Framework for Enhancing Anthrax Prevention & Control
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Illustration of long chains of *Bacillus anthracis* rods
Introduction to Anthrax

Anthrax is a serious infectious disease caused by gram-positive, rod-shaped bacteria known as Bacillus anthracis.

1. Transmission

The bacteria that cause anthrax can be found naturally in soil and commonly affect domestic and wild animals around the world. The animals can become infected when they ingest spores from contaminated soil, plants, or water.

Spores form when bacilli in blood or body fluids from carcasses are exposed to air, or when carcasses are opened by scavengers. The spores begin to form 4 to 10 hours after death, and the process of sporulation is complete within 24 to 48 hours. These spores are very hardy and they contaminate the soil, where they can survive for many years (Figure 1). Vegetative cells within an intact carcass will be outcompeted by other bacteria and die within 2 to 3 days.


Figure 1—The cycle of anthrax infection in livestock.
2. Ecologic factors

Ecological factors can influence when anthrax outbreaks occur.

Precipitation

Rain concentrates spore-containing soil into low-lying areas and surface waters. The spores are hydrophobic and float from groundwater to surface of soil, and they cling to vegetation or roots. Outbreaks occur primarily in hot, dry months following spring rains, which promote pasture growth and grazing. In addition, prolonged spring rains promote large tabanid (biting) fly populations, which may serve as mechanical vectors.

Seasonality

Anthrax is a hot season disease, as the outbreaks most often occur during hottest summer months or at the end of drought. Animals may gather in low-lying, high-anthrax risk areas to graze on remaining vegetation as spring growth dries up in the heat. Additionally, animals are drawn to new vegetation that occurs following rains at the end of a drought. In both instances, animals may graze down to surface soil or roots. This dry vegetation is abrasive and may cause mucosal trauma to the animals, thus increasing the chances of infection. Also, the animals may consume anthrax spores along with the surface soil and roots. Finally, drought conditions may reduce the animal's resistance to infection by increasing stress and causing nutritional changes.

Soil factors

Soil alkalinity, high calcium content, moisture, and high organic matter content favor spore survival. Calcium preserves spore latency. Spores will disappear from soils with pH less than 6.1.

Soil disruption by human activity (loosening and excavating soil from prior anthrax graves or contaminated sites) or natural events causes spores to surface and promotes increased growth of vegetation, which may be contaminated and attract more animals, resulting in new infections.

3. Host Susceptibility

Susceptibility varies by animal species (Figure 2). Cattle and sheep are highly susceptible and can have hyperacute to acute disease, including sudden death without prior signs of illness. Horses have hyperacute to acute disease with signs for 2 to 3 days before death. Pigs and carnivores are more resistant and may have subclinical disease. Scavengers are relatively resistant.

The incubation period in livestock is typically 3 to 7 days (range 1 to 14 days). The OIE international trade regulation incubation period is 20 days.

Figure 2—Animal susceptibility to anthrax infection. Ruminants (cattle, sheep, and goats) are the most susceptible, followed by pseudoruminants (e.g. horses and pigs), with carnivores and scavengers such as wild cats and vultures being the least susceptible.
4. Human Infection

People become incidental hosts through contact with infected animals or contaminated animal products. They can become ill if they:

- Get spores in a cut or scrape of the skin
- Eat food or drink water that is contaminated with spores
- Breathe in spores
- Inject spore-contaminated illicit drugs (e.g. heroin)

The type of anthrax infection (cutaneous, gastrointestinal, inhalation, or injection) depends on how anthrax enters the body—while some types of infection are more severe than others, all forms can cause systemic illness and result in death if untreated. Incubation period in people ranges from 1 day to more than 2 months.

Presentations

- **Cutaneous anthrax**—a clump of small blisters or lumps that may itch, swell, and eventually develop into an ulcer with a black center; the lesion may be painless and is often located on the face, neck, arm, or hands
  - Incubation period: up to 17 days, but most disease occurs in 1 to 7 days
  - Exposure: butchering an animal that died of anthrax or contact with contaminated animal products such as meat, hide, blood, or hair
  - Scratches or cuts on skin may increase risk
  - Handwashing may decrease risk

- **Inhalation anthrax**—initially, fever, chills, and fatigue may be accompanied by cough; slightly later, chest discomfort, headache, and nausea/vomiting occur; finally, shortness of breath and confusion
  - Incubation period: up to 60 days, but most disease occurs in 1 to 7 days
  - Exposure: working with spore-contaminated hides in an industrial setting or bioterrorism

- **Gastrointestinal anthrax**—fever/chills, fatigue, nausea/vomiting, and abdominal pain are common; diarrhea, headache, and confusion occur in about a quarter of patients; swelling of neck, sore throat, or painful swallowing suggest pharyngeal disease
  - Incubation period: up to 16 days, but most disease occurs in 1 to 7 days
  - Exposure: eating meat from an animal that died of anthrax

- **Injection anthrax**—similar to cutaneous anthrax, but injection anthrax has the potential to spread more rapidly throughout the body
  - Incubation period: up to 20 days, but most disease occurs in 1 to 7 days
  - Exposure: injecting spore-contaminated illicit drugs (e.g. heroin)

Treatment

All types of anthrax infection can be treated with antibiotics. Doctors will determine whether oral or intravenous and how many antibiotics are needed based on the patient’s history and physical exam (see Treatment section in References).

Another option for treatment is anthrax antitoxin—antitoxins target anthrax toxins in the body, but must be administered in conjunction with antibiotics.

Patients with serious cases of anthrax will need to be hospitalized and may require aggressive treatment, including fluid drainage, blood pressure support, and mechanical assistance with breathing.
5. Diagnosis

**Animals**
Rapid diagnostic methods require testing the carcass while it is still fresh. Once the carcass is putrefied or scavenged, culture is required to isolate *B. anthracis*. Samples should be collected without opening the carcass. Specimens can include blood, tissue, exudates, other fluids, and nasal turbinates.

**Humans**
Specimens can include blood, skin lesion exudates, pleural or ascitic fluid, cerebrospinal fluid, or stool. Specimens should always be collected prior to antibiotic therapy. Culture and Gram stains will likely be negative if specimens are collected after antibiotic therapy has been initiated, regardless of the form of disease. The likelihood that antigen or molecular testing methods will be positive decreases with the length of antibiotic treatment prior to sample collection. All samples (except sera for serology) must be collected prior to the initiation of antibiotics.

<table>
<thead>
<tr>
<th>Available tests</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram stain</td>
<td>Gram-positive rods, square-ended, in pairs or short chains</td>
</tr>
<tr>
<td>Polychrome methylene blue stain (M’Fadyean stain)</td>
<td>Dark blue square-ended rods surrounded by pink capsule. Rods are in pairs or short chains, sometimes as single rods</td>
</tr>
<tr>
<td>Direct antigen detection</td>
<td>Detection of antigen (usually protective antigen, but test will specify)</td>
</tr>
<tr>
<td>Serology</td>
<td>Seroconversion (use as a retrospective diagnosis, as need paired sera collected at least 2 weeks apart)</td>
</tr>
<tr>
<td>PCR</td>
<td>Detection of toxin and capsule DNA</td>
</tr>
<tr>
<td>Culture (Gold standard)</td>
<td>Identification of <em>B. anthracis</em> by: colonial morphology, non-motile, non-hemolytic, gamma phage and penicillin-sensitive, and capsule producing</td>
</tr>
</tbody>
</table>

6. Control and Prevention

The primary actions for animal outbreak management include:

- Rapid identification and treatment of affected animals
- Enhanced case surveillance
- Prophylaxis, vaccination, and quarantine
- Restrict access to suspected sources (feed or pastures)
- Appropriate carcass disposal
- Disinfection of affected premises and materials

The primary actions for human outbreak management include:

- Rapid identification of
  - animal source of outbreak
  - persons exposed to source
  - human cases
- Outpatient treatment of uncomplicated cutaneous cases
- Provision of antibiotics and supportive care for systemically ill patients
- For control measures, see animal outbreak control, as human cases are secondary to animal cases

Sheep are highly susceptible to anthrax. Livestock vaccination is necessary to prevent anthrax in humans and animals.

The objective of outbreak management is to break the infection cycle. Animal vaccination is a key component in a long-term prevention and control program. This framework and references provide information on vaccination program planning and implementation.
Introduction to Framework

This framework outlines a proposed start-to-finish approach to improve the prevention of anthrax outbreaks. Outbreak prevention is achieved primarily through vaccination of livestock against anthrax, which is the principle method for prevention and control of anthrax in animals and subsequent anthrax in humans. Surveillance of animal and human cases is important to identify suspect cases, estimate incidence, and evaluate the impact of control programs. Enhancing outbreak response is key to rapidly implementing control programs and halting the outbreak. Laboratory diagnostic capacity at biosafety level 2 is critical to the rapid identification of animal and human cases. These steps augment effective and efficient vaccination of livestock to prevent and control anthrax.

The principles and methods described in this framework can apply to any anthrax-endemic country, and can be modified to meet specific areas needing improvement. As epidemiological information is accrued about a given region, this framework can be expanded to include detailed protocols, system descriptions, and in-depth evaluations.

This framework is subdivided into 2 general phases:

- **Phase I—Assessment:**
  - Assessment of the current situation and systems at national and regional levels
  - Identification of target region(s) for initial prevention and control activities
  - Assessment of the current situation and systems in selected region(s)
  - Evaluation of system’s strengths, weaknesses, and barriers to improvement

- **Phase II—Implementation and Recommendations:**
  - Improvement of current systems in targeted region(s) with high disease burden
  - Implementation of prevention and control measures

This illustration is part of an anthrax prevention educational series developed by CDC. Here, the health message is to avoid slaughtering sick animals and cooking or drying their meat for human consumption.
Phase I—Assessment

1. Assessment of the current situation and surveillance systems at national and regional levels

   A. Surveillance
   
   I. Describe current surveillance capabilities and activities at the national level
   
   1. Are there any surveillance systems at the national level capturing information on anthrax cases in humans?
      a. Describe available systems and reporting flow.
   
   2. Are there any surveillance systems at the national level capturing information on anthrax cases in animals?
      a. Describe available systems and reporting flow.

   II. Review studies or estimates on the burden of anthrax at the national/regional levels
   
   1. Are there estimates of the burden of anthrax in humans—number of outbreaks, illnesses, hospitalizations, deaths, associated costs?
   
   2. Are there estimates on the burden of anthrax in animals—number of outbreaks, deaths, associated costs?

   B. Laboratory
   
   I. Describe current capabilities at national and regional laboratories.
   
   1. Which labs, if any, are performing anthrax diagnostics?
   
   2. Describe current safety measures, procedures, training, and equipment.
   
   3. Describe current capabilities at clinic and hospital levels

   II. Describe the current diagnostics available and performed.
   
   1. Are cultures and stains routinely performed for other bacterial illnesses (or is most treatment empiric)?
   
   2. Describe current safety measures, procedures, training, and equipment.

   C. Anthrax vaccine and vaccination
   
   I. Describe the vaccine(s) used/available in the country/regions.
   
   1. Where is the currently used vaccine produced?
   
   2. How is the vaccine manufactured? What strain is used? Are different vaccines used for different animal species?
   
   3. Are any anthrax vaccines produced in country, if not the currently used vaccine?

   II. Describe the current vaccination situation throughout the country/regions.
   
   1. Logistics for vaccine acquisition, distribution, and delivery.
   
   2. Affordability of livestock anthrax vaccination to livestock producers.
      a. Purchasing mechanism: do owners request and purchase through local veterinarians; is vaccine and/or vaccination provided by government; or a combination?
   
   3. Knowledge and acceptance of vaccine use by livestock producers.
   
   4. Estimates on the vaccination coverage of livestock.

   III. Describe vaccination policies and regulations for livestock animals.
   
   1. Timing, frequency of vaccinations, who administers, minimum age of animals at vaccination.

   D. Stakeholders
   
   I. Identify national and regional key partners and stakeholders (national institutes, universities, hospitals, animal industry, NGO's, etc.) for anthrax surveillance.
2. Identification of target region(s) for initial prevention and control activities

Anthrax is typically endemic in only some regions of a country, and thus control programs are most useful and cost effective when targeted to these areas. In countries where there is more than one endemic region or state, a phased implementation is a prudent approach. Several factors should be considered when selecting the region for the initial phase of implementation. These include:

- **Surveillance**—where burden is greatest based on human or animal disease surveillance data
- **Stakeholders**—presence of partners who are willing and able to implement the program
- **Security**—adequate for national-level staff to visit
- **Support**—sufficient funding and buy-in to implement the program, whether fully government-funded or costs are shared with animal owners

In countries where current surveillance is poor, hold discussions with regional human and animal health authorities to estimate disease incidence.

3. Current situation and systems in selected region(s)

Once a target region (likely a state/district) has been selected, the available surveillance data and outbreak investigation processes should be documented for the state/district.

**A. Surveillance**

I. Identify the case definitions used for human and animal cases in the selected regions.

II. Identify current and retrospective cases/outbreaks in both humans and animals.

III. Review human cases to understand source and exposure:

1. Cutaneous or gastrointestinal cases are typically reported in agricultural settings.
2. Inhalation cases may be observed in industrial settings such as (for example, processing animal hides).
3. Identify exposure sources (livestock, wildlife, or animal products).
   a. If surveillance data are limited, assess presence/absence of human cases at the lowest level possible (village, district, state or region by speaking to local animal/human health providers or authorities).

IV. Review animal cases:

1. What animals are primarily affected: livestock species or wildlife species?
2. What are the sources of exposure (grazing, feed, water)?

V. Describe in detail the current surveillance systems for human and animal case reporting in the selected regions.

1. What is the purpose and operation? What resources are used to operate the systems?
2. Describe the data: what is collected, how is it collected, who reports the data, who has access to and works with the data, what is done with the data, and how are the data reported back to the field?
3. What proportion of cases are laboratory confirmed or have a laboratory diagnosis?

**B. Outbreak Investigations**

I. Describe the current investigation procedures used for human cases/outbreaks in the selected regions.

1. Which agencies are involved and what are their roles?
2. Determine how many historical outbreaks were investigated.
3. How promptly are outbreaks reported and investigated?
4. Describe typical actions that result from investigation findings.
II. Describe the current investigation procedures used for animal cases/outbreaks in the selected regions.
   1. Which agencies are involved and what are their roles?
   2. Determine how many historical outbreaks were investigated.
   3. How promptly are outbreaks reported and investigated?
   4. Describe typical actions that result from investigation findings.

C. Laboratory
I. Describe current capabilities at the selected regions.
   1. Describe the current diagnostics available.
   2. Are cultures and stains routinely performed for other bacterial illnesses (or is most treatment empiric)?
   3. Describe current safety measures, procedures, training, and equipment.

D. Anthrax vaccine and vaccination
I. Describe the vaccine(s) used/available in the selected regions.
II. Describe the current vaccination situation in the selected region.
   1. Logistics for vaccine acquisition, distribution, and delivery.
   2. Affordability of livestock anthrax vaccination to livestock producers.
      a. Purchasing mechanism: do owners request and purchase through local veterinarians; is vaccine and/or
         vaccination provided by government; or a combination?
   3. Knowledge and acceptance of vaccine use by livestock producers.
   4. Estimate the vaccination coverage of livestock in the selected region.
III. Describe vaccination policies and regulations for livestock animals.
   1. Timing, frequency of vaccinations, who administers, minimum age of animals at vaccination.

4. Evaluation of system’s strengths, weaknesses, and barriers to improvement
A. Surveillance
I. Review the case definitions for human and animal cases.
   1. Are these in line with international case definitions?
II. Evaluate process of case reports of human cases
   1. Sensitivity of reporting from healthcare provider → local health authority → state → national.
   2. Is the number of human cases associated with each animal case similar to the regional-level ratios?
   3. Are the data timely? Is any action taken when cases are reported? Are specimens collected for lab diagnosis?
III. Is the quality of the data adequate for human case surveillance?
   1. Are case records complete? Are there known errors?
   2. Do human health authorities trust the data reported from these systems?
IV. Evaluate process of case reports of animal cases
   1. Sensitivity of reporting from veterinary provider or owner → local veterinary authority → state → national.
   2. Are the data timely? Is any action taken when cases are reported? Are specimens collected for lab diagnosis?
V. Is the quality of the data adequate for animal case surveillance?
   1. Are case records complete? Are there known errors?
   2. Do animal health authorities trust the data reported from these systems?
B. Outbreak investigations

I. Are the current investigation procedures in line with examples of One Health investigations?
   2. For examples of outbreak investigations, see references at the end of this document.
   3. Example of data collection tool used by CDC (Case Investigation Form) is available in Appendix A.

II. What proportion of reported human cases or outbreaks are investigated? Animal cases?
   1. What is needed to improve this?

III. Are the implemented actions appropriate and effective to control the outbreak?

IV. How well do human, animal, and wildlife agencies interact or participate in an outbreak investigation?
   1. Are agency roles defined and respected by stakeholders?

C. Lab capacity

I. Evaluate performance of the labs carrying out anthrax diagnostics.
   1. Are the labs located in regions where cases are occurring or close to current demand?
   2. Are there challenges transporting samples to laboratories to perform diagnostics?
   3. Are results being reported back to the healthcare providers and agencies?
   4. Is the timeliness sufficient to affect treatment/prevent additional cases?

II. Are the current diagnostics recommended for presumptive or confirmatory identification of B. anthracis?

III. Do the labs have appropriate safety measures to conduct current testing or implement recommended testing?
   1. Review biosafety protocols to ensure safe handling of Bacillus anthracis in the laboratory: Biosafety in Microbiological and Biomedical Laboratories (BMBL): http://www.cdc.gov/biosafety/publications/bmbl5/BMBL.pdf

D. Vaccine and vaccination


II. Is the efficacy or safety of the currently used vaccine(s) uncertain?

III. Compare the current vaccination policies to the Model Country Program Vaccine Template: Anthrax in Humans and Animals, 4th edition, pg 111, Table 10.

IV. Identify barriers to vaccination: consider logistics, cost, and acceptance.
Phase II—Implementation and Recommendations

1. Improvement of current systems in targeted region(s) with high disease burden

Based on evaluation findings and needs assessment, the following steps should be considered to begin addressing the needs for anthrax prevention and control.

A. Enhance surveillance

I. Encourage reporting of cases by local animal/human health providers.

II. Conduct training, provide resources and equipment to conduct work.

III. Integrate human and animal disease epidemiologic and laboratory surveillance data, and clinical and environmental laboratory data.
   1. Hold meetings with the public and animal and wildlife health groups to discuss importance of integrated surveillance, develop protocols for joint investigations, and build relationships.
   2. Implement a system to recognize and reward good quality reporting.
   3. Share and combine case data in maps and reports.
   4. Use combined surveillance data to identify anthrax foci, guide vaccination, and plan communication.

IV. Guidelines for improving animals and human disease surveillance can be found in Anthrax in Humans and Animals, 4th edition, pg 101.

B. Improve outbreak investigations

I. Conduct training and provide resources and equipment to conduct work.

II. Develop standard operating procedures describing how to conduct joint investigations with human and animal health authorities, including a clear description of roles and responsibilities by agency.

III. Human case as sentinel—investigate source of exposure, additional human cases with same exposure, source of animal exposure.

IV. Animal case—trace meat and animal products to destination (market, neighbors, owner); investigate additional animal cases nearby, human exposures and cases, source of animal exposure (contaminated feed or grazing); determine animal vaccination status.

V. Safely collect samples and perform diagnostic testing of suspect cases.

VI. Remove contaminated meat or products from consumer supply, safely dispose of animal carcasses, and implement ring vaccination. Follow guidelines for control of outbreak in animals.

C. Build lab capacity

I. Consider options to improve timeliness of testing and result reporting.
   1. Add anthrax diagnostics to laboratories located in regions where cases are occurring.
   2. Implement shipping, testing, and reporting procedures that specify rapid turn-around.
   3. Establish relationships between laboratory, veterinary, and public health groups.
   4. Develop or update existing procedures on actions to take based on presumptive or confirmatory results, for example quarantine, vaccination, public health messaging.

II. Implement diagnostics that are recommended for presumptive or confirmatory identification of *B. anthracis*

III. Conduct training, implement protocols, provide resources and equipment to safely and effectively conduct lab work

1. Implement the following at peripheral and reference laboratories as needed to ensure safe handling of anthrax samples and accurate results:
   a. Update laboratory infrastructure and equipment to safely receive and test suspect anthrax samples.
   b. Diagnostic service procedures—ensure laboratories are performing tests that are appropriate for the equipment and have adequate control measures in place.
   c. Review and provide training, if needed, in biosafety protocols—physical and operational.
   d. Ensure awareness about and adherence to protocols on Good Laboratory Practices
      01. See References: WHO, Good Laboratory Practice.
   e. Review updates with staff and provide appropriate training.

D. Educate veterinarians, animal workers, physicians, and other healthcare providers

I. Build diagnostic and therapeutic acumen of physicians and their understanding of the purpose of reporting.

II. Teach relevant professionals what anthrax looks like, how to make presumptive and confirmed diagnosis, what to do, how to treat it, and what public health activities are triggered by a report.

E. Evaluate progress and identify new goals for improvement

I. Biannually evaluate each component of the anthrax framework that has been addressed using the questions in the above Evaluation section.
   1. Share the findings of each evaluation with the personnel involved in each component (surveillance, outbreak investigation, laboratory, and vaccination).
   2. Request feedback on identified issues from these personnel, and request input to make changes.
   3. Implement changes.

II. Evaluate the level of knowledge among veterinarians, animal workers, physicians and healthcare providers through formal surveys, and pre-and post-evaluations during anthrax trainings.

2. Implementation of prevention and control measures

The principles of anthrax control are described in Anthrax in Humans and Animals, 4th edition, pg 89–100.

A. Initiate community education

I. Develop messages based on sources of exposure, identified barriers, other information identified in investigations and studies.

II. Train local animal/human health providers to disseminate messages.

III. Identify and utilize other mechanisms to disseminate messages (e.g., radio, print materials, etc.), and use images in areas with low literacy.

B. Test vaccine efficacy and safety
   I. Review efficacy and safety data on vaccines used in region.
   II. If no data are available from the manufacturer, consider testing efficacy and safety to ensure a quality product is being used.
   III. Address barriers identified from operational studies, if any, to vaccination and reporting.

C. Conduct cost-effectiveness studies
   I. Identify the most sustainable vaccination programs and degrees of public-private shared responsibility to help ensure long-term sustainability of the vaccination program.
   II. Relevant perspectives should be modeled:
      1. Governmental perspective, including all costs (e.g., vaccination program, laboratory, loss of productivity, treatment and compensation) and the cost per human case of anthrax averted and per livestock case of anthrax averted,
      2. Producer perspective, examining costs per livestock case of anthrax averted.

D. Vaccination campaign planning and implementation
   I. Establish partnerships to assist with planning and implementation.
      1. Partner organizations experienced in mass animal vaccination could include FAO, US Department of Agriculture, local veterinary associations, and non-government organizations.
   II. Use results from surveillance, social and operational studies, vaccine efficacy studies, and cost-effectiveness studies to determine the modifications needed for the campaign.
      1. Use integrated case data to guide target areas for vaccination.
      2. Determine if more frequent vaccinations are indicated based on epidemiologic data (when is anthrax season) and duration of vaccine efficacy.
      3. Use findings to develop and refine communication messages, determine when and how to disseminate the messages, and target audiences.
      4. Identify an efficacious vaccine that will be used.
      5. Develop policies clearly describing the responsibilities of animal owners and the government, and how this will change over time; notify all stakeholders of the policies before a campaign starts.

E. Control of anthrax in wildlife
   I. Vaccination campaigns are effective for controlling anthrax outbreaks in livestock; however, control strategies for outbreaks in wildlife populations are limited.
   II. Controlling an outbreak primarily focuses on preventing transmission from dead animals:
      1. Burning, covering, or burying carcasses to prevent access by scavengers, adopting fly control measures, restricting access to suspected contaminated areas or water sources, and when practical, safely disposing of animal carcasses.
   III. Prevention messaging and frequently asked questions which may be useful for educating public and wildlife management/ranger staff should be provided
   IV. Guidance and examples for messaging are provided in Anthrax in Humans and Animals, 4th edition, pp 172–175
References


Outbreak Investigation Reports


Treatment


