Slide 1

Anthrax

Malignant Pustule, Malignant Edema, Woolsorters' Disease, Ragpickers' Disease, Maladi Charbon, Splenic Fever

Anthrax is a serious zoonotic disease that can affect most mammals and several species of birds, but is particularly important in herbivores. The word anthrax is derived from a Greek word meaning charcoal or carbuncle. Anthrax, the disease, likely originated 6,000 to 7,000 years ago in Mesopotamia and Egypt, where agricultural civilization was first recorded. Scientific literature first contained a reference to anthrax in 1769, by Fournier. Common names include: Malignant Pustule, Malignant Edema, Woolsorters' Disease, Ragpickers' Disease, and Maladi Charbon.

Slide 2

Overview

- Organism
- History
- Epidemiology
- Transmission
- Disease in Animals
- Disease in Humans
- Prevention and Control

In today's presentation we will cover information regarding the organism that causes anthrax and its history. We will also talk about the epidemiology of the disease, how it is transmitted, species that it affects and clinical and necropsy signs observed. Finally, we will address prevention and control measures for anthrax, including actions to take if anthrax is suspected.

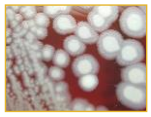
Slide 3

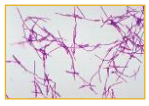
THE ORGANISM

Slide 4

The Organism

- *Bacillus anthracis*
- Large, gram-positive, non-motile rod
- Two forms
  - Vegetative, spore
- Over 1,200 strains
- Nearly worldwide distribution





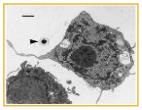
Bacillus anthracis is a gram-positive rod that exists in two forms: the vegetative bacillus and the spore. Within an infected host, spores germinate to produce the vegetative forms which eventually kill the host. These bacilli are released by the dying or dead animal into the environment (usually soil under the carcass). There they sporulate, ready to be taken up by another animal. Although vegetative forms of *B. anthracis* grow and multiply readily in normal laboratory nutrient agars or broths, they are more "fragile" than the vegetative forms of other *Bacillus* species, dying in simple environments such as water or milk. *B. anthracis* is dependent on sporulation for species survival making it an obligate pathogen. Anthrax can be found nearly worldwide and has roughly 1,200 various strains.

[The top photo show non-hemolytic *Bacillus anthracis* on sheep blood agar with "Medusa head" appearance (non-pigmented, dry, ground glass surface, edge irregular with comma projections); the bottom image shows Gram stained *B. anthracis* bacilli. Both images from CDC Public Health Image Library.]

Slide 5

The Spore

- Sporulation requires:
  - Poor nutrient conditions
  - Presence of oxygen
- Spores
  - Very resistant
  - Survive for decades
  - Taken up by host and germinate
- Lethal dose 2,500 to 55,000 spores



When conditions are not conducive to growth and multiplication of vegetative bacilli, *B. anthracis* tends to form spores. Sporulation requires a nutrient poor environment and the presence of free oxygen. The spore form is the predominant phase in the environment, can survive for decades in soil, and it is through the uptake of spores that anthrax is contracted. Heavy rains, alternating with dry periods, may concentrate the spores and result in outbreaks among grazing animals. The spore form of anthrax is markedly resistant to biological extremes of heat, cold, pH, desiccation, and chemicals (and thus to disinfection). Spores are not produced in the unopened carcass (within the anaerobic environment of an infected host the organism is in the vegetative form). It is estimated that 2,500 to 55,000 spores represent the lethal inhalation dose for humans.

[The image shows an electron photomicrograph of a *Bacillus anthracis* spore (arrowhead) partially surrounded by the pseudopod of a cultured macrophage (x137,000) from Dixon TC et al. Anthrax. N.Engl.J.Med. 1999;341:815-26.]

Slide 6

HISTORY

Slide 7

Sverdlovsk, Russia, 1979

- 94 people sick – 64 died
- Soviets blamed contaminated meat
- Denied link to biological weapons
- 1992
  - President Yeltsin admits outbreak related to military facility
  - Western scientists find victim clusters downwind from facility
- Caused by faulty exhaust filter

On April 2, 1979, there was an outbreak of anthrax in the Soviet city of Sverdlovsk (now called Ekaterinburg) about 850 miles east of Moscow. Ninety-four people were affected, and at least 64 people died from inhalational anthrax. The Soviet government claimed that the outbreak was caused by intestinal anthrax from contaminated meat. The US believed that the Soviet Union was violating the Biological Weapons Convention signed in 1972. Thirteen years later, in 1992, President Boris Yeltsin admitted that the anthrax outbreak was the result of military activity at the facility. Western scientists were allowed to investigate in 1992 and found that all the victims were clustered along a straight line downwind from the military facility. Livestock in the same area also died of anthrax. The outbreak was caused by a faulty exhaust filter which was removed and not immediately replaced allowing aerosolized anthrax spores to escape the facility.

Slide 8

South Africa, 1978-1980

- Anthrax used by Rhodesian and South African apartheid forces
  - Thousands of cattle died
  - 10,738 human cases
  - 182 known deaths
  - Black Tribal lands only

South Africa's National Party and apartheid regime of the late 1970s are known to have used biological and chemical weapons. These efforts included covert attacks throughout neighboring nations including Rhodesia (present day Zimbabwe). It is believed that within Rhodesia, from 1978 - 80, thousands of cattle died from intentionally introduced anthrax resulting in a critical food shortage. 10,738 people contracted the disease, resulting in 182 deaths. Outbreaks were almost wholly limited to black inhabited Tribal Trust Lands.

Slide 9

Tokyo, 1993

- Aum Shinrikyo
  - Japanese religious cult
  - "Supreme truth"
- Attempt at biological terrorism
  - Released anthrax from office building
  - Vaccine strain used
  - No human injuries

In 1993, the Aum Shinrikyo, a Japanese religious cult meaning "supreme truth" made several unsuccessful attempts at biological terrorism through the release of anthrax in Tokyo. Anthrax was released from the cult's Tokyo office building laboratory. Police and media reported foul smells, brown steam, some pet deaths, and stains on cars and sidewalks. Fortunately, the strain of anthrax used in the attacks was the vaccine strain, lacking in essential toxic properties. As a result no human injuries were reported in any of these events.

[The image shows Aum Shinrikyo leader Shoko Asahara. Source: Chronology of Aum Shinrikyo's CBW activities, Center for Nonproliferation Studies, Monterey Institute of International Studies. Mangold,T.; Goldberg,J. Plague wars: The terrifying reality of biological warfare.]

Slide 10

U.S., 2001

In 2001, anthrax-contaminated letters were mailed to prominent figures in the U.S. Four recovered letters were sent to: Tom Brokaw at NBC, the New York Post, Senator Tom Daschle, and Senator Patrick Leahy. All were believed to have been mailed from Trenton, NJ. This terrorist attack showed how readily anthrax could spread if manufactured in specific ways. Anthrax spores were able to escape sealed envelopes, contaminate postal machinery, and infect postal workers and mail recipients. For example, a 94 year-old woman died in Connecticut from anthrax, possibly from contaminated mail. In addition, mail sorting machines were also found to be positive at the facility.

[These screen captures are from CNN media postings in 2001]

Slide 11

U.S., 2001

- 22 cases
  - 11 cutaneous
  - 11 inhalational; 5 deaths
- Cutaneous case
  - 7 month-old boy
  - Visited ABC newsroom
  - Open sore on arm
  - Anthrax positive

There were a total of 22 cases of anthrax in the U.S. in 2001; eleven inhalation and 11 cutaneous. Five deaths occurred. The index case was a photojournalist in Florida; two postal workers died in Maryland, and a hospital supply worker died in New York City. The elderly Connecticut farm woman previously described also died.

A 7 month-old boy who visited the ABC newsroom on September 28, 2001 became infected. The child had an elevated white blood count, was afebrile, and had a 2-cm open sore with surrounding erythema and induration that oozed clear yellow fluid. There was swelling and erythema of the entire arm. The initial diagnosis was *Loxosceles reclusa* spider bite. After anthrax exposure was reported at another television network, two punch biopsies were taken. PCR and immunostaining for *Bacillus anthracis* were positive.

[This photo shows the open sore lesion in the child previously described. Source: Roche K, Chang W., Lazarus H. Cutaneous Anthrax Infection. New England Journal of Medicine 2001;345:1611.]

Slide 12

U.S., 2001

- CDC survey of health officials
  - 7,000 reports regarding anthrax
    - 1,050 led to lab testing
  - 1996-2000
    - Less than 180 anthrax inquiries
- Antimicrobial prophylaxis
  - Ciprofloxacin
    - 5,343 prescriptions

During the time period September 11 – October 17, 40 state and territorial health officials responded to a CDC telephone survey. An estimated 7,000 reports had been received at the health departments; approximately 4,800 required phone follow-ups, and 1,050 reports led to testing of suspicious materials at a public health laboratory. In comparison, fewer than 180 anthrax threats were reported between 1996 and 2000.

The antibiotic Ciprofloxacin was offered to many people in the aftermath of the anthrax mailings in 2001. 5,343 people were prescribed the medication for 60 days; 44% adhered to the 60 day treatment. Side effects were experienced by 3,032 people (57%) of those taking antibiotic prophylaxis, and included diarrhea, abdominal pain, dizziness, nausea, and vomiting.

Slide 13

TRANSMISSION

Slide 14

Human Transmission

- Cutaneous
  - Contact with infected tissues, wool, hide, soil
  - Biting flies
- Inhalational
  - Tanning hides, processing wool or bone
- Gastrointestinal
  - Undercooked meat

There are three main routes of anthrax transmission in humans. Cutaneous anthrax may occur when handling infected tissues, wool, hides, soil, and products made from contaminated hides or hair, such as drums, rugs, or brushes. Biting flies are also suspected of being mechanical vectors of anthrax to humans under certain conditions. Inhalational anthrax has been associated with tanning hides and processing wool or bone. Gastrointestinal anthrax occurs when individuals eat undercooked contaminated meat from animals that have died of anthrax. Laboratory acquired cases have also occurred.

[The top image shows wool hanging outdoors. Bottom image: Cattle hides. Source (for both): pixabay.com-public domain]

Slide 15

Human Transmission

- Tanneries
- Textile mills
- Wool sorters
- Bone processors
- Slaughterhouses
- Laboratory workers

People with occupational exposure to animal products are at risk of anthrax infection. This includes workers in tanneries, textile mills, wool sorters, and others. In the 1960s, unvaccinated mill workers were 'chronically exposed' to anthrax; case rates of 0.6 to 1.4% were observed. *B. anthracis* was recovered from the nose and pharynx of 14% of healthy workers in one study; in another study, workers were inhaled 600 to 1300 spores during the working day with no ill effect. A well-documented outbreak of pulmonary anthrax occurred in one mill with a similar level of contamination.

[Photo shows two men shearing sheep. Source: geograph.org.uk-creative-commons]

Slide 16

Animal Transmission

- Bacteria present in hemorrhagic exudate from mouth, nose, anus
- Oxygen exposure
  - Spores form
  - Soil contamination
- Sporulation does not occur in a closed carcass
- Spores viable for decades

In infected animals, large numbers of bacteria are present in hemorrhagic exudates from the mouth, nose, and anus. When they are exposed to oxygen, these bacteria form spores and contaminate the soil. Sporulation also occurs if a carcass is opened and oxygen exposure occurs – sporulation does not occur inside a closed carcass. Anthrax spores can remain viable for decades in the soil or animal products, such as dried or processed hides and wool. Spores can survive for two years in water, 10 years in milk, and up to 71 years on silk threads. Vegetative organisms are thought to be destroyed within a few days during the decomposition of unopened carcasses.

Slide 17

Animal Transmission

- Ingestion
  - Most common
  - Herbivores
    - Contaminated soil
    - Heavy rainfall, drought
  - Carnivores
    - Contaminated meat
- Inhalation
- Mechanical (insects)

In animals, transmission occurs by ingestion and possibly inhalation of spores, although entry through skin lesions has not been ruled out. Herbivores usually become infected when they ingest sufficient numbers of spores in soil or on plants in pastures. Outbreaks are often associated with heavy rainfall, flooding, or drought. Contaminated bone meal and other feed can also spread this disease. Carnivores usually become infected after eating contaminated meat. Vultures and flies may disseminate anthrax mechanically after feeding on infected carcasses.

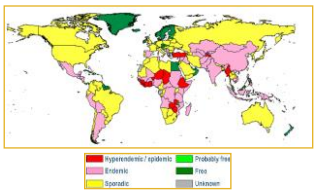
[This photo shows cattle grazing in a pasture. Source: U.S. Department of Agriculture, NRCS]

Slide 18

EPIDEMIOLOGY

Slide 19

Anthrax Distribution



20,000 to 100,000 cases estimated globally/year
http://www.vetmed.lsu.edu/whocc/mp_world.htm

Bacillus anthracis is found worldwide with an estimated 20,000-100,000 human cases each year (M. Swartz. Recognition and Management of Anthrax- An Update. *Anonymous. New England Journal of Medicine.* 345(22):1621-1626, 2001). Anthrax remains common in various countries of Africa and Asia, but is relatively rare in Europe, America, and Australasia.

[This image show the distribution of anthrax cases worldwide. Source: http://www.vetmed.lsu.edu/whocc/mp_world.htm]

Slide 20

Anthrax in the U.S.

- Cutaneous anthrax
  - Early 1900s: 200 cases annually
  - Late 1900s: 6 cases annually
- Inhalational anthrax
  - 20th century: 18 cases, 16 fatalities

In the early 20th century, cutaneous anthrax cases in the U.S. averaged 200 cases per year. During the second half of the century this decreased to approximately 6 cases per year. During the entire 20th century, there were 18 diagnosed cases of inhalational anthrax, 16 of which were fatal.

Slide 21

Anthrax in the U.S.

- Alkaline soil
- "Anthrax weather"
  - Wet spring
  - Followed by hot, dry period
- Grass or vegetation damaged by flood-drought sequence
- Cattle primarily affected

Outbreaks in the U.S. are most often associated with alkaline soil, and there are some areas where anthrax is endemic. Wet conditions followed by hot, dry weather in summer or fall are considered good conditions under which anthrax cases in livestock (cattle primarily) are likely to be seen. Vegetation may be damaged by this wet-dry cycle.

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DISEASE IN HUMANS

Slide 23

Cutaneous Anthrax

- 95% of all cases globally
- Incubation: 2 to 3 days
- Spores enter skin through open wound or abrasion
- Papule → vesicle → ulcer → eschar
- Case fatality rate 5 to 20%
- Untreated – septicemia and death

The cutaneous form of anthrax accounts for 95% of all cases globally. Incubation is typically 2 to 3 days, but can be longer. Spores typically enter the skin via abrasions or other open wounds. A papule develops and progresses into a vesicle. The vesicle ruptures, becomes necrotic, and enlarges, forming an ulcer covered by a characteristic black eschar in 7 to 10 days. The eschar may be surrounded by moderate to severe non pitting, gelatinous edema. Low-grade fever and malaise are frequent. The eschar dries and tails of within one to two weeks. The case fatality rate for cutaneous anthrax is 5 to 20%. If left untreated it can lead to septicemia and death. Death can occur through asphyxiation from the edema if the lesion is around the head or neck.

Slide 24

[This slide shows the progression of cutaneous lesions. The head, forearms, and hands are most often affected. Source: Centers for Disease Control and Prevention at http://www.bt.cdc.gov/agent/anthrax/anthrax-images/cutaneous.asp]

Slide 25

Case Study: Cutaneous Anthrax

- North Dakota, 2000
- 67 year old man
- Helped in disposal of 5 cows that died of anthrax
- Developed cutaneous anthrax
- Recovered with treatment

During the year 2000, 32 farms were quarantined for anthrax in the U.S. From July 6-Sept 24, 157 animals died. A 67 year old man, who helped dispose of 5 cows that had died of anthrax, developed cutaneous anthrax several days later. He was prescribed ciprofloxacin and recovered fully.

Slide 26

Gastrointestinal Anthrax

- Incubation: 2 to 5 days
- Severe gastroenteritis common
  - Consumption of undercooked or contaminated meat
- Case fatality rate: 25 to 75%
- GI anthrax not documented in U.S.
  - Suspected in Minnesota outbreak

The symptoms of gastrointestinal anthrax appear typically two to five days (15 hours up to 7 days) after the ingestion of undercooked meat containing anthrax spores. Two forms of gastrointestinal anthrax can occur. The oropharyngeal form is not well known. Symptoms include sore throat, dysphagia, fever, hoarseness, and swelling of the neck. The abdominal form is more common, and consists of severe gastroenteritis consisting of nausea, vomiting, fever, and abdominal pain progressing rapidly to severe, bloody diarrhea. The primary intestinal lesions are ulcerative and occur mainly in the terminal ileum or caecum. The case fatality rate is 25 to 75%. GI anthrax has rarely been described as occurring in the US; however, there have been no confirmed clinical cases reported to public health authorities.

Slide 27

Case Study: Gastrointestinal Anthrax

- Minnesota, 2000
- Downer cow approved for slaughter by local veterinarian
- 5 family members ate meat
  - 2 developed GI signs
- 4 more cattle died
- *B. anthracis* isolated from farm but not from humans

In late July 2000, a downer cow was approved for slaughter and family consumption by the local veterinarian on a farm in Northern Minnesota. Five family members ate well-cooked steak and hamburgers over the next few weeks; two reported gastrointestinal signs of diarrhea, abdominal pain, and fever. When four more animals died, a carcass was tested and *B. anthracis* was isolated. While anthrax was never isolated from the human cases, they were placed on chemoprophylaxis and anthrax vaccinination was initiated.

[Source: CDC. Human Ingestion of *Bacillus anthracis*-Contaminated Meat- Minnesota, August, 2000. Anonymous. *MMWR* 49(36):813-816, 2000.]

Slide 28

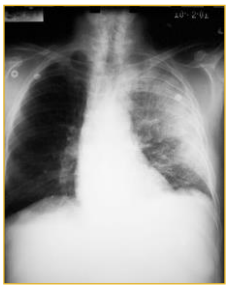
Inhalational Anthrax

- Incubation: 1 to 7 days
- Initial phase
  - Nonspecific (mild fever, malaise)
- Second phase
  - Severe respiratory distress
  - Dyspnea, stridor, cyanosis, mediastinal widening, death in 24 to 36 hours
- Case fatality: 75 to 90% (untreated)

The incubation period for inhalational anthrax is 1 to 7 days. There is some evidence that inhaled anthrax spores may take as long as 60 days to cause illness. In the initial phase, anthrax signs are nonspecific; they may include mild fever, malaise, myalgia, nonproductive cough, and some chest or abdominal pain. Illness progresses within 2 to 3 days leading to fever, dyspnea, cyanosis, stridor, mediastinal widening, and subcutaneous edema of the chest and neck. The second stage of disease is characterized by rapidly deteriorating health within 24 to 36 hours. The case fatality rate is 75 to 95% if untreated. Antibiotics and medical care within the first 48 hours of the onset of signs are indicated.

[Source: M. Swartz. Recognition and Management of Anthrax-An Update. *New England Journal of Medicine* 345(22):1621-1626, 2001.]

Slide 29



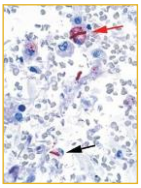
This photo shows X-ray evidence of mediastinal widening and pleural effusion, two common findings of inhalational anthrax.

[Source: J. Jernigan, D. Stephens, D. Ashford, C. Omenaca, M. Topiel, M. Gallbraith, M. Tapper, and et al. Bioterrorism-Related Inhalational Anthrax: The First 10 Cases Reported in the United States. *Emerging Infectious Diseases* 7:933-944, 2001.]

Slide 30

Diagnosis in Humans

- Identification of *B. anthracis*
  - Blood, skin, secretions
- Culture
- PCR
- Serology
  - ELISA
- Nasal swabs
  - Screening tool



Anthrax is diagnosed by finding *B. anthracis* in clinical samples (i.e. blood, skin lesions, or respiratory secretions), or by isolating the organism in culture. Polymerase chain reaction (PCR) techniques can also be used to identify *B. anthracis*. Antibodies develop late in the course of disease, and serology is only useful in retrospective studies. An ELISA test was approved by the FDA (in collaboration with the CDC) in 2004. This test is quicker and easier to interpret than previous antibody testing methods, and it can be completed in less than one hour. In 2001, nasal swabs were used as a rapid exposure assessment tool, and as a tool for rapid environmental assessment. Nasal swabs are not used for diagnosing anthrax and are not 100% effective in determining all who may have been exposed.

[Photo: Lung tissue from a fatal case showing *Bacillus anthracis* granular antigen staining inside a perihilar macrophage (red arrow) and intra- and extracellular bacilli (black arrow). (Immunohistochemical assay with a mouse monoclonal anti-*B. anthracis* cell-wall antibody and detection with alkaline phosphatase and naphthol fast red, original magnification 100X). Source: J. Jernigan, D. Stephens, D. Ashford, C. Omenaca, M. Topiel, M. Gallbraith, M. Tapper, and et al. Bioterrorism-Related Inhalational Anthrax: The First 10 Cases Reported in the United States. *Emerging Infectious Diseases* 2001;7:933-944.]

Slide 31

Treatment

- Penicillin
  - Most natural strains susceptible
- Additional antibiotic options
  - Ciprofloxacin
    - Treatment of choice in 2001
    - No strains known to be resistant
  - Doxycycline
- Course of treatment: 60 days

Penicillin has been the drug of choice for anthrax for many decades, and only very rarely has penicillin resistance been found in naturally occurring isolates. Some strains, particularly those used in bioterrorist attacks, may be resistant to penicillin. For this reason, the CDC recommends other antibiotics as the initial treatment, particularly for systemic disease, until antibiotic susceptibility has been determined. Antibiotics are effective only against the vegetative stage of *B. anthracis*, and not against spores. Treatment is continued for at least 60 days in inhalational anthrax, as spores may be able to remain dormant in the lungs and germinate during that time. Supportive therapy may also be necessary, particularly for the inhalational and gastrointestinal forms. Effective treatment depends on early recognition of the symptoms: treatment for cutaneous anthrax is usually effective, but the inhalational and gastrointestinal forms are difficult to recognize early and the mortality rates are higher.

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	Cold	Flu	Inhalational Anthrax
Symptoms			
Fever at or above 100°F	Uncommon in adults and older children.	Usual and can last 3 to 4 days.	Usual.
Headache	Usual.	Usual with sudden onset, and can be severe.	Sometimes.
Muscle Aches	Mild.	Usual, and often severe.	Sometimes.
Tiredness and Exhaustion	Mild.	Usual with sudden onset, can be severe, and can last 2 or more weeks.	Usual.
Runny Nose	Usual.	Usual.	Rare.
Cough	Usual.	Usual, and can become severe.	Usual.
Chest Discomfort	Uncommon.	Uncommon.	Usual.
Vomiting	Uncommon.	Uncommon in adults but more likely in very young children.	Usual.

Effective treatment depends on early recognition of the symptoms; however, anthrax may resemble the common cold or flu. This chart describes some of the differences between inhalational anthrax and more common diseases. With inhalational anthrax, there is no runny nose. However, chest discomfort and vomiting are common.

[Source: MMWR. Considerations for Distinguishing Influenza-Like Illness from Inhalational Anthrax Vol 50, No 44; 986-6 11/09/2001]

Slide 33

Prevention and Control

- Humans protected by preventing disease in animals
  - Veterinary supervision
  - Trade restrictions
- Improved industry standards
- Safety practices in laboratories
- Post-exposure antibiotic prophylaxis

Humans can protect themselves by preventing disease in animals. Veterinary supervision of animal production and slaughter also helps prevent contact with infected livestock or animal products. Trade restrictions may be placed on certain animal products from countries where anthrax is common and uncontrolled. Improvements in industry standards have decreased the occupational risks for people exposed to imported hides, wool, bone meal, and other animal products. In laboratories, good safety practices, including the use of biological safety cabinets, should be employed. Veterinarians should use protective clothing and equipment when examining sick animals. They should also avoid opening the carcasses of suspected cases. Post-exposure antibiotic prophylaxis is recommended for people who have been exposed to aerosolized anthrax spores. Treatment should be continued for at least 60 days. Simultaneous antibiotics and vaccination can be used in exposed humans, as human anthrax vaccines, unlike livestock vaccines, are not live.

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Vaccination

- Cell-free filtrate
- At risk groups
  - Veterinarians
  - Lab workers
  - Livestock handlers
  - Military personnel
- Immunization series
  - Five IM injections over 18-week period
  - Annual booster

The U.S. human anthrax vaccine is a cell-free filtrate produced from an avirulent strain; it contains no whole bacteria, dead or alive. The vaccine was developed during the 1950s and 1960s for humans, and was licensed by the FDA in 1970. Since then, it has been administered to at-risk wool mill workers, veterinarians, laboratory workers, livestock handlers, and others than handle animal hides or furs. Anthrax vaccination is mandatory for designated military and emergency-essential personnel, as well as comparable Department of Defense civil employees. The vaccine is manufactured by one company, the BioPort Corporation. The primary immunization series consists of five intramuscular injections given at day 0, week 4, months 6, 12, and 18. Following the priming series, annual booster injections of the vaccine are recommended.

[This photo shows a military corpsman receiving a vaccine. Source: U.S. Navy via commons.wikimedia.org]

Slide 35

Vaccine Side Effects

- Injection site reactions
  - Mild: 30% men, 60% women
  - Moderate:1 to 5%
  - Severe:1%
- Systemic effects rare
  - Muscle or joint aches, headache, rash, chills, fever, nausea, loss of appetite
- No long-term side effects noted

Vaccine side effects include injection site reactions. About 30% of men and 60% of women experience mild local reactions -- not unlike other vaccinations. 1 to 5% of individuals experience moderate local reactions. Severe local reactions occur at a rate of 1%. System reactions occur in less than 0.2% of people. There have been no patterns of long-term side effects from the vaccine, neither persistent nor delayed side.

Slide 36

ANIMALS AND ANTHRAX

Slide 37

Clinical Signs

- Many species affected
  - Ruminants at greatest risk
- Three forms
  - Peracute
    - Ruminants (cattle, sheep, goats, antelope)
  - Acute
    - Ruminants and equine
  - Subacute-chronic
    - Swine, dogs, cats

Virtually all mammals and some birds can contract anthrax. Clinical signs in animals differ by the species, with ruminants being the most at risk. The peracute form most often affects ruminants, including cattle, sheep, and goats. The acute form will affect ruminants, as well as horses. The subacute or chronic form most often affects swine, dogs, and cats. The incubation period varies from 1-20 days. In herbivores, infections become apparent after 3-7 days, while in pigs it usually takes 1-2 weeks.

[This antelope is hemorrhaging from the nose. Source: World Health Organization]

Slide 38

Ruminants

- Peracute
  - Sudden death
- Acute
  - Tremors, dyspnea
  - Bloody discharge from body orifices
- Chronic (rare)
  - Pharyngeal and lingual edema
  - Death from asphyxiation

In ruminants, peracute systemic disease is common; sudden death may be the only sign. Staggering, trembling, and dyspnea may be seen in some animals, followed by rapid collapse, terminal convulsions, and death. In the acute form, clinical signs may be apparent for up to 2 days before death. In this form, fever and excitement may be followed by depression, stupor, disorientation, muscle tremors, dyspnea, and congested mucous membranes. Pregnant cows may abort, and milk production can drop severely. Bloody discharges from the nose, mouth, and anus are sometimes seen. Occasionally, infections in ruminants are characterized by subcutaneous edematous swellings, most often in the ventral neck, thorax, and shoulders. Anthrax in wild herbivores varies with the species, but tends to resemble the disease in cattle.

Subacute to chronic infections occur in less susceptible species such as pigs, but can also be seen in cattle, horses, dogs, and cats. The main symptoms are pharyngeal and lingual edema, with animals dying from asphyxiation. Extensive, localized, subcutaneous edema of the ventrum, including the neck, sternum, and flank can also be seen. The carcass will decompose fairly rapidly leading to bloating, but rigor mortis will not be complete. Dark, tarry blood may ooze from body orifices. Treatment with antibiotics can be successful if begun early in the course of the disease.

[Photo shows a cow carcass with hemorrhaging from the nose. Source: Dr. Danelle Bickett-Weddle, Iowa State University, College of Veterinary Medicine]

Slide 39

Differential Diagnosis (Ruminants)

- Blackleg
- Botulism
- Poisoning
  - Plants, heavy metal, snake bite
- Lightning strike
- Peracute babesiosis

Differential diagnoses for anthrax in ruminants include other potential causes of acute death, such as blackleg, botulism, poisoning (plants, heavy metals, and snake bite), lightning strike, and peracute babesiosis.

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Equine

- Acute
  - Fever, anorexia, colic, bloody diarrhea
  - Swelling in neck
    - Dyspnea
    - Death from asphyxiation
  - Death in 1 to 3 days
- Insect bite
  - Hot, painful swelling at site

Photo from WHO

Horses typically develop acute disease. Common symptoms in this species include fever, chills, anorexia, depression, severe colic, and bloody diarrhea. Swellings may be seen in the neck, sternum, lower abdomen, and external genitalia. Dyspnea can occur due to the swelling of the neck. Affected animals usually die within 1 to 3 days, but some animals can survive up to a week. If a horse contracts anthrax via a bite from an insect, a localized, hot, painful, subcutaneous swelling will occur. The swelling will soon spread to the throat (causing dyspnea), sternum, abdomen, and external genitalia.

[This photo shows a dead zebra with hemorrhaging from the nose. Source: World Health Organization]

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Pigs

- Acute disease uncommon
- Subacute to chronic
  - Localized swelling of throat
    - Dyspnea
    - Asphyxiation
  - Anorexia
  - Vomiting, diarrhea

Septicemia and sudden death occurs occasionally in pigs. More often, pigs have mild subacute to chronic infections characterized by localized swelling and systemic signs, such as fever and enlarged lymph nodes. Some animals develop rapidly progressive swelling of the throat, with dyspnea and difficulty swallowing; these animals may suffocate. Intestinal involvement with anorexia, vomiting, diarrhea, or constipation is less common. Some pigs with anthrax recover. Recovered, asymptomatic animals may have signs of localized infections in the tonsils and cervical lymph nodes at slaughter.

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Carnivores

- Relatively resistant
  - Ingestion of contaminated raw meat
- Subacute to chronic
  - Fever, anorexia, weakness
  - Necrosis and edema of upper GI tract
  - Lymphadenopathy and edema of head and neck
  - Death
    - Due to asphyxiation, toxemia, septicemia

Anthrax infection is generally rare in dogs and cats, but can occur when they ingest contaminated carcasses or animal by-products. Clinically apparent anthrax in dogs, cats, and wild carnivores resembles the disease in pigs. A recent review of published cases in dogs suggests that massive swelling of the head, neck, and mediastinum is the most common symptom in this species. In the published cases, death was usually the result of toxemia and shock, but swelling of the throat and suffocation could also have been a factor. Hemorrhagic gastroenteritis was reported in one dog, in addition to a swollen foreleg and ptyalism. Severe acute gastroenteritis has also been reported in other carnivores and omnivores.

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Diagnosis and Treatment

- Necropsy not advised!
- Do not open carcass!
- Samples of peripheral blood needed
  - Cover collection site with disinfectant soaked bandage to prevent leakage
- Treatment
  - Penicillin, tetracyclines
- Reportable disease

Necropsy of affected carcasses is not advised. Due to poor clotting, a blood sample can be taken post-mortem from a superficial vessel, such as an ear vein, or with a Anthrax syringe from any available vein. The collection site should be covered with a disinfectant-soaked bandage to prevent leakage of contaminated blood. Blood smears should be made and the blood submitted for isolation of *B. anthracis*. The organism is very sensitive to penicillin and tetracyclines, and these are the antibiotics of choice if infection is detected early. Care must be taken in handling infected tissues or carcasses because the organism can penetrate cuts in the skin, resulting in localized infection with subsequent dissemination. Anthrax is a notifiable disease.

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Case Study: Canine Anthrax

- Golden retriever, 6 yrs old
  - 2 day history of ptyalism and swelling of right front leg
  - Temperature 106°F, elevated WBC
  - Died same day
- Necropsy
  - Splenomegaly, friable liver, blood in stomach
  - 2x2 cm raised hemorrhagic leg wound
  - Some pulmonary congestion

In 1991 in Mississippi a 6 year old golden retriever presented with a 2 day history of ptyalism and swelling of the right front leg, elevated temperature (106°F), and elevated white blood cell count (25,900/µl). The dog died the same day. Necropsy showed splenomegaly, a friable liver, blood in the stomach and intestines, a 2x2 cm raised hemorrhagic wound on the RF leg, some pulmonary congestion, and bacteria in hepatic sinusoids, renal glomerular capillaries, and myocardial blood vessels. Death was attributed to toxemia/septicemia. Anthrax was confirmed with electron microscopy.

[This photo shows a golden retreiver. Source: commons.wikimedia.org]

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Case Study: Canine Anthrax

- Source of exposure in question
  - Residential area
  - 1 mile from livestock
  - No livestock deaths in area
  - Dove hunt on freshly plowed field 6 days prior to onset
- Signs consistent with ingestion but cutaneous exposure not ruled out

The circumstances of this case leave several unanswered questions regarding the source of exposure of this dog to anthrax. Exposure was considered unlikely during the 6 days prior to death because the dog was kept at home, albeit unrestrained, in a residential area with no livestock within approximately 0.8 km. No livestock deaths had been reported at this site. Exposure of the dog was presumed to have occurred 6 days prior to initial clinical signs (7 days prior to death) during a dove hunt over a freshly plowed field. One possible source includes carrion ingested in adjacent wooded areas, although a carcass was not found. Ingestion would be the most likely explanation for the gastrointestinal hemorrhage found at necropsy. A second possibility is percutaneous infection, such as a wound or an insect bite. Although cutaneous anthrax has not been described in animals, wound contamination could not be ruled out.

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Vaccination

- Livestock in endemic areas
- Sterne strain
  - Live encapsulated spore vaccine
- No U.S. vaccine for pets
  - Used in other countries
  - Adjuvant may cause reactions
- Working dogs may be at risk

Annual vaccination of livestock in endemic areas is recommended. The most widely used vaccine is the Sterne-strain vaccine. It is a non-encapsulated, live variant strain of *B. anthracis* developed in 1937. Immunity develops 7 to 10 days after vaccination. The vaccine produced in the U.S. is licensed for use in livestock only (cattle, sheep, horses, goats, and swine). No U.S. anthrax vaccine is licensed for use in pets. In other countries, live spore vaccines produced from the Sterne strain have been used to vaccinate pets and exotic species. The vaccine contains saponin as an adjuvant and its use in cats and dogs may produce injection site reactions. Cases in domestic cats are very rare. Working dogs might put themselves at risk by exposure to dead carcasses.

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Animals and Anthrax

- Anthrax should always be high on differential list when:
  - High mortality rates observed in herbivores
  - Sudden deaths with unclotted blood from orifices occur
  - Localized edema observed
    - Especially neck of pigs or dogs

Anthrax should always be high on a differential list when there is high mortality in a group of herbivores, sudden death occurs with unclotted blood from orifices, and localized edema occurs, especially of the neck in pigs and dogs.

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PREVENTION AND CONTROL

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Prevention and Control

- Report to authorities
- Quarantine the area
- Do not open carcass
- Minimize contact
- Wear protective clothing
  - Latex gloves, face mask

Anthrax is a notifiable disease; if anthrax is suspected the state veterinarian and local health officials should be contacted. Do not open the carcass to perform a necropsy due to the potential for contamination and exposure. Make sure there is minimal contact with the carcass by establishing a quarantine area, generally for 21 days after the last anthrax death. Wear protective clothing, such as a face mask and gloves, if it is necessary to work with the dead animal. Be sure to cover any areas of broken skin on yourself so that no infectious organisms come in contact with those areas. [Photo of a veterinarian in Mali preparing to vaccinate cattle for anthrax. Source: J. VanAcker/Food and Agriculture Organization of the United Nations (FAO)]

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Prevention and Control

- Local regulations determine carcass disposal options
  - Incineration
  - Deep burial
- Decontaminate soil
- Remove organic material and disinfect structures

Since necropsies are not advised, it is best to burn or bury the carcasses and all contaminated materials, then decontaminate the soil with 5% lye or quicklime (anhydrous calcium oxide). If structures have been contaminated, remove the organic material and disinfect with an approved chemical. [Photo of carcass burial. Source: Environmental Health Services, Department of Public Health, Kings County, California]

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Prevention and Control

- Isolate sick animals
- Discourage scavengers
- Use insect control or repellants
- Prophylactic antibiotics
- Vaccination
  - In endemic areas
  - Endangered animals

Other measures to prevent disease in animals include isolating sick animals from the rest of the herd immediately, discouraging scavengers from the area, and using insect repellants to prevent fly dispersal of the organism. In endemic areas, modified live vaccines can prevent anthrax in livestock, if authorities feel it is necessary. Livestock can be vaccinated annually, before the season when outbreaks generally occur. These vaccines have also been used to protect cheetahs and endangered ruminants, including the black rhinoceros (photo from Lewa Wildlife Conservancy, http://www.lewa.org). Because the vaccine is a modified live type, prophylactic antibiotics cannot be given concurrently; however, animals may be vaccinated when antibiotic treatment has concluded. [This photo shows a black rhinoceros from Etosha National Park in Namibia. Source: Frank Vassen, www.flickr.com/creative-commons]

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Disinfection

- Spores resistant to heat, sunlight, drying and many disinfectants
- Disinfectants
  - Formaldehyde (5%)
  - Glutaraldehyde (2%)
  - Sodium hydroxide (NaOH) (10%)
  - Bleach
- Gas or heat sterilization
- Gamma radiation

Anthrax spores are resistant to heat, sunlight, drying, and many disinfectants. They can be killed with formaldehyde or 2% glutaraldehyde; overnight soaking is recommended. A 10% NaOH or 5% formaldehyde solution can be used for stockyards, pens, and other equipment. Sodium hypochlorite has also been recommended for some purposes. The sporicidal effectiveness of hypochlorite solutions varies with the pH and the concentration of free available chlorine. To become an effective sporicidal agent, household bleach must be diluted with water to increase the free available chlorine, and adjusted to pH 7. Prolonged contact is recommended. Gaseous sterilization can be accomplished with chlorine dioxide, formaldehyde gas, and other methods, under specific conditions of humidity and temperature. Sterilization is also possible by heating to 121°C (250°F) for at least 30 min. Gamma radiation has been used to decontaminate animal products, as well as mail from contaminated postal facilities. Exposed arms and hands can be washed with soap and hot water then immersed for one minute in a disinfectant such as an organic iodine solution or 1 ppm solution of mercuric perchloride. Clothing should be cleaned and boiled.

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Disinfection

- Preliminary disinfection
  - 10% formaldehyde
  - 4% glutaraldehyde (pH 8.0-8.5)
- Cleaning
  - Hot water, scrubbing, protective clothing
- Final disinfection: one of the following
  - 10% formaldehyde
  - 4% glutaraldehyde (pH 8.0-8.5)
  - 3% hydrogen peroxide,
  - 1% peracetic acid

Where practical, cleaning of all surfaces should be done by straightforward washing and scrubbing using ample hot water. Protective clothing should be worn. For final disinfection, one of the following disinfectants should be applied at a rate of 0.4 liters per square meter for an exposure time of at least 2 hours: 10% formaldehyde (approximately 30% formalin), 4% glutaraldehyde (pH 8.0-8.5), 3% hydrogen peroxide, or 1% peracetic acid. Hydrogen peroxide and peracetic acid are **not** appropriate if blood is present. When using glutaraldehyde, hydrogen peroxide, or peracetic acid, the surface should be treated twice with an interval of at least one hour between applications. Formaldehyde and glutaraldehyde should not be used at temperatures below 10^{o}C. After the final disinfection, closed spaces, such as rooms or animal houses, should be well ventilated before use. The effectiveness of the disinfection procedure cannot be assumed, and attempts should be made to confirm it has been adequate by means of swabs and culture.

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Biological Terrorism: Estimated Effects

- 50 kg of spores
  - Urban area of 5 million
  - Estimated impact
    - 250,000 cases of anthrax
    - 100,000 deaths
- 100 kg of spores
  - Upwind of Wash D.C.
  - Estimated impact
    - 130,000 to 3 million deaths

Previous acts of biological terrorism have been small in scale. It is estimated that in a city of 5 million people, a release of 50 kg of anthrax spores (10 km upwind and 2 km wide) would extend over 20 km in 2 hours. This would result in 500,000 people placed at risk. There would be an estimated 250,000 illness and 125,000 deaths. A 1993 report by the U.S. Congressional Office of Technology Assessment estimated that 130,000 to 3 million deaths may occur following the aerosolized release of 100 kg of anthrax spores upwind of Washington D.C.

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Additional Resources

- World Organization for Animal Health (OIE)
  - www.oie.int
- U.S. Department of Agriculture (USDA)
  - www.aphis.usda.gov
- Center for Food Security and Public Health
  - www.cfsph.iastate.edu
- USAHA Foreign Animal Diseases ("The Gray Book")
  - www.aphis.usda.gov/emergency_response/downloads/nahems/fad.pdf

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