern Africa (8). It has also been shown that genomics has a strong impact on strain distribution, and this includes the possibility of

niche specialisation within a sublineage. This may improve our understanding of the genetic–ecological dynamics of *B. anthracis* and may lead to more refined predictive modelling for different regions (9, 10).

Host factors

Anthrax is a multispecies disease that can infect mammals of most taxonomic groupings. Ruminants and hindgut-digesting herbivores are the most susceptible. Carnivores and primates (including humans) are more resistant to infection, and ostriches are the only avian species in which natural infection has been regularly reported (11). Carcass scavengers are generally highly resistant to anthrax. Most mammalian domesticated livestock are highly susceptible, and Hugh-Jones and de Vos listed 4 free-ranging perissodactyl, 24 artiodactyl, 9 carnivore and 2 primate species in southern Africa in which natural infection has been confirmed (12). On a broader geographical scale, Cormack Gates *et al.* listed 23 free-ranging bovid, 6 cervid, 17 carnivore and 2 primate species worldwide of which representatives were confirmed to have died of anthrax, as well as several free-ranging zebra and rhino species, and Asian and African elephants (3). In most outbreaks of anthrax, no gender or age predilections are generally reported. However, bison bulls (*Bison bison*) and African buffalo bulls (*Syncerus caffer*) are generally over-represented (this is probably linked to their behaviour), and younger animals of most species tend to be spared because most of the nutritional requirements of unweaned animals come from their mothers' milk, and not the environment (12).

Pathogenesis and transmission

It is well established that *B. anthracis* is not a highly invasive organism. The 50% lethal dose (LD_{50}) for anthrax challenge is much higher by the oral or inhalation route than via the parenteral route. Once the anthrax spore has entered the mammalian body, germination is triggered by moisture, warmth and the presence of L-alanine in the blood serum. The bacterium undergoes exponential replication within regional nodes, then passes via the lymphatic vessels into the bloodstream. Coker *et al.* (2003) showed that a major factor determining virulence is the number of plasmids controlling the cellular capsule: the thicker the capsule, the higher the virulence (13). The bacilli are taken up in other parts of the reticuloendothelial system, particularly the spleen, to establish secondary centres of infection and proliferation (14, 15, 16). The vegetative anthrax bacilli produce a lethal combination of exotoxins, responsible for the severe clinical signs and post-mortem lesions of anthrax. The toxin complex consists of two separate protein toxins, designated *oedema factor* (OF) and *lethal factor* (LF), and a cell receptor-binding protein called *protective antigen* (PA). Protective antigen combines with OF or LF to form *oedema toxin* (OT) and *lethal toxin* (LT), respectively (15, 17). The toxin complex acts to reduce phagocytosis, increase capillary permeability and compromise blood clotting mechanisms. The net effect produces massive oedema (including in the lungs and brain), haemorrhage, renal failure and terminal hypoxia (14, 15). Various mammalian taxa have differing sensitivity to these exotoxins, reflected in the course of infection and terminal bacteraemic counts (18). Higher terminal bacteraemic counts are required to kill animals with lower sensitivity to exotoxins (Fig. 1), and *vice versa.*

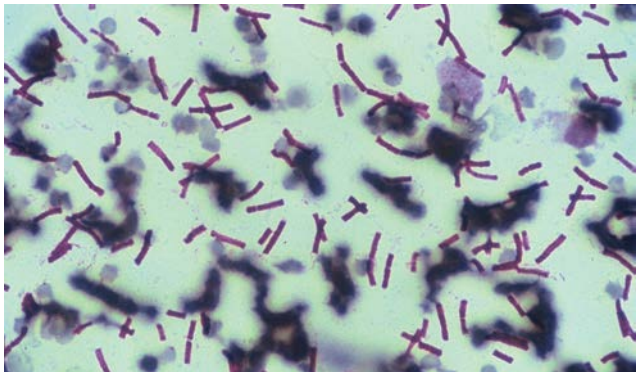

Fig. 1
High terminal bacteraemia in a greater kudu
© R. Bengis

In all *Bacillus* species, sporulation is a response to low nutrient conditions or dehydration, which effectively limit the diffusion of nutrients to the bacillus. Although limited sporulation may occur prior to death, generally the anaerobic conditions within the carcass prevent the anthrax bacilli from replicating, despite the nutrient-rich medium, or sporulating to any large extent (1, 7). In addition, putrefactive anaerobic bacteria from the gastrointestinal tract cause the carcass to start to decompose rapidly. The vegetative forms of *B. anthracis* are very susceptible to competition from other microbes, and if putrefactive organisms dominate before the carcass is opened, the anthrax bacilli are quickly eliminated (11, 14, 18). In nature, however, carcasses are rarely left intact long enough for this to occur. Scavengers opening the carcass help to disperse vegetative *B. anthracis* into aerobic microenvironments where, through either metabolic activity or dehydration, nutrients become limited and sporulation can proceed (1). Pools of blood and tissue fluids, kept under aerobic conditions around the carcass site, favour sporulation. Many of these spores remain at the site of the dead animal, but some may be dispersed by water run-off, wind and scavengers (19, 20). Following sporulation, the part of the life-cycle involving environmental dormancy of the organism repeats itself.

Transmission of anthrax relies on ingestion, percutaneous/parenteral inoculation, or inhalation of spores. Ingestion of spores is generally associated with drinking from a contaminated water source, or ingesting contaminated grazing, browse, flesh or bones. Ingestion is probably the most common route of infection in animals. In predators

and porcine species, oedematous lesions generally develop in the oral and pharyngeal area, whereas in domestic and wild herbivores, necro-haemorrhagic lesions develop in Peyer's patches or segmental regions of the small intestine, eventually progressing to septicaemia (21, 22). Osteophagia by pregnant or lactating animals, or animals on rangeland with phosphate-deficient soils, is an important cause of infection in certain regions (18).

Bacillus anthracis may penetrate broken skin or mucous membranes, and this route of infection is most commonly seen in humans who have handled anthrax-infected animal products. The animal equivalent is infection of subcutaneous tissues, generally as a result of mechanical transmission by the contaminated mouthparts of biting insects. Cellulitis characterised by subcutaneous swelling is particularly common in equine and porcine species (11). In carnivores, the massive facial and oral oedema and necrosis are thought to be due to penetration of oral or pharyngeal mucous membranes by bone spicules while the animals chew the bones of infected carcasses (12, 18). Following percutaneous or mucous membrane penetration, the spores germinate and give rise to a small oedematous area containing encapsulated vegetative bacilli. The lesion then progresses in size, macrophages and fibrin deposits appear, the lymphatics dilate and fragmentation of connective tissue occurs with increasing oedema. Phagocytosis appears minimal, and the infection then progresses to a lymphangitis followed by lymphadenitis (16). If the infection is not halted at this stage it may become systemic, and result in fatal septicaemia.

Inhalation is probably the least common route of infection in livestock and wildlife living in the 'open air' because anthrax spores tend to clump together with surrounding organic material, and are not easily aerosolised. Anthrax outbreaks in animals are commonly associated with low-lying depressions and rocky seep areas with high moisture content, high organic content and an alkaline pH. Successive cycles of flood run-off and evaporation appear to concentrate the anthrax spores in these depressions, referred to as 'concentrator areas' (7, 12). With the seasonal decrease in water levels in these concentrator areas, the resident animals (livestock or wildlife) using the water source may be increasingly exposed to higher concentrations of accumulated spores. In addition, water and wind erosion, or large- or small-scale excavations or seismic events, may expose spores hidden in the soil column or may expose carcass remnants of earlier anthrax victims (7, 12).

During an anthrax outbreak, each successive victim may become an additional source of infection. The modes of transmission from the infected carcass or bacteraemic animals to the surrounding population at risk will vary in the different environments with their associated species (18). Anthrax spores may directly contaminate pasture in close proximity to a carcass, and terminally ill animals that are febrile and thirsty may die close to water or even in it (Fig. 2). In addition, anthrax bacilli and spores from a carcass may be dispersed by water run-off, scavenging birds and carnivorous mammals (12, 19, 20). Vegetative anthrax bacilli do not survive the digestive processes of carnivorous birds and mammals, but the hardy anthrax spores pass through the gastrointestinal tract unscathed to indirectly contaminate distant sites. In southern Africa, browse

Fig. 2
Dead buffalo contaminating a water pool
© R. Bengis

Fig. 3
Necrophilic flies on vegetation close to an anthrax carcass
© R. Bengis

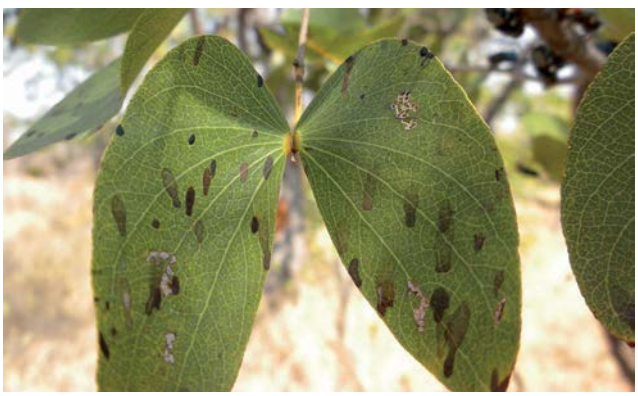

Fig. 4
Browse contaminated by necrophilic flies
© R. Bengis

contamination occurs through the agency of non-biting necrophagic flies (e.g. genera *Lucilia* and *Chrysomyia*), which feed on the body fluids and proteins of infected carcasses and then alight on nearby vegetation, depositing infectious vomit and faecal droplets on the leaves (Figs 3 and 4). This is an important transmission mode in ecosystems that are well populated by browsing herbivores such as greater kudu (*Tragelaphus strepsiceros*) and nyala (*Tragelaphus angassi*) (11, 13, 18). These necrophagic flies have been referred to as 'case multipliers' (4), and cause localised clustering of cases. Most outbreaks in southern Africa involving the above-mentioned modes of transmission tend to occur in the dry season or winter.

In certain regions of the world, haemophagic biting flies have been implicated as important mechanical transmitters of anthrax infection in herbivores (12). These flies have been referred to as 'space multipliers', because they are responsible for both local clustering and centrifugal spatial spread of infection (4). Haemophagic flies (mainly tabanids and stomoxids) have been documented as important transmitters of anthrax in white-tailed deer (*Odocoileus virginianus*) and bison in North America. In southern Africa this transmission mode involves mainly hippoboscid biting flies, and it has been documented in greater kudu, plains zebra (*Equus burchelli*), and horses. In Uganda, Zambia and South Africa, large biting flies of the genus *Pangonia* may play an important role in anthrax outbreaks in hippopotami (*Hippopotamus amphibious*). In northern Russia, including the Taimyr Peninsula, tabanid flies appear to be the most important mechanical vectors of anthrax in reindeer (*Rangifer tarandus*).

In general, haematophagic fly transmission is closely related to rainfall patterns and resulting vector abundance, and is mainly a summer season phenomenon. In west Texas, late winter/early spring rainfall followed by a dry summer frequently results in multiple outbreaks (4, 12).

Patterns of disease in animals

The general pattern seen in anthrax endemic regions is that of sporadic cases occurring on an irregular basis, but with some form of seasonal pattern. These sporadic events are interspersed with periodic outbreak clusters, or even propagating epidemics (12, 23, 24) that are generally linked to increased densities or concentrations of preferred host species, or abundance of arthropod vectors. These propagating epidemics are generally self-limiting, and tend to follow a normal epidemic curve (12). Where anthrax outbreaks are a winter or dry season phenomenon, infection by ingestion appears to be the most important transmission mode, whereas summer outbreaks are generally associated with peaking populations of biting flies and percutaneous transmission, but may also be linked to forage flushes in low-lying concentrator areas that have formed around rain pools. A feature of dry season outbreaks in southern Africa is that they are dramatically terminated by the onset of the summer rains (12, 18).

Fig. 5
Typical posture and body condition of a nyala that has died of anthrax
© R. Bengis

Clinical signs in animals

Anthrax may present as a peracute or acute disease in ruminants. Clinical signs include disorientation, ataxia, respiratory distress, and apoplectic seizures followed by acute death. The victims are generally in good body condition, and carcasses frequently demonstrate opisthotonus with extensor rigidity of the forelimbs (Fig. 5). In equine and porcine species, abdominal pain (colic) is frequently evident and there may be diarrhoea. Cutaneous and localised swellings, which may be present at various anatomical sites, are also common in these two taxa (11, 22).

Although predators in general are less susceptible to infection by *B. anthracis*, they are highly vulnerable to massive exposure when they feed on infected carcasses, ingesting billions of organisms. Clinical cases in predators are generally more common during the early phases of an epidemic in a new locality. If predators survive their first few exposures to anthrax, they appear to develop a strong immunity. Most predators in anthrax endemic areas appear to become totally resistant (18, 24, 25).

Post-mortem and external macroscopic pathology

Post-mortem examination of animals that have died of anthrax is not recommended, because opening the carcass assists sporulation. There is also a zoonotic danger to the veterinarian or pathologist. In animals that have died of anthrax, *rigor mortis* is incomplete or absent, and rapid bloating occurs. Typical of an acute disease, the animals are generally in good body condition. Blood-stained fluid may exude from one or more body orifices (Fig. 6). Petechiae and

ecchymoses are often present in unpigmented or hairless areas of the skin (Fig. 7). The blood is dark and tarry and frequently does not clot. The principal macroscopic lesions seen in septicaemic anthrax in herbivores are widespread oedema, haemorrhage and necrosis (12, 14, 18, 21). Extensive pulmonary and mediastinal oedema is a common finding. Most lions (*Panthera leo*) and leopards (*Panthera pardus*) present with grossly swollen heads due to cellulitis of the head and oral structures (Figs 8 and 9). The lesions vary in severity and are frequently localised to the subcutaneous tissues of the head, the oral cavity and regional lymph nodes. These lesions may vary from localised glossitis or stomatitis to extensive necrotic cellulitis of the lips and face, resulting in severe oedema. Important and practical diagnostic samples to collect from suspect cases include a blood smear for light microscopy and cotton swabs or filter paper blots of blood for culture. These swabs/blots should be allowed to dry in order to reduce viable contaminants and encourage sporulation. In putrefied carcasses that are several days old, swabs of the nasal turbinates or hoof lamellae are excellent options for culture.

Fig. 6
Facial oedema and bleeding from nose and mouth – buffalo
© R. Bengis

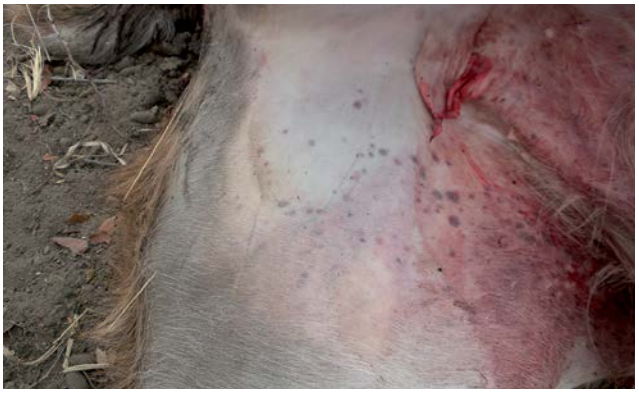

Fig. 7
Cutaneous haemorrhages, inner thigh of a greater kudu
© R. Bengis

Fig. 8
Lioness showing facial oedematous swelling
© R. Bengis

Fig. 9
Leopard showing oedematous swelling of the face and neck
© R. Bengis

Human anthrax

Anthrax is an important zoonotic disease and the World Health Organization (WHO) estimates that between 20,000 and 100,000 human cases occur globally per year (14). All evidence suggests that humans are relatively resistant to anthrax. The clinical classification of anthrax refers to the route of infection, i.e. cutaneous, enteric or inhalational (pulmonary). Cutaneous anthrax accounts for 95% of human cases reported. The site of infection is exposed skin, usually of the arms, hands, face, and neck, where anthrax spores come into contact with minor cuts and abrasions. This is commonly related to butchering or handling meat from infected animals. Suspected transmission of anthrax to humans by biting flies during animal outbreaks has also been recorded (26). Infections in drug users have resulted from the injection of heroin contaminated with anthrax spores (27). Cutaneous anthrax is characterised by an initially pruritic papule, which develops around vesicles,

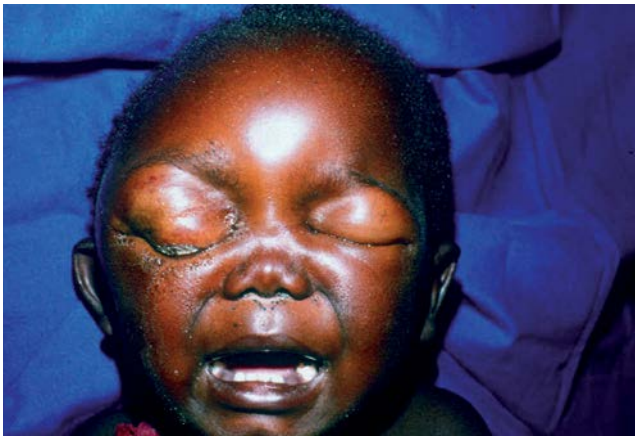

Fig. 10
Cutaneous anthrax affecting the eyelid of a child
Note widespread facial oedema (© M. Isaäcson)

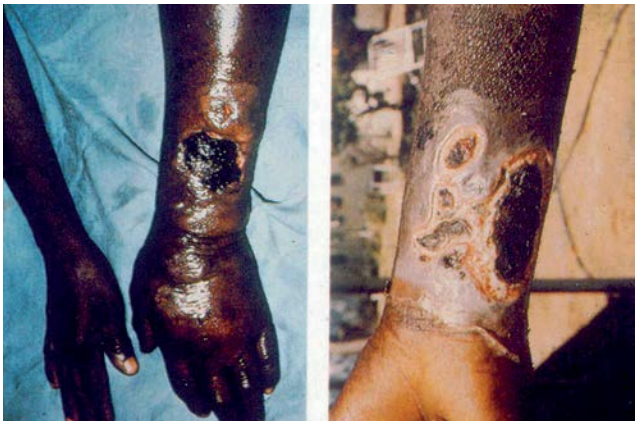

Fig. 11
Cutaneous anthrax in acute (left) and convalescent (right) stages
Note eschar and marked swelling in the acute stage, and their resolution in convalescence (© M. Isaäcson)

plus regional oedema that is often very marked, affecting a large anatomical area (Fig. 10). The lesion ulcerates to form a painless eschar, variable in size, with a typically black necrotic centre (Fig. 11). There is regional lymphadenopathy and low-grade fever. Uncomplicated cutaneous anthrax will heal with minimal scarring (Fig. 11). Antibiotic treatment does not stop or reverse the development of the skin lesion but prevents bacteraemia and systemic spread (14). If left untreated, 20% of cases will progress to severe systemic, and potentially fatal, infection.

Enteric anthrax is more common in rural areas of the developing world where carcasses are considered a windfall by protein-deprived people. The source of infection is probably a large dose of vegetative bacilli in raw or undercooked meat, rather than spores. There are two patterns of disease, both variable in severity. Oropharyngeal infection is characterised by high temperature, ulceration of the oropharynx, dysphagia, and marked neck swelling and lymphadenopathy. The tonsils are frequently involved, and a whitish pseudomembrane develops in the base of the ulcer. Occasionally the airway may be compromised (28). As with all forms of anthrax, systemic sepsis may occur. In intestinal anthrax, oedema, ulceration and haemorrhage usually involve the lower ileum and caecum, which results in symptoms of acute diarrhoea, nausea, vomiting and abdominal pain. There may be serosanguineous or haemorrhagic ascites. Abdominal radiography may suggest obstruction, with distension and air–fluid levels. Depending on its severity, the illness may resolve, respond to treatment, or progress to haematemesis, bloody diarrhoea and 'acute abdomen', followed by shock and death, in a variable proportion of patients (28).

Inhalational anthrax was historically an occupational disease of 'woolsorters' handling the skins or wool of infected sheep within the confines of a sorting shed, in the 18th to 20th Centuries. It has more recently been described in musicians playing drums that were covered with skins sourced from anthrax-infected carcasses. However, with the exception of deliberate release (bioterrorism) events, inhalational anthrax is the least common presentation of this disease. Clinically, patients have an initial non-specific, influenza-like illness with fever and malaise; cough, nausea, chest pain and vomiting are frequent. After a variable period, from hours to a few days, dyspnoea, shock and collapse progress rapidly to fulminant sepsis and death, unless early and aggressive antibiotic treatment is instituted. Radiologically, typically there is mediastinal widening, hilar lymphadenopathy and pleural effusion. Although anthrax does not cause classical bronchopneumonia, radiographs may show air-bronchograms and necrotising pneumonitis or consolidation that may be indistinguishable from other pneumonias (29, 30). Haemorrhagic meningitis secondary to sepsis may complicate any of the three main forms of anthrax.

In recent decades, the anthrax organism has been propagated for biological warfare and bioterrorism. Deliberate (30) and accidental (31) release of weaponised anthrax organisms has provided unfortunate but valuable insights into epidemiological and clinical aspects of the human disease.

Treatment and prophylaxis of anthrax

Bacillus anthracis is susceptible to most antibiotics; however, because of the peracute nature of anthrax disease in herbivores, by the time the victims show clinical signs it is usually too late to treat the disease with antibiotics. However, during a herd outbreak in cattle, it may be useful to treat any sick or febrile animals as well as any suspect incubating cases with long-acting penicillin or tetracyclines. Anthrax has a less acute course in carnivores, and during outbreaks

in southern Africa, lions and leopards with typical clinical signs (swollen faces and lips) have been successfully treated with mega-doses of long-acting penicillin (18). Prophylactic treatment may also be indicated prior to moving animals out of an outbreak zone. These animals can then be vaccinated at their destination a minimum of 14 days after the date of antibiotic administration. Antibiotics and vaccine should never be given together (18).

Human patients with anthrax need not be isolated (person-to-person spread is not normally a risk). Cutaneous lesions should be covered, and standard contact precautions taken with blood, secretions and other body fluids. In the case of drug users with injection anthrax, the lesions that develop are frequently in deeper tissues and should be drained and flushed. The antibiotic of choice is penicillin G or amoxycillin. In penicillin-allergic persons, doxycycline or ciprofloxacin may be used as an alternative. Intravenous (IV) hydrocortisone may be life-saving in patients with massive oedema threatening to obstruct the airways. In cutaneous anthrax, corticosteroids may help to control excessive oedema. Intravenous penicillin G (18 to 24 million units/day) or IV amoxycillin is used in inhalational anthrax. It is recommended that this be combined with other effective agents such as doxycycline and quinolones, because it appears from the 2001 anthrax attacks in the United States that combination therapy may confer a therapeutic advantage, although this is unproven (14, 30). There is also a theoretical concern that an inducible beta-lactamase present in *B. anthracis* could cause penicillin treatment failure in the case of a high infecting dose (particularly in inhalational anthrax) but, provided that adequate doses are used, this is not a practical problem outside the biowarfare/terrorism scenario (30). The addition of an antibiotic that reaches high therapeutic concentrations in the central nervous system (e.g. vancomycin or rifampicin) will provide additional cover for anthrax meningitis, a risk in severe sepsis. Three to seven days of treatment is sufficient for uncomplicated cutaneous anthrax; severe disease is treated for 10 to 14 days.

While scientific evidence suggests that only very significant exposure warrants the use of antibiotic prophylaxis, it is nevertheless often given in instances of casual or accidental contact with anthrax-infected animals. The anthrax guidelines published jointly by the World Organisation for Animal Health (OIE), the Food and Agriculture Organization of the United Nations and the WHO (14) suggest that where 'sufficient fear of substantial exposure in a natural situation exists (e.g. consumption of meat from a poorly cooked anthrax carcass), antibiotic prophylaxis may be considered but should only be of five to seven days' duration'. However, potentially exposed persons should be advised to immediately report any skin lesions and/or general illnesses that develop within a week of exposure.

Control of anthrax

Anthrax is a listed (internationally reportable) disease; in 2012 the OIE reported that anthrax was still present in most countries of Africa and Asia, some European countries, parts of North, Central and South America, and areas of Australia (32). Anthrax control measures are aimed at breaking the cycle of soil contamination, infection and transmission, and consist of continuous scanning and targeted surveillance of high-risk (endemic) areas, prophylactic procedures (vaccination and carcass disposal) and disease regulatory actions (quarantine and enforced treatment or vaccination) (14, 33).

In the face of an anthrax outbreak in animals, it is important to embark on an immediate vaccination campaign that targets the livestock at immediate risk (34). Multimedia public awareness campaigns are important, and local communities should be informed of the disease outbreak, and of disease prevention in livestock and the zoonotic risk, and be warned not to handle or consume animal carcasses. People should be encouraged to report carcasses, and carcasses should be disposed of efficiently (2, 14). In remote areas where animal anthrax is prevalent or has occurred previously, local medical clinics or rural hospitals should be informed, and be reminded of the clinical presentations of anthrax in humans. Cultural practices that promote transmission to humans (for example, the utilisation of infected carcasses for meat, hides and horns) may need to be discouraged through public education campaigns (14).

The mainstay for the control of anthrax in domestic livestock is vaccination using the non-capsulating strain 34F of *B. anthracis* (Sterne spore vaccine), in combination with various adjuvants (2, 14, 33, 34). This is an inexpensive and highly effective method of maintaining herd immunity in livestock, but needs to be repeated annually. Care should be taken when using these vaccines in caprine species and llamas, because these animals may develop severe reactions. Vaccination of wildlife has been practised from ground vehicles, hides or helicopter platforms. This requires remote injection by means of 'drop-out' darts or biodegradable ballistic implant projectiles (for thin-skinned species). These techniques are useful for solitary or 'small group' species such as larger antelopes, rhinoceroses and large predators. Another technique relies on mass capture of herd animals in a corral, followed by inoculation using multi-dose handheld or pole syringes from the sides of an exit chute. These techniques can be highly effective, but are both time consuming and prohibitively expensive, and the need to repeat vaccination annually is daunting (18). There is therefore a definite need for the development of an effective oral vaccine for ranched and habituated wildlife, which can be delivered by means of water or feed.

Carcass disposal

The primary source of environmental contamination by anthrax spores is the carcass of an animal that has died of anthrax. To minimise sporulation, carcasses should not be opened, and they should preferably be disposed of intact. Disposal options are limited to incineration, rendering (not practical for free-ranging wildlife) or burial. Incineration can be effected using local fossil fuels, inflammable chemicals (napalm), down-directed blow torches or portable incinerators (7, 14). Other fuel options include rubber tyres, charcoal briquettes (30 kg for a deer-sized animal) and large hay bales wetted with diesel fuel. The blood-contaminated soil is shovelled onto the carcass to be burned.

Burial is not ideal: it is labour intensive without earth-moving equipment, and spores will tend to surface again at a later date. Carcasses should be buried to a depth of at least two metres, and one part chloride of lime should be mixed with three parts of soil during the filling of the grave to accelerate lysis of the carcass tissues and reduce the survival of spores (14).

It is important to know that keeping carcasses intact until significant putrefaction has occurred will theoretically kill most vegetative anthrax bacilli and reduce their opportunity to sporulate. Therefore, making a carcass unattractive to scavengers will reduce the number of carcasses that are opened. In Canada, 5% formaldehyde sprayed on and around a carcass was found to be an effective deterrent against scavengers, and had the positive spin-off of disinfecting the surrounding contaminated vegetation and soil (12).

Another relatively new and promising, but unproven, technique relies on making the carcass inaccessible to invertebrate, avian and small mammalian scavengers for an adequate period to allow putrefaction to proceed to an advanced state and eliminate most anthrax bacilli. This entails covering or wrapping the carcass in thick agricultural plastic sheeting or placing the carcass in a purpose-built 'body bag' and leaving it *in situ* to decompose for several days (depending on environmental temperature) (18). At a later stage, the carcass remnants can be buried or incinerated at a central site. This technique may only be practical for animals up to the size of a large antelope, but it is important to remember that these thin-skinned animals are also those species with high terminal bacteraemias, and which are relatively easily opened by small scavengers.

Other control techniques

In regions where invertebrates have been shown to be epidemiologically important, e.g. regions where there is transmission by biting flies or environmental contamination by necrophagic flies, targeted control of these insects may be attempted.

In certain habitats where 'hot spots' have been identified during an anthrax outbreak, rangeland burning may be considered as a method of reducing transmission and mortality. The rationale behind this intervention is that the fire destroys many spores on the vegetation, kills many invertebrate vectors, disperses resident mammals from the area, and then makes the area unattractive to herbivores for a varying period. This technique has been effectively used in certain African savannah systems where anthrax has a winter/dry season pattern (18).

Discussion

It is important to appreciate that anthrax organisms spend the greater part of their existence as dormant spores in suitable environments, and that replication and persistence appear to depend on extreme virulence, with exponential replication resulting in acute death of the host, followed by sporulation and survival for prolonged periods outside a host. Different ecosystems have different 'preferred' replication hosts, but in general these hosts fall into the category of social ungulates, both domesticated and wild. Primates (including humans), carnivores and ostriches may be considered to be 'incidental' hosts.

In the context of the One Health concept, the contaminated environment is intermittently the source of infection for resident or migrant 'preferred' replication hosts, including domesticated livestock or wildlife. The activity of *B. anthracis* then shifts from a dormant state to one of exponential replication within these hosts, with multimodal transmission of infection occurring among sympatric populations of hosts during the outbreak. Each victim in turn becomes a potential source of increased contamination of the environment. Incidental hosts (including humans) most frequently become infected when handling or eating the carcasses of infected ungulates, but may also rarely become infected by contact with contaminated animal products (e.g. hides and wool) or contaminated biting insects. In areas where anthrax is endemic in wildlife, or where there is an active outbreak of anthrax in wildlife, the organisms may be transmitted from this source to adjacent livestock populations by means of water run-off, and dispersal by birds and other carrion feeders, as well as necrophagic and haemophagic flies.

Conclusions

In view of the environmental resilience of this organism, plus its endemic persistence and circulation in certain

wildlife-dominated ecosystems, and because of the practical difficulties encountered with disease surveillance and vaccination of free-ranging wild animals, anthrax outbreaks will continue to occur at regular intervals in many wildlife populations in various regions of the globe. These infected wildlife areas present a continuing risk to livestock (and humans) in surrounding areas. In addition, spores may persist in certain livestock farming areas, and any complacency or false sense of security in farmers or animal health regulators regarding vaccination of livestock may result in continued or escalating outbreaks in livestock. Particularly in areas of subsistence farming in Africa, livestock anthrax inevitably poses a risk for outbreaks of human cases, because animals that die acutely will often be utilised as a source of protein. Long-term health education is required to alter such cultural practices.

La fièvre charbonneuse : une illustration du concept « Une seule santé »

R.G. Bengis & J. Frean

Résumé

La fièvre charbonneuse est une infection bactérienne pouvant prendre une forme suraiguë, aiguë ou subaiguë qui affecte de nombreuses espèces sur plusieurs continents. C'est l'une des plus anciennes maladies connues ; les cinquième et sixième fléaux bibliques (*Exode*, chapitres 7 à 9) qui se sont abattus d'abord sur le bétail puis sur la population humaine faisaient probablement référence à la fièvre charbonneuse. Depuis les plus anciens rapports historiques jusqu'à la mise au point d'un vaccin efficace au milieu du XX^{e} siècle, la fièvre charbonneuse a été l'une des principales causes de mortalité incontrôlée chez les bovins, les ovins, les caprins, les équidés et les porcins, avec des cas d'infection chez l'homme en tant qu'hôte incident partout dans le monde. De 1930 à 1980, le nombre de foyers de fièvre charbonneuse affectant le bétail a connu un déclin spectaculaire grâce à l'utilisation du vaccin sporulé mis au point par Sterne. Des programmes nationaux de vaccination ont rencontré un grand succès dans nombre de pays pendant cette période, soutenus par l'utilisation sans restriction d'antibiotiques et la mise en œuvre de mesures de quarantaine et de destruction des cadavres d'animaux. Toutefois, nous assistons aujourd'hui à une résurgence de cette maladie chez les animaux d'élevage de certains pays ayant interrompu leur programme de vaccination par négligence ou par l'effet d'un sentiment trompeur de sécurité. L'épidémiologie de la fièvre charbonneuse possède une composante environnementale, en plus de celles liées au bétail, à la faune sauvage et à l'homme. C'est ce qui fait de la fièvre charbonneuse un exemple intéressant à appliquer dans le cadre d' « Une seule santé ». Nombre de foyers de fièvre charbonneuse affectant la faune sauvage demeurent inaperçus ou font l'objet d'une sous-déclaration, en raison des insuffisances et des difficultés de la surveillance. L'homme contracte généralement l'infection de manière accidentelle lors des foyers affectant le bétail ou la faune sauvage. La prise pour cible délibérée de populations humaines dans le cadre d'une guerre biologique ou d'actes de bioterrorisme constitue une exception.

Mots-clés

Fièvre charbonneuse – Persistance dans l'environnement – Sensibilité de l'hôte – Transmission – Une seule santé – Zoonose.

El carbunco bacteridiano como ejemplo del concepto de «Una sola salud»

R.G. Bengis & J. Frean

Resumen

El carbunco es una infección de origen bacteriano que puede presentarse en forma de patología hiperaguda, aguda o subaguda. Afecta a numerosas especies y está presente en muchos continentes. Es una de las enfermedades infecciosas más antiguas que se conocen: la quinta y la sexta plagas bíblicas (capítulos 7 a 9 del *Éxodo*), que afectaron en primer lugar al ganado y después al hombre, eran probablemente carbunco bacteridiano. Desde los primeros registros históricos hasta la elaboración de una vacuna eficaz, a mediados del siglo XX, el carbunco fue en todo el mundo una de las principales causas de mortalidad incontrolada de bovinos, ovinos, caprinos, equinos y porcinos, con episodios de extensión al ser humano. Tras la aparición de la vacuna esporulada de Sterne se produjo, entre 1930 y 1980, un acusado descenso del número de brotes en el ganado. En muchos países se implantaron durante esos años fructíferos programas nacionales de vacunación, acompañados de un uso liberalizado de antibióticos, normas de cuarentena y medidas de eliminación de los animales muertos. Sin embargo, últimamente se ha notificado la reaparición de esta enfermedad en el ganado en algunas regiones, donde la complacencia y una falsa sensación de seguridad han generado disfunciones en los programas de vacunación. Además de incumbir al ganado, la fauna salvaje y el ser humano, la epidemiología del carbunco bacteridiano tiene un componente ambiental, lo que hace de esta enfermedad un ejemplo idóneo para reflexionar a la luz del concepto de «Una sola salud». Debido a las carencias y dificultades de la vigilancia, muchos brotes de carbunco bacteridiano en la fauna salvaje pasan desapercibidos o se notifican por debajo de su nivel real (subnotificación). Lo más común es que el ser humano contraiga la enfermedad accidentalmente en el curso de brotes que afectan al ganado doméstico o los animales salvajes, con la salvedad de los casos de ataque deliberado con carbunco que constituyen actos de guerra biológica o bioterrorismo.

Palabras clave

Carbunco bacteridiano – Persistencia ambiental – Sensibilidad del anfitrión – Transmisión – Una sola salud – Zoonosis.

References

1. Choquette L.P.E. (1970). – Anthrax. *In* Infectious diseases of wild mammals (J.W. Davis, L.H. Karstadt & D.O. Trainer, eds). Iowa State University Press, Ames, Iowa, 256–266.

2. Sterne M. (1959). – Anthrax. *In* Infectious diseases of animals: diseases due to bacteria (A.W. Stableforth & I.A. Galloway, eds). Academic Press, New York, 16–52.

3. Cormack Gates C., Elkin B. & Dragon D. (2001). – Anthrax. *In* Infectious diseases of wild mammals, 3rd Ed. (E.S. Williams & I.K. Barker, eds). Iowa State University Press, Ames, Iowa, 396–412.

4. Hugh-Jones M. & Blackburn J. (2009). – The ecology of *Bacillus anthracis*. *Molec. Asp. Med.*, **30** (6), 356–367.

5. Koshikawa T., Tamazaki M. & Yoshimi M. (1989). – Surface hydrophobicity of spores of *Bacillus* spp. *J. gen. Microbiol.*, **135**, 2717–2722.

6. Gould G.W. (1984). – Mechanisms of resistance and dormancy. *In* The bacterial spore (A. Hurst & G.W. Gould, eds). Academic Press, Toronto, 173–209.

7. Dragon D.C. & Rennie R.P. (1995). – The ecology of anthrax spores: tough but not invincible. *Can. vet. J.*, **36**, 295–301.

8. Keim P., Kalif A., Schupp J., Hill K., Travis S.E., Richmond K., Adair D.M., Hugh-Jones M., Kuske C.R. & Jackson P. (1997). – Molecular evolution and diversity in *Bacillus anthracis* as detected by amplified fragment length polymorphism markers. *J. Bacteriol.*, **179**, 818–824.

9. Mullins J.C., Garofolo G., Van Ert M., Fasanella A., Luknova L., Hugh-Jones M.E. & Blackburn J.K. (2013). – Ecological niche modelling of *Bacillus anthracis* on three continents: evidence for genetic–ecological divergence? *PLoS ONE*, **8** (8), e72451. doi:10.1371/Journal.pone.0072451.

10. Smith K.L., de Vos V., Bryden H., Price L.B., Hugh-Jones M.E. & Keim P. (2000). – *Bacillus anthracis* diversity in the Kruger National Park. *J. clin. Microbiol.*, **38** (10), 3780–3784.

11. De Vos V. & Turnbull P.C. (2004). – Anthrax. *In* Infectious diseases of livestock, 2nd Ed. (J.A.W. Coetzer & R.C. Tustin, eds). Oxford University Press, Oxford, 1788–1818.

12. Hugh-Jones M.E. & de Vos V. (2002). – Anthrax and wildlife. *In* Infectious diseases of wildlife: detection, diagnosis and management (Part Two) (R.G. Bengis, ed.). *Rev. sci. tech. Off. int. Epiz.*, **21** (2), 359–383.

13. Coker P.R., Smith K.L., Fellows P.F., Rybachuck G., Kousoulas K.G. & Hugh-Jones M.E. (2003). – *Bacillus anthracis* virulence in guinea pigs vaccinated with anthrax vaccine adsorbed is linked to plasmid quantities and clonality. *J. clin. Microbiol.*, **41** (3), 1212–1218.

14. World Organisation for Animal Health, Food and Agriculture Organization of the United Nations & World Health Organization (WHO) (2008). – Manual on anthrax in humans and animals, 4th Ed. (P.C. Turnbull, ed.). WHO, Geneva.

15. Hoover D.L., Friedlander A.M., Rogers L.C., Yoon I.K., Warren R.L. & Cross A.S. (1994). – Anthrax edema toxin differentially regulates lipopolysaccharide-induced monocyte production of tumor necrosis factor alpha and interleukin-6 by increasing intracellular cyclic AMP. *Infect. Immun.*, **62** (10), 4432–4439.

16. Cromartie W.J., Bloom W.L. & Watson D.W. (1947). – Studies on infection with *Bacillus anthracis*. 1. A histopathological study of skin lesions produced by *B. anthracis* in susceptible and resistant animal species. *J. infect. Dis.*, **80**, 1–13.

17. Ianaco-Connors L.C., Schmaljohn C.S. & Dalrymple J.M. (1990). – Expression of the *Bacillus anthracis* protective antigen gene by baculovirus and vaccinia virus recombinants. *Infect. Immun.*, **58** (2), 366–372.

18. Bengis R.G. (2012). – Anthrax in free-ranging wildlife. *In* Fowler's zoo and wild animal medicine: current therapy, Vol. 7 (R.E. Miller & M. Fowler, eds). Elsevier Saunders Press, St Louis, Missouri, 98–107.

19. Turnbull P.C., Carman J.A., Lindeque P.M., Joubert F., Hubschle O.J.B. & Snoeyenbos G.H. (1989). – Further progress in understanding anthrax in Etosha National Park. *Madoqua*, **16** (2), 93–104.

20. Lindeque P.M. & Turnbull P.C.B. (1994). – Ecology and epidemiology of anthrax in Etosha National Park, Namibia. *Onderstepoort J. vet. Res.*, **61**, 71–83.

21. Kriek N.P.J. & de Vos V. (1996). – Species differences in the pathology of wildlife in the Kruger National Park, South Africa. *Salisbury med. Bull.* (Suppl.), **87**, 82.

22. Smith H.A. & Jones T.C. (1966). – Diseases due to simple bacteria (anthrax). *In* Veterinary pathology, 3rd Ed. Lea and Febiger, Philadelphia, 463–466.

23. De Vos V. & Bryden H.B. (1996). – Anthrax in the Kruger National Park: temporal and spatial patterns of disease occurrence. *Salisbury med. Bull.* (Suppl.), **87**, 26–30.

24. Ebedes H. (1976). – Anthrax epizootics in Etosha National Park. *Madoqua*, **10**, 99–118.

25. Turnbull P.C. (1992). – Serology and anthrax in humans, livestock and Etosha National Park wildlife. *Epidemiol. Infect.*, **108**, 299–313.

26. Fasanella A., Garofolo G., Galella M., Troiano P., De Stefano C., Pace L., Aceti A., Serrecchia L. & Adone R. (2013). – Suspect vector transmission of human cutaneous anthrax during an animal outbreak in Southern Italy. *Vector-borne Zoonotic Dis.*, **13** (10), 769–771.

27. Powell A.G., Crozier J.E., Hodgson H. & Galloway D.J. (2011). – A case of septicaemic anthrax in an intravenous drug user. *BMC infect. Dis.*, **11**, 21.

28. Beatty M.E., Ashford D.A., Griffin P.M., Tauxe R.V. & Sobel J. (2003). – Gastrointestinal anthrax: review of the literature. *Arch. internal Med.*, **163** (20), 2527–2531.

29. Ross J.M. (1957). – The pathogenesis of anthrax following the administration of spores by the respiratory route. *J. Pathol. Bacteriol.*, **73**, 485–494.

30. Inglesby T.V., O'Toole T., Henderson D.A., Bartlett J.G., Ascher M.S., Eitzen E., Friedlander A.M., Gerberding J., Hauer J., Hughes J., McDade J., Osterholm M.T., Parker G., Perl T.M., Russell P.K., Tonat K.; Working Group on Civilian Biodefense (2002). – Anthrax as a biological weapon. *In* Bioterrorism: guidelines for medical and public health management (D.A. Henderson, T.V. Inglesby & T. O'Toole, eds). AMA Press, Chicago, 63–97.

31. Meselson M., Guillemin J., Hugh-Jones M., Langmuir A., Popova I., Shelokov A. & Yampolskaya O. (1994). – The Sverdlovsk anthrax outbreak of 1979. *Science*, **266**, 1202–1208.

32. World Organisation for Animal Health (OIE) (2013). – Terrestrial Animal Health Code, 22nd Ed. OIE, Paris. Available at: www.oie.int/en/international-standard-setting/terrestrial-code/access-online/ (accessed on 10 June 2014).

33. Sterne M. (1939). – The use of anthrax vaccines prepared from avirulent (uncapsulated) variants of *Bacillus anthracis*. *Onderstepoort J. vet. Sci.*, **13**, 307–312.

34. Jackson F.C., Wright G.G. & Armstrong J. (1957). – Immunization of cattle against experimental anthrax, with alum-precipitated protective antigen or spore vaccine. *Am. J. vet. Res.*, **18**, 771–777.