**Anthrax**

**Control Tools**

**Diagnostics availability**

Commercial diagnostic kits available worldwide

No

**GAP:**

Need rapid, reliable, validated and, inexpensive diagnostic kits.

Commercial diagnostic kits available in Europe

No.

**GAP:** See above.

Diagnostic kits validated by International, European or National Standards

None.

Diagnostic method(s) described by International, European or National standards

Diagnostic methods are described in the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals, Chapter 2.1.1 on Anthrax.


**GAP:** To define an official method for diagnosing anthrax and requirements to validate existing and new tests. Development of procedure for recovering spores from environmental samples.

Commercial potential for diagnostic kits in Europe

Limited.

DIVA tests required and/or available

Not available or required, but would complement the diagnostic process.

Opportunities for new developments

Need for specific rapid diagnostic test that yields clear unequivocal results and can be operated with minimal training in the field.

Test to verify the presence of anthrax spores in soil or other suspected contaminated materials.

Vaccines availability
Commercial vaccines availability (globally)

Commercial vaccines are available.

**GAPS:**

Improve the stability of the vaccine and decrease the cost of production.

To develop therapeutics that can protect and vaccinate simultaneously. Improve vaccine for long-lasting immunity. More recent information on vaccine efficacy in different geographical areas.

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**Commercial vaccines authorised in Europe**

Yes.

**Marker vaccines available worldwide**

No.

**Marker vaccines authorised in Europe**

None.

**Effectiveness of vaccines / Main shortcomings of current vaccines**

Efficacy on different animal species unclear. Window of protection is too short. Requirement for annual vaccination to ensure protection. Live vaccine cannot be used in combination with antibiotics. Requirement for manual immunization.

**GAP:** Need information on the effectiveness of the vaccine on different animal species.

**Commercial potential for vaccines in Europe**

The commercial potential is limited and it depends on the anthrax situation in individual countries.

**Regulatory and/or policy challenges to approval**

Considerable.

**Commercial feasibility (e.g manufacturing)**

Feasible but expensive.

**Opportunity for barrier protection**

Vaccination can be used in the event of an anthrax outbreak or in an endemic area.

**Opportunity for new developments**

Improve the stability of the vaccine and decrease the cost of production.

To develop therapeutics that can protect and vaccinate simultaneously. To improve vaccine for long-lasting immunity. More recent information on vaccine efficacy in different geographical areas and animal species. Capability of mass vaccinations.

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**Pharmaceutical availability**

**Current therapy (curative and preventive)**
Treatment is rarely possible due to the rapid course of the disease. Many antibiotics are effective against *B. anthracis*.

Future therapy

Current antibiotics are effective and there is little need for new therapies to be developed.

Commercial potential for pharmaceuticals in Europe

There is no specific commercial potential as current antibiotics available are satisfactory for the treatment of anthrax.

Regulatory and/or policy challenges to approval

No.

Commercial feasibility (e.g. manufacturing)

Effective antibiotics already available.

Opportunities for new developments

Limited.

**GAP:** There is need to monitor drug resistance. There is need for research on the development of therapeutic agents that can both treat and confer long-term protection in the same formulation. There is need for the development of a vaccine that can be administered en mass.

New developments for diagnostic tests

Requirements for diagnostics development

There is need for a specific rapid diagnostic test that yields clear unequivocal results and can be operated with minimal training in the field.

A test is required to verify the presence of anthrax spores in soil or other suspected contaminated materials.

**GAP:** There is need to establish a test for other members of *Bacillus* group capable of causing anthrax (e.g. *B. cereus* bv *anthracis*).

Time to develop new or improved diagnostics

The development of new tests will take time to validate.

Cost of developing new or improved diagnostics and their validation

Variable.

Research requirements for new or improved diagnostics

**GAPS:**

Improved quicker diagnostic tests.

Specific tests to isolate *B. anthracis*

Selective medium for *B. anthracis*. Better understanding of the disease in animals to identify early markers of infection, which would underpin the development of diagnostic assays. Identify importance of non-typical anthrax through tests capable of detecting pXO1 and pXO2 independent from chromosomal background.

Technology to determine virus freedom in animals
Current available technology is unable to definitively confirm *B. anthracis*-free animals.

**GAP:** Research and collaboration is required.

### New developments for vaccines

**Requirements for vaccines development / main characteristics for improved vaccines**

Efficacy on different animal species. Window of protection should be life-long. Currently there is a requirement for annual vaccination to ensure protection.

**GAPS:**

Development of vaccines to allow mass vaccination.

Development of vaccines that can be used in combination with antibiotics.

#### Time to develop new or improved vaccines

The cost is variable, and the time to produce improved vaccines is likely to be 10 to 15 years.

#### Cost of developing new or improved vaccines and their validation

The cost is variable, but it is likely to be expensive.

### Research requirements for new or improved vaccines

Efficacy on different animal species. Window of protection should be life-long; currently there is a requirement for annual vaccination to ensure protection.

**GAPS:**

Vaccine and adjuvants that permits the development of high level of protective antibodies.

Development of vaccines to allow mass vaccination.

Development of vaccines that can be used in combination with antibiotics.

Generation of vaccines directed against the capsule, toxin and spore.

### New developments for pharmaceuticals

**Requirements for pharmaceuticals development**

None required.

#### Time to develop new or improved pharmaceuticals

Not applicable.

#### Cost of developing new or improved pharmaceuticals and their validation

Not applicable.
**Research requirements for new or improved pharmaceuticals**

To develop therapeutics that can protect and vaccinate simultaneously.

**Disease details**

**Description and characteristics.**

**Pathogen**

Anthrax is caused by *Bacillus anthracis*, which is a spore forming, gram-positive rod-shaped organism. Within the genus *Bacillus*, *B. anthracis* is the only obligate pathogen. There are cases of horizontal gene transfer within the *B. cereus* group, and this has implications for diagnostics.

**GAP:** Since horizontal gene transfer occurs, diagnostic methods should take this into account. Methods to identify horizontal gene transfer within *B. cereus* group must be developed.

**Variability of the disease**

Anthrax can be found worldwide and to date a number of genotypes have been identified. The pathogen can be modified genetically and there are strains that have antibiotic resistance. The routes of initiation of the disease can vary depending on a range of factors including the environment, host susceptibility and infectious dose. The clinical picture of anthrax can be caused by other members of the *Bacillus* group, which harbor the plasmids pXO1 and pXO2 (*Bacillus cereus* bv anthracis).

**GAP:** The epidemiology of *Bacillus cereus* bv anthracis in Africa needs to be investigated further.

**Stability of the agent/pathogen in the environment**

Bacilli released by the dying or dead animal into the environment, usually soil, sporulate. The spores predominate in the environment and are more resistant than the vegetative form to extremes of heat, cold, pH, desiccation, ultraviolet light, gamma radiation and chemicals. The spores can lie dormant for years, especially in calcium-rich alkaline soils. Environmental disinfection is not simple.

**GAP:** More research into the ecology of anthrax in the environment is required. Simple and reproducible methods to isolate spores from environmental samples are required. The development of environmentally friendly decontamination products and methods is paramount.

**Species involved**

**Animal infected/carrier/disease**

All mammals, including humans, appear to be susceptible to anthrax to some degree. Wild and domestic herbivores such as cattle, sheep, and goats are the most susceptible. Horses, swine, cats, and dogs are less susceptible and in them, the disease usually has a more protracted course. Occasionally, other species are affected.

**GAP:** To understand the route of infection. To characterise the pathology of anthrax in animals (existence of carrier state/subclinical infection). To investigate potential reservoir animals. To develop low-cost simple sero-prevalence tools.

**Human infected/disease**

There are three established forms of disease that are caused by *B. anthracis*, namely inhalation, gastrointestinal and cutaneous. Humans primarily contract the disease through contact with infected animals and their products. There have been fatal anthrax cases related to the injection of anthrax-contaminated heroin.

**GAP:** Characterization of the pathology of the disease in humans. Development of rapid and simple diagnostics. Development of effective therapeutics and vaccines.
**Description of infection & disease in natural hosts**

**Transmissibility**

Herbivores are usually infected by exposure to spores from soil-contaminated food or water. Wild carnivores can become infected through the consumption of infected animals. Experimental data has identified vector-mediated transmission, namely mechanical and biological transmission e.g. flies.

**GAP:** Investigate the role of insects in the transmission of anthrax spores. Research to characterize routes of infection in animals.

**Pathogenic life cycle stages**

*Bacillus anthracis* can take two forms: the vegetative bacilli and the spore. Herbivores become infected with the spores. There is no consensus on the fate of *B. anthracis* spores inside the host. Recently, some researchers have questioned the role of macrophages in the pathogenic life cycle of *B. anthracis*. The other school of thought was that once inside the host, spores are taken up by macrophages and transported to regional lymph nodes. The spores germinate inside the macrophages and produce capsulated and toxin producing vegetative cells, which lyse the macrophages, releasing the organism in the blood stream where it causes systemic infection. The bacteria then replicate to large numbers because of the production of toxins which suppress the immune system and kill the animal. In the late stages of infection, animals bleed through orifices. The bacteria released in the blood form spores, which contaminate the soil.

**GAP:** To understand sporulation in the context of the disease. To understand the fate of *B. anthracis* in carcasses. To determine whether subclinical infections occur in some animal species.

**Signs/Morbidity**

The progression of disease is dependent on the host species, immune status, dose and route of infection, be it cutaneous, gastrointestinal or inhalation. Anthrax in animals manifests in three different ways: per acute, acute and sub-acute to chronic, depending on the factors defined above. Generally, herbivores develop the per-acute and acute forms, whereas carnivores and omnivores develop the sub acute to chronic forms.

In the per-acute form of disease, signs preceding death often go unobserved. The clinical history usually describes the animal to be in good health a few hours before death. If the animal is observed shortly before death, fever, muscle tremors, dyspnoea, and mucosal congestion are common signs. Shortly afterwards, the animal will often have terminal convulsions, collapse and then die. Following death, unclotted blood may be seen to exude from the orifices (anus, vulva, nostrils, and/or mouth). Incomplete rigor mortis is also common.

In the acute form, the clinical signs are the same as the per-acute form, however, oedematous swellings may be observed up to 48 hours before death. Death usually occurs within 48-96 hours.

In the sub acute to chronic form, the organism tends to localise in the regional lymph nodes of the pharyngeal area where severe
swelling may occur resulting in death by occlusion of the airway. In some cases, a fatal bacteraemia may develop.

**GAP:** To understand the pathology of the disease in ruminants. To develop sensitive methods to detect small numbers of organisms, toxins and disease-specific antibodies.

**Incubation period**

Incubation period of anthrax under natural conditions is unknown, but probably ranges from 1 to 14 days.

**Mortality**

From the presentation of clinical signs, animals usually die within 1 to 3 days.

**GAP:** More information is required regarding pathology of the disease in different animal species.

**Shedding kinetic patterns**

Shedding bacteria after death.

**GAP:** To understand the mechanism of spore formation after death.

**Mechanism of pathogenicity**

The pathogenicity of *B. anthracis* is determined by two major components: a poly-D-glutamyl capsule and the anthrax toxin. The anthrax toxin consists of three distinct antigenic components: protective antigen (PA), the oedema factor (EF), and the lethal factor (LF). Strains of anthrax vary in virulence, the mechanism of which is to be determined.

**GAP:** Determine the basis of the variation in virulence for the different isolates of *B. anthracis* and *B. cereus* bv *anthracis*.

**Zoonotic potential**

**Reported incidence in humans**

The incidence of human disease is directly related to incidence of animal disease in a country. In developed countries, human disease is rare, although underreporting is possible due to lack of familiarity with the infection.

Worldwide, the incidence is unknown, though *B. anthracis* is present in most of the world. The actual incidence of human cases worldwide is difficult to assess due to under-reporting.

**GAP:** Better reporting systems are required. More information is required from areas where the disease is endemic. Improve public awareness, and clinical training.

**Estimated level of under-reporting in humans**

High level of under-reporting.

**GAP:** Better reporting systems required. More information is required from areas where the disease is endemic. Improve public awareness, and clinical training.

**Risk of occurrence in humans, populations at risk, specific risk factors**

It is perceived that humans appear to be relatively resistant to anthrax as compared with other susceptible species. Most cases of human anthrax have resulted from direct or indirect contact with infected animals, or occupational exposure to infected or contaminated animal products.
Symptoms described in humans

Symptoms of disease vary depending on how the disease was contracted, but usually occur within 7 days. **Cutaneous:** Most (about 95%) anthrax infections occur when the bacterium enters a cut or abrasion on the skin, when handling contaminated animal products or infected animals. Skin infection begins as a raised itchy bump that resembles an insect bite but within 1-2 days develops into a vesicle and then a painless ulcer, usually 1-3 cm in diameter, with a characteristic black necrotic (dying) area in the centre. Localised swelling is characteristic of infection and in severe cases can cause occlusion of the airway if the lesion is found around the face. Local lymphadenopathy may occur. Deaths are rare with appropriate antimicrobial therapy.

**Inhalation:** Initial symptoms may resemble a nonspecific respiratory infection. After several days, the symptoms may progress to severe breathing problems, shock and death.

**Intestinal:** The intestinal form of anthrax may follow the consumption of contaminated meat and is characterized by an acute inflammation of the intestinal tract. Initial signs include nausea, loss of appetite, vomiting and fever, followed by abdominal pain, vomiting of blood, and severe diarrhoea. Intestinal anthrax is usually fatal.

**GAP:** More information about pathology in humans is required.

Likelihood of spread in humans

Anthrax does not appear to be transmissible from person to person.

Impact on animal welfare and biodiversity

**Both disease and prevention/control measures related**

While there are no specific animal welfare considerations, vaccination is advisable in endemic areas. Prompt control measures should be instigated in the event of an outbreak.

**Endangered wild species affected or not (estimation for Europe / worldwide)**

Endangered mammalian species are susceptible.

**GAP:** More research required to determine the impact of infection.

**Slaughter necessity according to EU rules or other regions**

Not applicable.

Geographical distribution and spread

**Current occurrence/distribution**

*B. anthracis* can be found worldwide.

**GAP:** Knowledge of the genotypes in different geographical regions is required.

**Epizootic/endemic - if epidemic frequency of outbreaks**

In many countries, anthrax occurs sporadically as environmental conditions allow.

**Seasonal cycle (seasonality)**

Little agreement exists on the roles played by seasonal factors.

**GAP:** To understand whether there is seasonality related to anthrax infection and to determine the risk factors.
Speed of spatial spread during an outbreak

Insufficient information regarding the speed of spatial spread.

**GAP:** Research to address this issue is required.

Transboundary potential of the disease

Dependant on movement of infected animals and contaminated animal products.

Seasonal cycle linked to climate

Seasonal variation influences the host, vectors and the distribution of *B. anthracis* in the environment. In the case of animals, it affects feeding behaviour and overall health. In the case of bacteria, climatic conditions can affect both numbers and spatial distribution of the organisms.

**GAP:** To determine the major risk factor associated with climate variation.

Distribution of disease or vector linked to climate

See section “Seasonal cycle linked to climate”.

Outbreaks linked to extreme weather

Outbreaks in endemic areas have been associated with a prolonged hot dry spell, which in turn was preceded by heavy rains or flooding, or with rain ending a period of drought.

**GAP:** Comprehensive characterization of effect of climate on disease outbreaks.

Sensitivity of disease or vectors to the effects of climate change (environmental changes/land use)

Insufficient information is available.

**GAP:** To determine the impact of global warming.

Route of Transmission

**Usual mode of transmission (introduction, means of spread)**

Herbivores are usually infected by exposure to spores from soil-contaminated food or water. Wild carnivores can become infected through the consumption of infected animals. Experimental data has identified vector-mediated transmission namely mechanical and biological transmission e.g. flies.

**GAP:** Investigate the role of insects in the transmission of anthrax spores. Research to characterize routes of infection in animals.

**Occasional mode of transmission**

Bioterrorism.

**Conditions that favour spread**

Insufficient information is available.

**GAP:** Research required to determine conditions that favour the spread of anthrax.

**Detection and Immune response to infection**
Mechanism of host response

In general, animals mount a protective antibody response following vaccination and exposure. T cells have been proposed to contribute to protection, but further research is required. The innate immune system is also important.

**GAP:** Research required to determine the mechanism of host response to anthrax.

Immunological basis of diagnosis

Detection of antibodies.

**GAP:** Development of affordable more species-specific assays that can distinguish between natural infection and vaccination.

Main means of prevention, detection and control

Sanitary measures

The affected property should be quarantined and neighbouring properties should be notified. Staff dealing with suspect animals and material must wear full personal protective clothing and equipment. The following carcass disposal methods are currently being used: disposal by total burning (recommended) or deep burial (at least 2 m) above the water table.

**GAP:** There is a need to develop a validated effective method for disposal of infected carcasses and animal products.

Mechanical and biological control

Prompt disposal of dead animals and contaminated materials. Carcasses should not be opened. Restrict access of scavengers to contaminated carcasses. Decontaminate equipment that has been in contact with contaminated animals and animal products. Vaccination of livestock in endemic areas is recommended as per country guidelines.

**GAP:** Research to validate effectiveness of control measures.

Diagnostic tools

Identification of the agent: Demonstration of encapsulated *B. anthracis* in blood or tissues from fresh anthrax-infected carcasses and growth of the organism on blood agar plates is relatively easy to handle (methods for capsule visualisation, Polychrome methylene blue, culture on blood agar, susceptibility to gamma phage and confirmation of virulence markers by PCR).

**GAP:**
To develop field tests that are reliable and fast.

There is need for development of reliable kits for onsite field testing.

Methods for the detection of *B. cereus* bv anthracis need to be developed and validated.

Vaccines

The most widely used vaccine for the prevention of anthrax in animals is the Sterne-strain vaccine. This vaccine is a non-encapsulated live variant strain of *B. anthracis* developed by Sterne in 1937. Immunity develops 7-10 days after vaccination. A single vaccination produces short-lived immunity and two doses are recommended (three weeks apart). The initial vaccine should be administered about two months prior to the expected disease outbreak season. Annual vaccination is recommended in endemic areas. Other Sterne-like vaccines are used around the world.

**GAP:** Improve vaccine for long-lasting immunity.

Therapeutics

Treatment is rarely possible due to the rapid course of the disease. Many antibiotics are effective against *B. anthracis.*
**GAP:** To develop therapeutics that can protect and vaccinate simultaneously.

**Biosecurity measures effective as a preventive measure**

Wear personal protective equipment when dealing with suspected cases of anthrax.

**Border/trade/movement control sufficient for control**

Enforcement of quarantine regulation according to national guidelines.

**Prevention tools**

Annual vaccination is recommended in endemic and high-risk areas. Control movement of animals during outbreaks.

**GAP:** Active surveillance of the environment such as soil. Better communication tools prior to outbreaks.

**Surveillance**

Anthrax is a reportable disease.

**GAP:** More comprehensive pathogen typing tools and disease outbreak reporting system (GIS).

**Past experiences on success (and failures) of prevention, control, eradication in regions outside Europe**

The disease can be controlled by annual vaccination and effective disposal of infected carcasses and contaminated materials.

**GAP:** Quality control of anthrax vaccine.

**Costs of above measures**

Country dependent.

**GAP:** Encourage collaboration between countries with capability and countries with need.

**Disease information from the OIE**

**Disease notifiable to the OIE**

Anthrax is an OIE listed disease. Reports are updated every 6 months.

**OIE disease card available**

http://www.oie.int/fileadmin/Home/eng/Media_Center/docs/pdf/Disease_cards/ANTHRAX-EN.pdf

**OIE Terrestrial Animal Health Code (reference)**

http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_anthrax.htm

**OIE Terrestrial Manual (reference)**

http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.01.01_ANTHRAX.pdf

**Socio-economic impact**
Zoonosis: Impact on affected individuals and/or aggregated DALY figures

It depends on the severity of the outbreak, the countries/regions, and the type of enterprise. If left untreated, anthrax can cause serious disease and high mortality.

**GAP:** To improve communication.

Zoonosis: cost of treatment and control of the disease in humans

A large exposure of the human population to anthrax would have a huge an economic impact.

Direct impact (a) on production

Variable impact depending on size of outbreak. Loss or reduced efficiency of production, which reduces farm income. The severity of the impact will depend on specific circumstances.

**GAP:** To understand species susceptibility and the risk of introducing animals to a high-risk area.

Direct impact (b) cost of private and public control measures

Costs of control, vaccination, and effective disposal of infected carcasses and contaminated materials. Costs vary depending on country and size of outbreak.

Indirect impact

Outbreaks can affect marketability of animal products. Tourism can be affected, particularly wildlife reserves.

**GAP:** It is important to have a public communication strategy, which provides accurate and authoritative information.

Trade implications

**Impact on international trade/exports from the EU due to existing regulations**

Limited impact.

**Impact on EU intra-community trade due to existing EU regulations**

Limited impact.

**Impact on national trade due to existing regulations**

Limited impact.

Main perceived obstacles for effective prevention and control

Lack of effective veterinary services in some affected countries and local cultural practices concerning slaughter and consumption of sick or dead animals.

**GAP:** Provision of effective veterinary services, diagnostic capabilities and education of the public. Effective disposal of infected carcasses and contaminated material.

Main perceived facilitators for effective prevention and control

Effective veterinary services, diagnosis, reporting and annual vaccination in endemic areas. Implementation of quarantine and effective disposal practices.
Risks

Risks mainly associated with the handling of infected carcasses and contaminated animal products. Failure to vaccinate in endemic areas, or to follow effective disposal procedures, will lead to continued environmental contamination with spores. Cultural practices (slaughter and consumption of sick animals) could put certain groups at high risk of contracting anthrax. One should not discount the potential for bioterrorism.

**GAP:** More information about the risk of anthrax is required.

Conclusion

Anthrax can be controlled if vaccination programmes are adhered, to and if effective disposal of carcasses and contaminated materials are practised. Effective veterinary services and diagnostic capability are necessary to prevent and control anthrax. It is important to have a public communication strategy, which provides accurate and authoritative information. In areas of the world where the disease is uncommon, medical professionals and veterinarians often lack the experience to correctly diagnose anthrax.

Sources of information

Name of expert group leader

Names of expert group members are published where permission has been given.

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Project Management Board

Date of submission by expert group

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