Agents of Bioterrorism

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What does "bioterrorism" make you think of?

Nobody has responded yet.

Hang tight! Responses are coming in.

Overview

- Brief Historical Outline
  - Early, Modern, and State-sponsored Biowarfare
  - Modern Bioterrorism
- Category A Agents
  - Anthrax
  - Smallpox
  - Tularemia
  - Viral hemorrhagic fevers
  - Botulinum toxin
- Category B Agents
  - Brucellosis
  - Burkholderia

Why Biological Agents?

- **Military use (biological warfare):**
  - Focus is on disabling or hindering an enemy, state-actor force
  - Agents are chosen based on:
    - Ease of targeted dispersal (don't want to use an agent that could easily infect or blow back on your own forces/people)
    - Difficult to rapidly diagnose and treat
    - Longer symptomatic phase, with disabling symptoms
  - Historic agents of interest:
    - Burkholderia
    - Plague
    - Smallpox
    - Tickborne diseases

- **Terrorist use (bioterrorism):**
  - Designed to inflict terror, panic, or instability in a population (non-military) for political or ideologic reasons
  - Agents are chosen based on:
    - Dramatic, rapid pathology
    - Ease of rapid spread
    - Ease of acquisition or production
    - Case fatality rate
  - Historic agents of interest:
    - Viral hemorrhagic fevers
    - Smallpox
    - Anthrax

A Brief History of Bioterrorism – Early

- 15th c. BCE
  - Hittites drove rams with a disease suspected today to be Tularemia into enemy territory to cause outbreaks
- 6th c. BCE
  - Assyrians poison enemy wells and water supplies with ergot (*Claviceps purpurea* fungus)
  - Poisoning of water supplies with cadavers/animals would be a relatively common technique well into the 20th century.
- 4th c. BCE
  - Scythians dipped arrows into decomposing animal cadavers or excrement (Romans, a bit later, do the same with their swords) → *Clostridium*
- 190 BCE
  - Hannibal (Carthaginian) fires earthen vessels filled with venomous snakes at enemy ships
- 1344
  - Mongol army sieges Kaffa (Crimea). After the invading army was struck by bubonic plague traveling east from China, they began firing corpses over the city walls.

A Brief History of Bioterrorism - Modern

- 1710
  - Russian forces besieging Swedish fort in Reval, Estonia were the last recorded users of “cadaver launching” technique
- 1763
  - British commander Colonel Henry Bouquet has blankets from smallpox victims given to neighboring Native American tribes
- 1797
  - Napoleonic army floods plains around Mantua, Italy to enhance spread of malaria
- 1863
  - Dr. Blackburn, a Confederate surgeon, is arrested while trying to import clothes from yellow fever victims into the north during the Civil War.
  - Confederate soldiers purposely shoot farm animals in ponds and streams to make water unusable for incoming Union troops
- 1915 – 1918
  - Germany attempts to ship Bacillus anthracis and Burkholderia pseudomallei-infected horses and cattle to the US and allies.
  - Germany alleged to have airdropped cholera and plague-infected children’s toys, fruit, and chocolates on Romanian, Italian, and Russian cities (never proven, but suspected).
- 1925
  - Protocol for the Prohibition of the Use in War of Asphyxiating, Poisonous, or Other Gases and of Bacteriological Methods of Warfare
    - Updated version signed in 1972
- WW2-era
  - More formal transition into state-sponsored research programs due to advances in biochemistry and microbiology

A Brief History of Bioterrorism – State-sponsored Programs

- **Germany**:
  - Offensive biowarfare program began around 1933, as did military training on dispersal of biological agents
  - Some evidence of focus on spreading disease among crops, but most research seems to have shifted to defensive work due to a ban on offensive use by Hitler. They were more concerned about Russian and French biological attacks.
- **Japan**:
  - VERY active offensive biowarfare program from 1928 onward. Still considered one of the most aggressively active biowarfare programs.
  - Unit 731 – covert biological and chemical research and development unit
    - Performed human experimentation, largely in occupied China (based in Harbin) using plague, cholera, smallpox, and botulism (among others)
    - Released plague-infected fleas from planes
    - Developed “defoliation bacilli bombs” that were later used to disperse anthrax, plague-carrying fleas, typhoid, cholera
    - Had planned to disperse plague in San Diego on Sept 22, 1945 but Japan surrendered prior to this attack

A Brief History of Bioterrorism – State-sponsored Programs

- **Soviet Union**
  - Biopreparat
    - Association of multiple labs and production facilities
  - Research included anthrax, plague, tularemia, Brucella, smallpox, Marburg, Machupo virus
  - One of the first to mass-produce highly refined anthrax
    - That we know of, they had the capacity to produce 300 metric tons per 10-month production cycle.
    - Sverdlosk anthrax leak → occurred in 1979, admitted in 1992 under Yeltsin
  - Claims to have largely disbanded all biowarfare research as part of terms for western lab reconditioning grants/funds.

A Brief History of Bioterrorism – State-sponsored Programs

- **United States**
  - Operation Paperclip → Co-opted research from captured German scientists in exchange for not putting them on trial post-WW2
    - Similar program for captured Japanese scientists from Unit 731
  - Fort Detrick, MD
  - Similar agents of interest in US BW program and Unit 731 (likely owing to information gained from co-opted research)
  - Operation Sea-spray (1950)
    - Similar tests conducted in:
      - Minnesota (1950s: zinc cadmium sulfide, now known to be carcinogenic)
      - NY subway (1966: *Bacillus subtilis*, delivered by dropping lightbulbs filled with agent)
      - Reagan National Airport and Greyhound Lines terminal (1965, *Bacillus globigii)*
      - Between 1949 and 1969, over 230 open-air tests were performed.

Modern Bioterrorism Incidents

- Oregon 1984 – Rajneeshee cult
  - Contaminated local restaurant salad bars with *Salmonella typimurium*
  - 751 illnesses, 0 deaths
- Tokyo 1990s – Aum Shinrikyo cult
  - Multiple failed attempts at dispersing *B. anthracis* and *C. botulinum* from the roof of their 8-story building and from cars driving around government buildings
  - Culminated in deadly Tokyo subway Sarin gas attack
- USA 2001 – Amerithrax attacks
  - Letters containing highly-refined anthrax (Ames strain) sent to multiple media offices and senatorial offices
  - 22 infected, 5 deaths
  - Still no clear perpetrator, though US DOJ points to a DOD/USAMRID scientist (Ivins).

Categorization of Agents

- Categories based on ease of ability to disseminate, transmissibility, morbidity, and mortality. (We will just focus on Category A and B here)
- Category A
  - Anthrax*
  - Botulism*
  - Smallpox*
  - Plague
  - Tularemia
  - Viral hemorrhagic fevers
- Category B
  - Brucellosis*
  - *Clostridium perfringens* toxin
  - Foodborne threats (Salmonella, Shigella, E. coli)
  - Glanders (*Burkholderia mallei)**
  - Psittacosis
  - Coxiella burnetii
- Category C
  - Emerging pathogens and those made more virulent through genetic engineering
  - Hantavirus, Nipah virus, yellow fever virus, MDROs

Category A Agents

Bacillus anthracis

- Spore-forming GPR
- Exists naturally in the environment, mostly infecting grazing animals through ingestion of soil-derived spores
- 20,000 – 100,000 cases of human disease annually, worldwide (though rare in US)
  - Only 18 cases of inhalational anthrax reported in the US in 20th century

Bacillus anthracis

- One major risk is persistent contamination
  - Spores can persist on environmental surfaces for prolonged periods, meaning decontamination of suspected attack sites is key (wetting them down helps prevent spread, though some facilities in the Amerithrax attacks were unusable for months/years due to ongoing detection of spores)
- WHO estimates that 50kg release of lab-derived (highly potent) Anthrax spores upwind of a city of 500,000 would results in 125,000 cases of inhalational anthrax and 95,000 deaths.
  - Lab-derived strains are engineered to cause less spore clumping, allowing spores to penetrate into distal airway.
  - This is also what allowed spores to pass through microscopic pores in envelope paper, causing disease in those who handled, but did not open, infected mail in Amerithrax attacks
- Sverdlosk Accident – 1979
  - Accidental release of weaponized anthrax spores from a secret Soviet bioweapons lab
  - 79 cases, 68 deaths the surrounding town, covered up as being due to “tainted meat consumption” until Deputy Director of Biopreparat (Soviet bioweapons program) Kenatzhan Alibekov defected in 1990.

Bacillus anthracis

- Cutaneous anthrax
  - Most common form of human infection
  - Animal handlers, butchers
  - Can see secondary cases from contact with primary lesion
  - Itchy, raised lesion at site of contact that develops into papule then vesicle.
    - Significant edema around site, which develops a black eschar over several days.
    - Edema is typically disproportionate to the size of the lesion. Site is often painless.
- Inhalational anthrax
  - Primary route used in bioweapon, though can see cutaneous, as well
  - No human-human transmission documented
  - Flu-like illness within minutes – hours of inhalation, develops into severe dyspnea, high fever, confusion, pleuritic chest pain within 48 hours followed by respiratory failure
  - CLASSIC!! → Widened mediastinum on CXR with pleural effusions
  - Germinating spores spread through bloodstream
  - Always consider meningitis and parenchymal brain infection (around 50% of patients experience this)
- Gastrointestinal anthrax
  - Ingestion of contaminated meat
  - Can see clusters of disease from this route due to communal distribution of meat from infected animal
  - Inflammation of pharynx with ulcers and pseudomembrane formation, edema of face/neck, diarrhea, abdominal pain, N/V

Bacillus anthracis

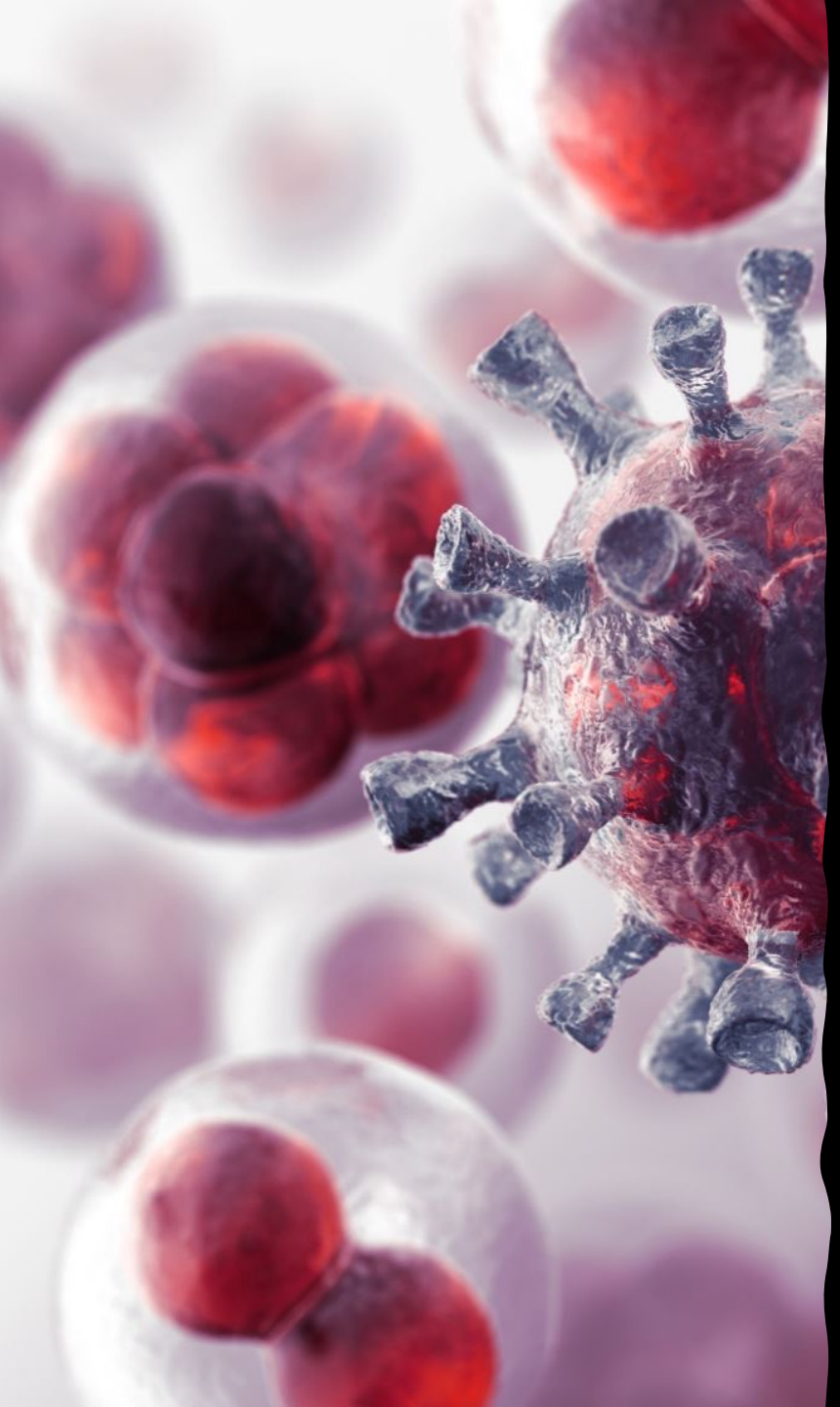
- Diagnosis
  - Can be cultured on standard media (blood, nasal, sputum, CSF, skin swab)
  - PCR/histology of skin biopsies from suspected cutaneous lesions
  - Serology
    - 4-fold rise in IgG between acute and convalescent samples is diagnostic
  - CXR/CT
  - All in the context of clinical background
    - Mass triage event? Postal worker with questionable exposure? Farmer? Butcher?
  - If one specific symptom related to anthrax is present, or two nonspecific features but with high risk factors, immediately contact CDC

Bacillus anthracis

- Management
  - Patient isolation not required
  - Gown/gloves/mask when collecting samples
  - Give antitoxin for all suspected inhalational disease (raxibacumab, obiltoxaximab)
    - Counteracts extracellular toxins and helps prevent binding
    - Limited supply, so in mass casualty event prioritize those with more severe disease or who are not responding to antibiotics
  - Suspected systemic anthrax:
    - Obtain CSF!
    - FQ + B-lactam + protein synthesis inhibitor
      - Cipro + Meropenem + Clindamycin or Linezolid
    - Once meningitis ruled out, can stop B-lactam
    - Duration: 3 weeks, followed by single agent post-exposure prophylaxis for total treatment of 60 days
- CNS anthrax
  - Usually a "harbinger of death" within hours/days.
  - Acute onset headache and rapid mental status deterioration
  - SAH, widespread parenchymal bleed, cerebral edema
- Cutaneous disease
  - Ciprofloxacin or Doxycycline x 7 – 10 days (60 days if suspecting bioterrorism
  - Note: If analysis shows strain is PCN-sensitive, FQ can be replaced with high dose PCN or Amoxicillin
- Prophylaxis
  - Ciprofloxacin or doxycycline x 3 months (or PCN/Amox as above)
  - Post-exposure vaccine can be given to those who respond quickly to deliberate release

Smallpox (*Variola* virus)

- Eradicated in 1978…well, sort of.
- Two nations kept samples: the United States (CDC) and the Soviet Union (State Research Center of Virology and Biotechnology – VECTOR)
  - Some evidence that Soviet Union experimented with “bomblets” that would aerosolize the virus over a wide area
  - Two calls for destruction of these samples (under WHO observation) have been blocked (chiefly by the DOD) for “strategic research purposes”
  - In 2019, Canadian researchers showed that, for less than $100,000 and with little experience, they were able to recreate a similar extinct horse pox virus (dual-use technology arguments abound).



Smallpox (*Variola* virus)

- Transmitted by airborne droplets and direct contact with vesicles and respiratory secretions
  - Attack rate ~30%
- High mortality at extremes of age
  - About 33% mortality in epidemic settings
- Infectious from onset of fever to last scab separation, with a 10-16 day incubation period
- Potent bioweapon due to transmissibility, low number of vaccinated individuals, lack of treatment, and high mortality rate.
  - Vaccination provides effective immunity for ~10-15 years, so vast majority of the world is currently non-immune.

Smallpox (*Variola* virus)

- Presents as short prodromal illness (3 days) with fever, myalgias, headache, fatigue, nausea/vomiting, followed by mouth sores and rash.
- Classic rash features:
  - Starts near day 3 of symptoms, first on face then spreads to body and extremities, appearing as a maculopapular rash that progresses to vesicles then pustules.
  - Pustules are deep and firm (as opposed to superficial ones seen in chickenpox)
  - About 7-10 days later, pustules begin to scab and heal. Once all scabs have fallen off, patient is no longer infectious.

Smallpox (*Variola* virus)

- Diagnosis:
  - Major criteria (CDC):
    - Severe prodromal illness with high fever 1 – 4 days pre-rash
    - Deep, hard, well-circumscribed vesicles
    - All vesicles at the same stage of development
      - Differentiates this from and chickenpox
      - What about monkeypox?
  - Vesicular fluid and throat swabs can be sent for PCR, but MUST be processed in BSL4 lab

- Management:
  - At first suspicion, patient should be in single room, given a surgical mask, and placed on contact/respiratory precautions.
  - Bedding used by patient needs to be incinerated
  - Call CDC *yesterday*.
  - No in vivo data for antivirals, though Cidofovir and tecovirimat have some in vitro data.
  - Supportive care
  - Give vaccine ASAP
    - Ideally within 3 days of exposure but can be given up to a week after.
    - Ring vaccination strategy
  - Strict isolation for 17 days for non-immune persons exposed to a known case due to long incubation period

Operation Dark Winter

- Simulated bioterror attack wargame carried out on June 22-23, 2001
  - Johns Hopkins Center for Civilian Biodefense Strategies, Center for Strategic and International Studies, ANSER Institute for Homeland Security
- Focused on measuring possible inadequacies in our national emergency response systems during a biological attack.
  - Purposely designed to spiral out of control.
- Simulation started with an isolated smallpox attack on Oklahoma City, followed by similar attacks in Georgia and Pennsylvania.
  - By day 13, disease had spread to 25 states and 15 foreign nations with 16,000 cases and 1,000 deaths.
- Main findings:
  - An attack on the US with biological weapons would threaten vital national security interests
  - Current organizational structures and capabilities are not well-suited for management of a biological attack
  - There is no surge capability in the US healthcare, public health, pharmaceutical, or vaccine industries
  - Dealing with the media would be a major challenge for all levels of government
  - Containing the spread of the disease would present significant ethical, political, cultural, operational, and legal challenges.

Clostridium botulinum

- Spore-forming GPR found naturally in soil and water.
- Disease is caused by botulinum toxin.
  - Can be aerosolized or introduced into food/water supplies, either as spores or purified toxin
- Incubation period:
  - Ingestion of toxin: 6 hours – 8 days
  - Inhalation: 1 – 3 days
- No person-person transmission
- Regardless of route of infection, predominant symptom is an acute, symmetric, flaccid paralysis with bulbar palsies (difficult swallowing/speaking, double vision)
  - May have GI symptoms if foodborne, as well.
  - Classically progresses to a descending flaccid paralysis, respiratory failure, autonomic instability

Clostridium botulinum

- Diagnosis:
  - Clinical history and examine are chief evidence
  - Prior to administration of antitoxin, can test for antitoxin antibodies in serum
  - May be able to culture *C. botulinum* from stool, wound, or food, depending on type of exposure (spore vs toxin)
  - Reference labs can detect toxin in serum, stool, or food

- Management:
  - Administer antitoxin as soon as disease is clinically suspected (ideally, get serum sample first, but don't delay treatment for this).
  - Supportive care
    - May require long-term care and vent support, part of the reason this is a potent bioweapon
  - No prophylaxis for contacts

Category B Agents

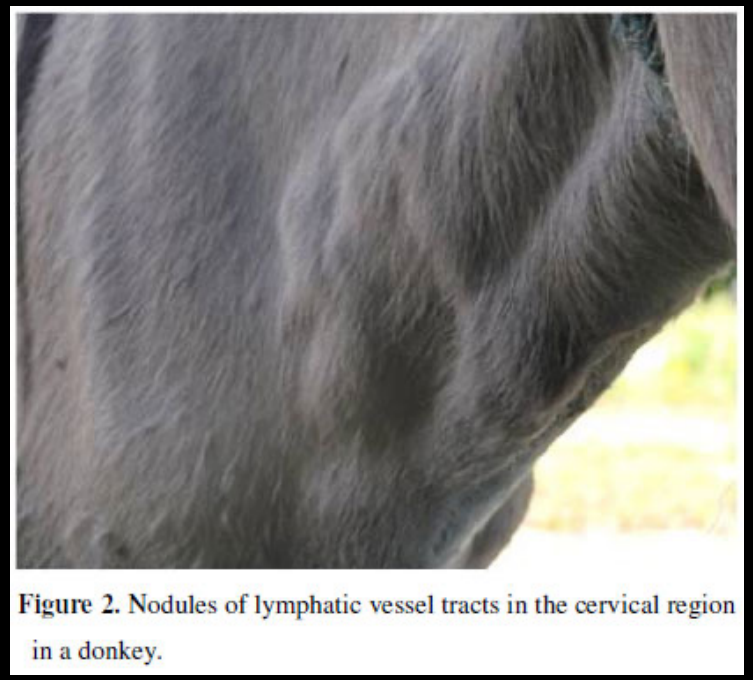
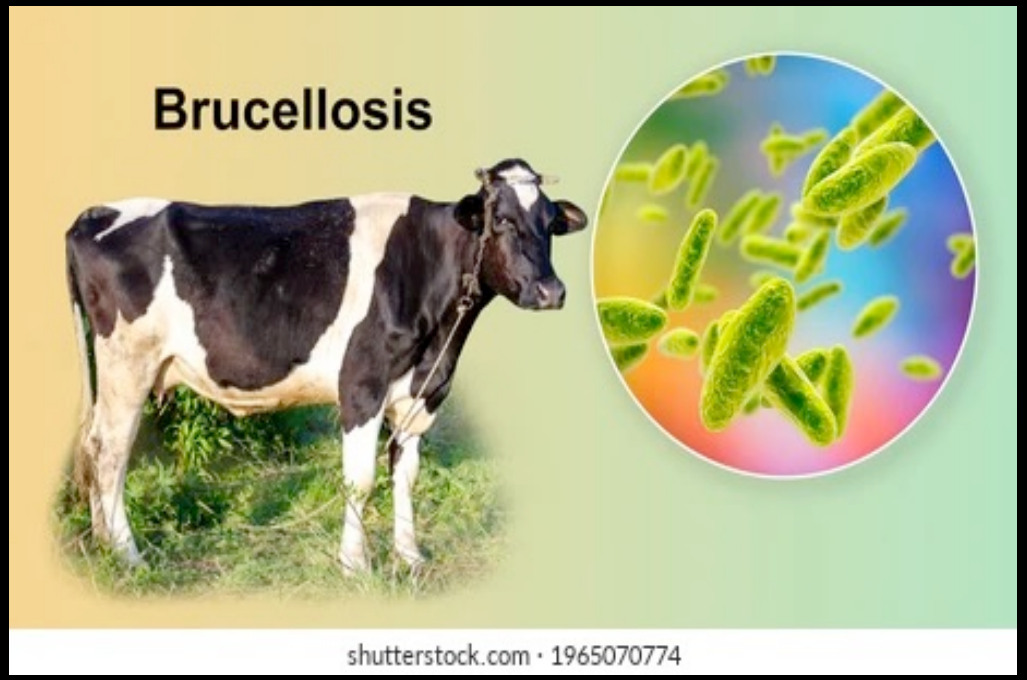


Figure 2. Nodules of lymphatic vessel tracts in the cervical region in a donkey.



Brucella melitensis, abortis, and *suis*

- Gram-negative intracellular coccobacilli
  - *B. melitensis* → Sheep, goat, camels
  - *B. abortis* → Cattle
  - *B. suis* → Pigs, feral swine
- Worldwide geographic distribution
  - Of note, has been eradicated from herds in the US, so all human cases should be linked to travel or exposure to imported unpasteurized dairy products.
- Common routes of transmission are ingestion of unpasteurized milk, direct contact with infected animal or secretions, or inhalation of aerosols from those animals

Brucella melitensis, abortis, and *suis*

- After infection, organism spreads to lymph nodes and uses RES to spread and form granulomas in tissues.
  - Can involve almost any tissue in the body
  - Most common localized infection (~50% of patients) is osteoarticular (sacroiliitis, spondylodiskitis).
    - Pedro-Pons sign → anterosuperior step-like erosion of infected vertebra
- One of the "great mimics", like TB or syphilis
- Incubation period of 1 – 4 weeks, followed by fever, moldy-smelling perspiration, myalgia/arthralgia, abdominal pain, malaise.
  - Exam may reveal hepatosplenomegaly, lymphadenopathy
  - "Undulant fever" → Symptoms and fever can persist or relapse for days, weeks, or years
  - About 20% can have urogenital involvement → epididymoorchitis
  - Can progress to <u>neurobrucellosis</u>
    - Meningoencephalitis, myelitis, cranial nerve palsies, radiculoneuropathy.
    - Can evolve slowly and be difficult to detect.
  - Other forms: endocarditis, pericarditis, myocarditis, peritonitis, skin/ocular lesions, hepatosplenic abscesses, colitis, pneumonia

Brucella melitensis, abortis, and *suis*

- Diagnosis
  - Gold standard is bone marrow culture.
    - Remains positive even with prior antibiotic use
    - Obtain if index of suspicion is high, even with negative serology
  - Serology:
    - IgG titer > 1:80 considered positive in non-endemic regions
    - IgG titer > 1:160 considered positive in endemic regions
    - Antibodies can cross-react with *Francisella tularensis*

- Management
  - Even with treatment, about 5-15% will experience relapse
  - Don't use serology alone to monitor treatment. Must couple titer with exam.
  - Uncomplicated, nonfocal disease:
    - Doxycycline + Gentamicin x 6 weeks
    - Doxycycline + Rifampin x 6 weeks
  - Osteoarticular disease:
    - Doxycycline + Gentamicin x 3 months
  - Neurobrucellosis:
    - Ceftriaxone x 1 month plus Doxycycline + Rifampin x 4-5 months
      - PO abx continued until CSF normalizes
  - Endocarditis:
    - Doxycycline + Rifampin + Gentamicin x 6 weeks

Glanders (*Burkholderia mallei*)

- Gram-negative bacillus
- Zoonoses of horses, donkeys, mules.
  - Endemic in Africa, Asia, Europe, Central/South America
- Can be transmitted by inhalation or contact with broken skin or mucous membranes.
  - On one hand, not ideal for bioweapon because it does not persist long in the environment and human-human transmission is rare.
  - This is countered, however, by a low infectious dose and broad susceptibility among the population.

Glanders (*Burkholderia mallei*)

- Wide range of clinical presentation, from asymptomatic infection to fatal disease.
  - Incubation: 1 – 2 days from inhalation
  - More severe presentations:
    - Ulcerative necrosis of the tracheobronchial tree with cervical and mediastinal lymphadenopathy.
    - Bacteremia with disseminated abscesses
    - Both of these are associated with inhalational route of infection and are typically fatal within 7-10 days.
      - Even those treated promptly with antibiotics have roughly 50% mortality risk if presenting with severe disease.
  - Can also present as focal pneumonia, empyema, pleural effusion, or military infection.
- <u>Diagnosis</u>
  - Growth of *B. mallei* from cultures of blood, exudates, pus
  - Formerly considered a Pseudomonas species, and can sometimes be misidentified as such in culture.

Glanders (*Burkholderia mallei*)

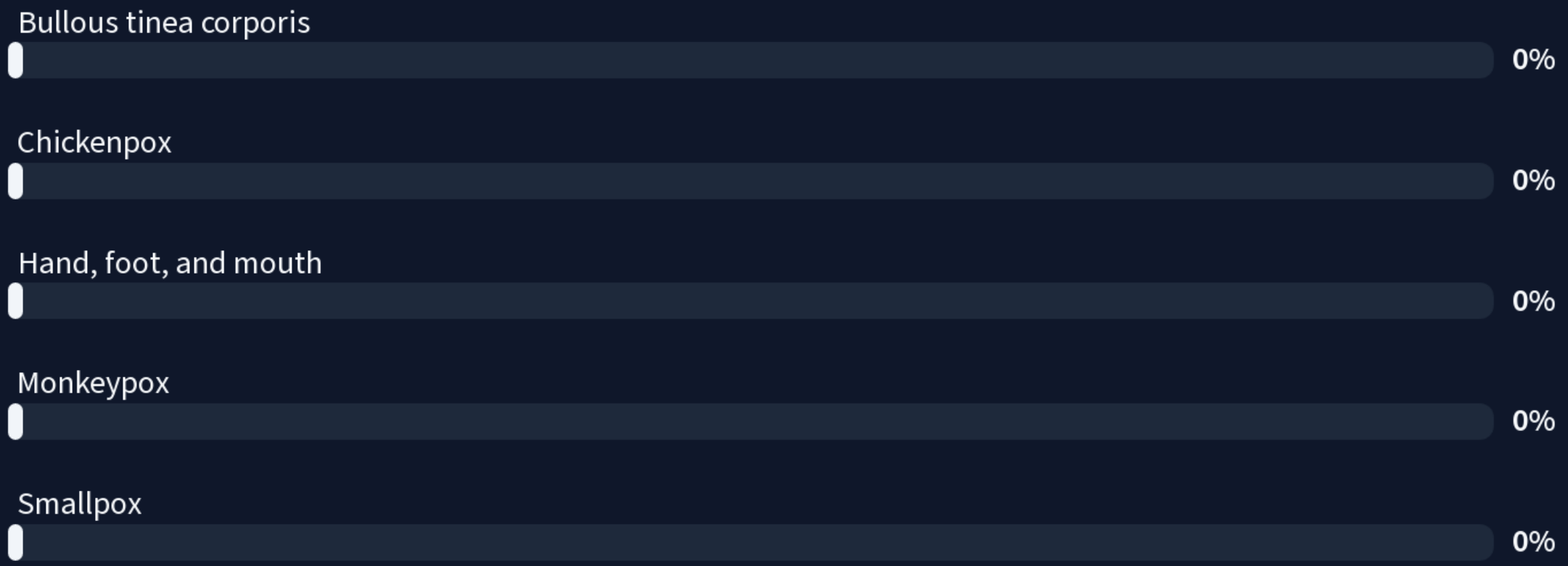
- Management
  - Standard precautions
  - **Initial phase**: Ceftazidime, meropenem, or imipenem
  - **Eradication therapy**: Bactrim or Augmentin for several months to prevent relapse
  - No good data on efficacy of post-exposure prophylaxis, but can give Bactrim or Augmentin.

Time for some questions!

A 45-year-old man presented with a 2-day history of rash and fever. He had returned 1 week before his symptoms began from a 4-week trip to Nigeria. He works as a postal worker. On examination his temperature was 38.7°C, his heart rate was 110 beats/minute, and his blood pressure was 110/64 mmHg. He had a vesicular rash affecting predominantly his trunk, with many vesicles that were easy to burst. There are some macular lesions as well as the vesicles.

What is the most likely diagnosis?

A 45yo male postal worker p/w a 2-day h/o rash and fever. He returned 1 week ago from a trip to Nigeria. He has a vesicular rash affecting his trunk, with many easily burst vesicles as well as some macular lesions. What is the most likely dx?



Chickenpox

- Trunk predominant (rather than limbs)
- Easily sloughed lesions
- Different stages of lesions
- These features are not consistent with smallpox or monkeypox (limb predominant, lesions will all be in the same stage)

A 54-year-old woman presented with a productive cough as well as a painful swollen nose with copious discharge. She reported a biphasic illness, as the current symptoms had been preceded by recovery from a 1-week history of malaise, fever, headache, and myalgia. She had a history of osteoarthritis but did not take any regular medications. She worked as an equine vet.

On examination her temperature was 37.5°C, her respiratory rate was 18 breaths/minute, and her oxygen saturations were 97% on room air. Her nose and surrounding facial skin were moderately swollen, and she had palpable cervical lymphadenopathy.

Flexible nasal endoscopy was performed, followed by bronchoscopy, which revealed multiple necrotic ulcers in the mucosal lining of the tracheobronchial tree.

Investigations:

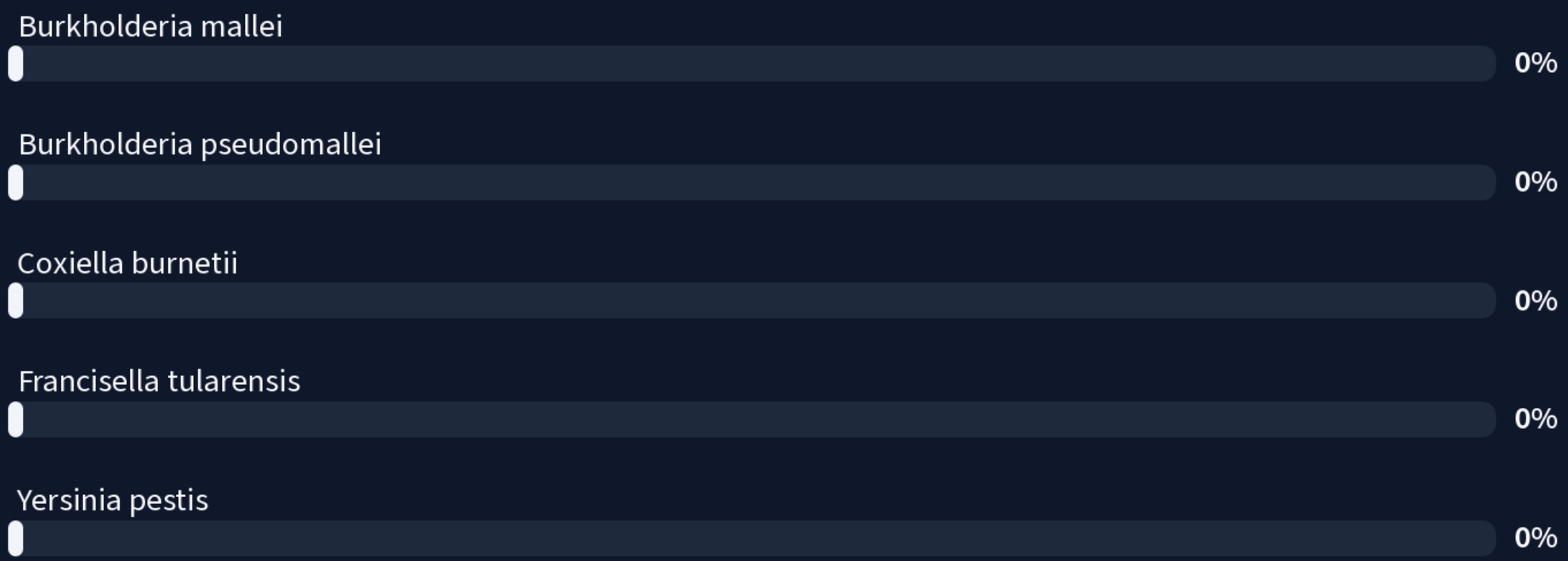
Biopsies were taken and sent for microscopy and culture

Results: gram-negative bacilli with rounded ends seen on direct microscopy

Chest X-ray was unremarkable

What is the most likely causative organism?

A 54yo F presents with productive cough, swollen nose with discharge. Illness has been biphasic, preceded by a week of malaise, fever, HA, myalgia that resolved. Necrotic ulcers of tracheobronchial tree seen on endoscopy. Gram stain of biopsy with GNR.



Burkholderia mallei

- Patient has glanders
- Likely inhalation (nasal involvement, tracheobronchial ulcerations) via horse exposure
- First line treatments → ceftazidime, imipenem, or meropenem +/- TMP-SMX
  - Common to have multiple drug resistances

A 46-year-old man presented with a 5-day history of dyspnea and a nonproductive cough. Four weeks earlier he had returned from a holiday in West Africa where he had bought components for drums, which he then crafted himself. He had a history of hypertension, obesity, and type 2 diabetes. On examination, he appeared ill. His blood pressure was 85/46mmHg, heart rate was 115 beats/minute, respiratory rate was 32 breaths/minute, and oxygen saturations were 86% on 4LPM oxygen. He required urgent intubation and transfer to the critical care unit.

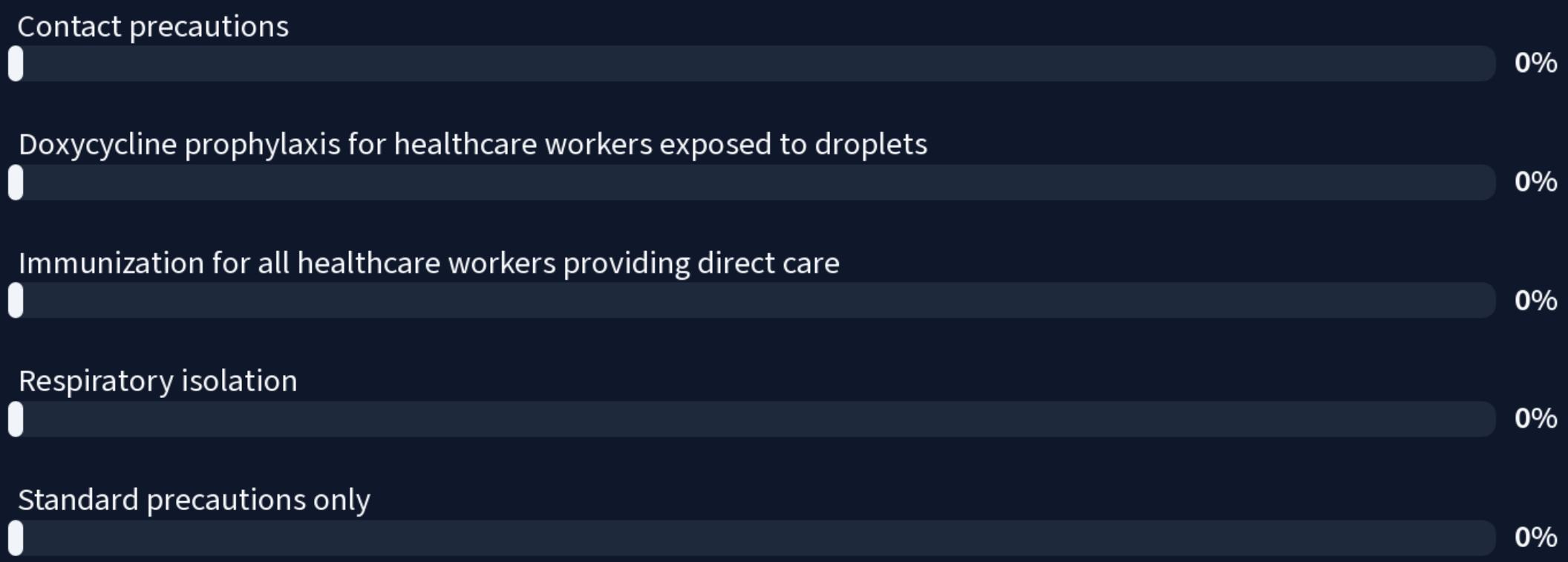
Investigations:

CXR: small bilateral effusions seen with cardiomegaly

4 sets of blood cultures positive at 12 hours with gram-positive rods

What infection prevention intervention is most appropriate?

46yo M with 5d h/o dyspnea and non-productive cough. Returned from West Africa 4w ago where he bought drum components. Becomes critically ill, requiring intubation. CXR with small b/l effusions, blood cultures with GPR. Infection prevention methods?



Standard precautions

- Drums components likely contaminated with anthrax spores
- No human-human transmission
- You do need to narrow down where patient was exposed, as family/close contacts my need chemoprophylaxis
- No need to chemoprophylax HCW

A 42-year-old man presented with a 3-week history of fever associated with progressive low back pain, malaise, nausea, vomiting, and diarrhea. He had a history of asthma, for which he used regular low-dose steroid inhalers. He was not on any oral medications and had no known drug allergies. He worked in an office. He had sustained a cut to his finger 6 weeks previously while on a hunting trip that involved slaughtering, cooking, and eating wild boar. None of his friends became sick although he said that their wilderness guide had been coughing during their entire trip. On examination, his temperature was 38.9^{o}C. He had hepatosplenomegaly on abdominal palpation. There was some mild epididymo-orchitis on genital exam. His respiratory and cardiovascular exams were unremarkable.

Investigations:

Total white cell count 2.5 ×109/L

Hemoglobin 8.2 g/dL

Platelet count 90,000/µL

Computed tomography scan of his abdomen and pelvis demonstrated enlarged liver and spleen and also showed evidence of sacroiliitis.

What was the most likely route of acquisition of his infection?

A. Direct contact

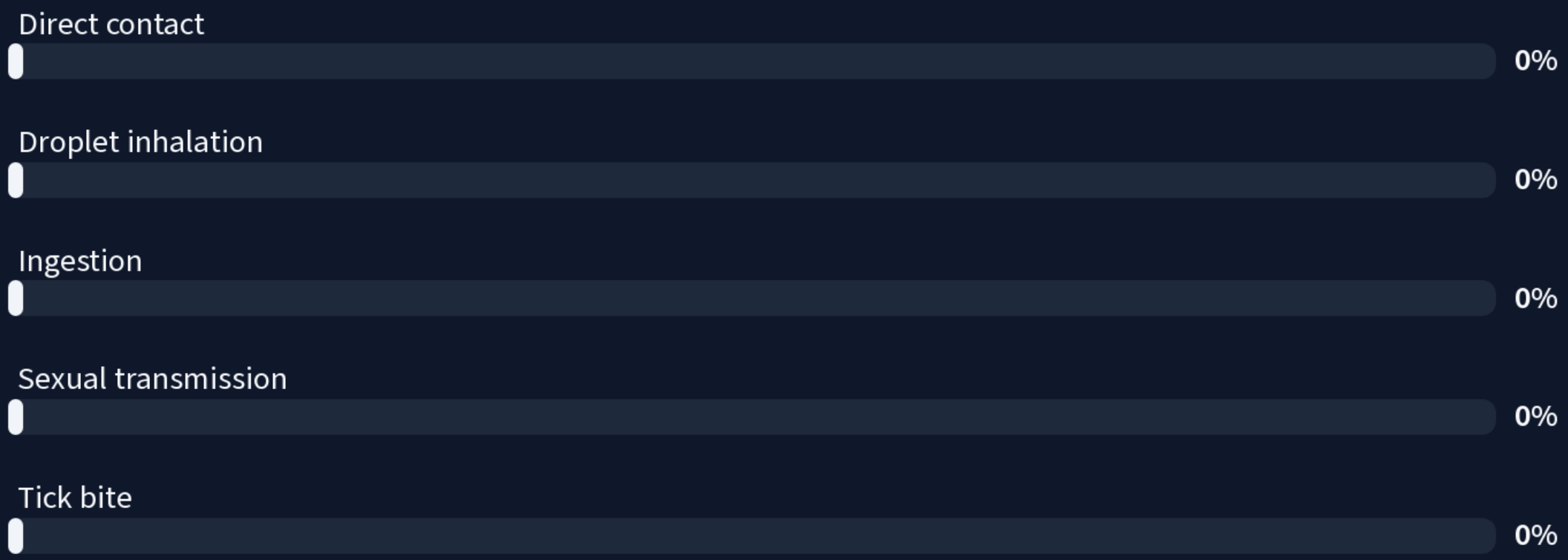
B. Droplet inhalation

C. Ingestion

D. Sexual transmission

E. Tick bite

42yo M with 3w hx of fever, low back pain, malaise, N/V/D. Had a cut 6w ago during a hunting trip while slaughtering/cooking/eating wild boar. No one else on the trip is sick. Has HSM, fever, sacroilitis, epididymoorchitis. Route of infection?



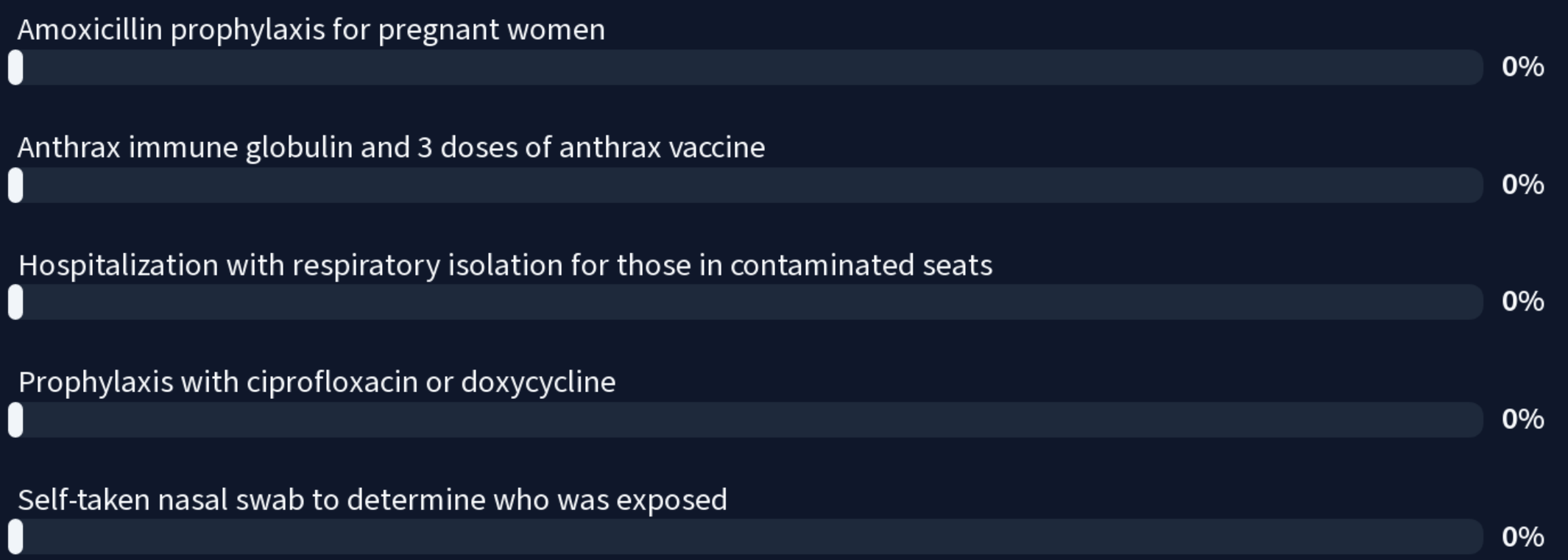
Direct contact

- Dx is acute brucellosis
  - Exposure plus fever, sacroiliitis, HSM, pancytopenia
  - Incubation week to months
  - 100-200 cases per year in the US
    - Mostly in California, Texas, Arizona, Florida
  - Mostly transmitted through exposure to blood or organs of hunted animals (boar, elk, moose, deer), or through occupational exposure (veterinary and slaughterhouse workers)
    - No person-to-person transmission
    - No transmission after ingestion of cooked meat

There was a reported bioterrorist release of anthrax spores in a crowd at a professional football game in an outdoor stadium. The announcement about the release of the spores was made 3 hours after the game ended. Rapid testing confirmed contamination at the stadium with anthrax spores, and PCR confirmed *Bacillus anthracis.*

What would be the most appropriate immediate management of those who attended the game?

Anthrax was released at a pro football game, announced 3 hours after the game ended. Rapid PCR confirmed B. anthracis. Best immediate management of attendees?



Prophylaxis with ciprofloxacin or doxycycline

- Assume everyone was exposed
  - No role for testing seats or using nasal swabs to identify exposed vs non-exposed
- Immune globulin not indicated for inhalational anthrax, and vaccine not given in combination with immune globulin (though may be used alone for a mass exposure event like this)
- No room for suboptimal prophylaxis
  - A dead mother is higher risk than cipro/doxy for a developing fetus
  - Can always change to amoxicillin if susceptibilities allow later

What to do when you see one of these?

- FIRST: Put patient in appropriate level of isolation
- SECOND: Notify staff working with patient about concern
  - This includes notifying the lab! Many of these infections are high risk for lab workers, and they need to be able to protect themselves when working with blood/secretions.
- THIRD: Contact MDH at 651-201-5414

DEPARTMENT OF HEALTH

High-yield Info Sources

- Center for Infectious Disease Research and Policy (CIDRAP)
  - www.cidrap.umn.edu
- USAMRIID Biodefense Tools (App, Blueobok)
  - https://www.usamriid.army.mil/education/instruct.htm
- CDC Bioterror Preparedness Resources
  - https://emergency.cdc.gov/bioterrorism/prep.asp

References

- Barras, V., and G. Greub. “History of Biological Warfare and Bioterrorism.” Clinical Microbiology and Infection, vol. 20, no. 6, Elsevier BV, June 2014, pp. 497–502. doi:10.1111/1469-0691.12706.
- Robertson, A. G., and L. J. Robertson. “From Asps to Allegations: Biological Warfare in History.” *Military Medicine*, vol. 160, no. 8, Aug. 1995, pp. 369–73.
- Spec, Andrej et al. *Comprehensive Review of Infectious Diseases*. Philadelphia, PA: Elsevier - Health Sciences Division, 2019. Print.
- Thavaselvam, Duraipandian, and Rajagopalan Vijayaraghavan. “Biological Warfare Agents.” Journal of Pharmacy and Bioallied Sciences, vol. 2, no. 3, Medknow, 2010, p. 179. Crossref, doi:10.4103/0975-7406.68499.
- Van Zandt, Kristopher E., et al. “Glanders: An Overview of Infection in Humans.” *Orphanet Journal of Rare Diseases*, vol. 8, Sept. 2013, p. 131. *PubMed*, https://doi.org/10.1186/1750-1172-8-131.
- Zajtchuk, Russ et al. *Medical Aspects of Chemical and Biological Warfare*. Office of the Surgeon General – Department of the Army. 1997. Online. https://www.medcoe.army.mil/borden-tb-med-aspects-chembio-war