

# Anthrax Scare in the Philippines Medical and Public Health Issues

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## INTRODUCTION

Since the early days, the deliberate use of microorganisms and toxins as weapons has been attempted. The use of biological agents have evolved from the crudest form like the use of infected cadavers to contaminate water supplies and being catapulted to the enemy side, to the development of specialized munitions for battlefield and covert use.

The history of biological warfare is difficult to assess because of a number of confounding factors. These include difficulties in verification of alleged or attempted biological attacks for propaganda purposes, the paucity of pertinent microbiological or epidemiological data, and the incidence of naturally occurring endemic or epidemic diseases during hostilities.

The greatest challenge in outbreak investigation is distinguishing reliably the difference between a natural infectious disease event from an intentional act. In highly developed countries like the United States where sourcing and funding for large-scale investigation do not pose a great problem compared to our country's current economic condition, how capable are we in recognizing deviations in the natural patterns of infectious diseases? How capable are we in identifying causative agents especially in a timely manner, so that real-time interventions can actually take place? What if the agent is one that has not been previously recognized?

The Center for Disease Control and Prevention in Atlanta, Georgia issued several statements and guidelines on the medical and public management of bio-terrorism that is patterned to their country's capacity and capabilities. The recommendations are however adaptable into our setting in terms of the prevention and treatment aspect.

Inasmuch as we want to compete with the technology of the western world in rapidly detecting causative agents, nothing beats a well-defined referral and communication systems that would readily answer suspected bio-terror attacks. With our country's present economic condition, we can only rely on the inventiveness and resourcefulness we Filipinos are known for.

Compared to conventional warfare, it is the local health service including the infectious disease specialists that stay in the "frontlines." If the local health service is not aware of the potential threats or has low index of suspicion for diseases caused by likely bio-terrorist agents such as anthrax or plague, even the best-laid plans won't play out as expected.

Last October 2001, 4 confirmed cases of anthrax (2 inhalational and 2 cutaneous forms) were reported in the United States from intentional delivery of *B. anthracis* spores through mailed letters or packages, rousing suspicion of a bio-terrorist attack. Extensive investigations are being done and the number of cases may even grow further. Consequently the anthrax scare spread like wildfire all over the globe. Here in our country, several reported incidents of potential bio-terrorist attacks in the form of letters laden with powdery substance suspected as contaminated with anthrax created panic and hysteria even reaching the Section of Infectious Diseases of the University of the Philippines-Philippine General Hospital. In response to the country's need for further information regarding biological agents, the section recommendations based on the key information presented by the Center for Disease Control (CDC) and the Johns Hopkins Working Group on Civilian Biodefense are being issued.

## THE ANTHRAX SCARE

Anthrax is among the top 5 zoonotic diseases in the Philippines that poses a problem in the veterinary community. Its occurrence in our country is commonly associated with exposure to anthrax infected farm animals or animal products such as in goats, sheep, cattle and mostly carabaos.

With the advent of the modern methods of biological warfare, the use of *Bacillus anthracis* spores, the causative agent of anthrax, as a weapon of mass destruction has drawn deep concerns among the medical and military community primarily because of how this disease behaves. In a worst-case scenario, the World Health Organization (WHO) expert committee in 1970, estimated that casualties following a theoretical aircraft release of 50 Kg of anthrax over a developed urban population of 5 million would be 250,000, 100,000 of whom are expected to die without treatment. In 1993, the US congressional office of Technology Assessment estimated that a 100-Kg of aerosolized release of anthrax spores would cause an estimated 130,000 to 3 million casualties. Based on the economic model developed by CDC, an economic spending of \$26.6 billion per 100,000 persons exposed is expected.

Historically, there were quite a number of incidents implicating this agent being used as a biological weapon. The most frequently cited incident was the Sverlovsk Accident (now Ekaterinburg, Russia) in 1979 wherein airborne spores were accidentally released and an epidemic of anthrax occurred among people who lived and worked within a distance of four kilometers. Sixty-six deaths occurred out of the 77 confirmed cases of inhalation anthrax.

### *How does anthrax manifest?*

Three types of anthrax infection occur in humans: inhalational, cutaneous and gastrointestinal. Naturally occurring inhalational anthrax is now a rare cause of human disease. Historically, wool sorters at industrial mills were at highest risk but since the advent of animal vaccination, the risk decreased significantly. A mere identification of inhalational anthrax today in the absence of naturally occurring identifiable source would rouse the suspicion of a bio-terrorist activity.

The initial symptoms appear like a non-specific flu-like illness such as fever, non-productive cough, myalgia and malaise. Early in the course of the disease, chest radiograph shows a widened mediastinum, which is an evidence of hemorrhagic mediastinitis, and marked pleural effusion. After 2-3 days, the disease takes a fulminant course with dyspnea, stringent cough and chills, culminating in death.

Cutaneous anthrax is the most common naturally occurring form. The disease can be acquired from infected herbivores through contact with abraded skin. It is however important to know that development of such without any obvious history of exposure to animals in an otherwise healthy individual should raise the suspicion of a possible bio-terrorist activity.

It usually starts as a pruritic papule or macule, which further enlarges to form an ulcer as early as the 2nd day. Vesicles may subsequently appear with clear or serosanguinous discharge. Gram stain of this discharge may contain numerous gram-positive organisms. Towards the last stage of the lesion before it resolves in 1-2 weeks, a painless, depressed black eschar is seen, often associated with extensive local edema. It further dries and falls off leaving no scars.

Gastrointestinal anthrax results from contamination of infected meat products. The manifestation is difficult to differentiate from other diseases unless a high index of suspicion is present and the organism is isolated from blood and stool specimens.

Following deposition and subsequent germination, it may present as the oral or pharyngeal form or as a primary intestinal lesion depending on the area of deposition. The former presents as an oral or esophageal ulcer leading to the development of regional lymphadenopathy,

edema and sepsis. The latter occurs predominantly in the ileocecal junction presenting initially with nausea, vomiting and malaise which progresses rapidly resulting to hematochezia, signs of acute abdomen or sepsis syndrome.

#### *When to suspect anthrax as a biological weapon?*

Owing to the rarity of this disease, the first suspected case of inhalational anthrax should be reported immediately to the Department of Health so that immediate investigation, epidemiological surveys and laboratory testing can be done to document the disease. For these investigations, the U.S. Department of Health and Human Services defines a confirmed case of anthrax as:

- 1) a clinically compatible case of cutaneous, inhalational, or gastrointestinal illness that is laboratory confirmed by isolation of *B. anthracis* from an infected tissue or site or
- 2) Other laboratory evidence of *B. anthracis* infection based on at least two supportive laboratory tests.

A suspected case is defined as:

- 1) a clinically compatible case of illness without isolation of *B. anthracis* and no alternative diagnosis, but with laboratory evidence of *B. anthracis* by one supportive laboratory test *or*
- 2) a clinically compatible case of anthrax epidemiologically linked to a confirmed environmental exposure, but without corroborative laboratory evidence of *B. anthracis* infection.

Laboratory criteria for diagnosis of anthrax consists of:

- 1) isolation and confirmation of *B. anthracis* from a clinical specimen collected from an affected tissue or site *or*
- 2) Other supportive laboratory tests, including:
  - a) evidence of *B. anthracis* DNA by polymerase chain reaction (PCR) from specimen collected from an affected tissue or site;
  - b) demonstration of *B. anthracis* in a clinical specimen by immunohistochemical staining; *or*
  - c) Other laboratory tests (e.g. serology) that may become validated by laboratory confirmation.

The sudden appearance of a large number of patients in a city or region with an acute-onset flu-like illness and a case fatality rate of 80% or more, with nearly half of all deaths occurring within 24 to 48 hours, is most likely secondary to anthrax or pneumonic plague. Because of the limited availability of rapid diagnostic test for its diagnosis such as the ELISA (Enzyme-linked immunosorbent assay) for protective antigen and PCR (polymerase chain reaction), these tests can only be used for confirming and managing anthrax hoaxes.

The Working Group on Civilian Biodefense outlined a diagnostic model shown below to guide us in the appropriate approach to the diagnosis and is not considered routine laboratory procedure (Table 1). It is important to emphasize that diagnostic tests outlined in the table above are not complicated and can be done in most centers trained in handling agents.

#### *What are the current treatment options?*

Because of the limited number of evidence in humans regarding treatment, the recommendations were largely based on limited number of studies in experimental animals, current understanding of antibiotic resistance patterns, and the potential need to treat a large number of casualties. The Working Group of Civilian Biodefense offered the following recommendations (Table 2), which are yet to be approved by the FDA.

Table 1. Diagnosis of inhaled anthrax infection

Epidemiology	Sudden appearance of multiple cases of severe flu-like symptoms with fulminant course and high mortality
Diagnostic test	Chest radiograph: widened mediastinum; Peripheral blood smear: Gram positive bacilli on unspun smear
Microbiology	Blood culture growth of large gram-positive bacilli with preliminary identification of <i>Bacillus</i> species
Pathology	Hemorrhagic mediastinitis, hemorrhagic thoracic lymphadenitis, hemorrhagic meningitis

Table 2. Medical therapy in the contained casualty setting

	Initial therapy	Optimal therapy if strain is proven susceptible	Duration in days
Adults, pregnant and immunosuppressed persons	Ciprofloxacin 400 mg IV q12 h	Pen G 4 MU IV q4h Doxycycline 100mg IV q12h	60
Children	Ciprofloxacin 20-30 mg/kg/day IV divided into 2 daily dose not to exceed 1 g/day	Age < 12: Pen G 50,000U/kg IV q6h Age ≥ 12: Pen G 4 MU IV q4h	60

IV – intravenous MU – million units

The first recommendation is for patients with clinically evident inhalational anthrax infection in a contained casualty setting. Because of the rapid course of symptomatic inhalational anthrax, the need for early antibiotic intervention is essential in determining a better survival outcome. A delay in antibiotic treatment for patients with anthrax infection even by hours may substantially lessen the chances for survival.

*Bacillus anthracis* is generally susceptible to penicillin and tetracyclines. However, reports have been published of a *B. anthracis* vaccine strain engineered by Russian scientists that is resistant to tetracyclines and penicillin. Although treatment of anthrax infection with ciprofloxacin has not been studied in humans, animal models suggest excellent efficacy. It is for this reason that the empiric choice of antibiotic pending sensitivity studies is ciprofloxacin.

It is common medical knowledge that fluoroquinolones should not be used in children younger than 16 years because of the risk of arthropathy. However, balancing the risks of anthrax caused by an engineered antibiotic-resistant strain, the working group recommends that ciprofloxacin be used in the pediatric and pregnant populations until subsequent sensitivity results show susceptibility to penicillin or tetracycline. Treatment protocol however is different in the mass casualty setting primarily because of the logistic difficulty in instituting intravenous medications to a large population. Table 3 outlines the recommended regimens and duration for this population.

#### *What about those who were exposed but without symptoms?*

There are no FDA approved antibiotic regimens following exposure to anthrax aerosol. For post exposure prophylaxis, it has been recommended that the same antibiotic regimen and duration as that recommended for treatment of mass casualties be given.

Table 3. Medical therapy in the mass casualty setting

	Initial therapy	Optimal therapy if strain is proven susceptible	Duration in days
Adults, pregnant and immunosuppressed persons	Ciprofloxacin 500 mg po BID	Amoxycillin 500 mg q8h Doxycycline 100mg p.o. q12h	60
Children	Ciprofloxacin 20-30 mg/kg/day IV divided into 2 daily dose not to exceed 1 g/day	Weight > 20 Kg: Amoxycillin 500 mg q8h Weight < 20 kg: Amoxycillin 40 mg/kg divided into 3 doses to taken every 8 hours	60

p.o.. – by mouth

*Is vaccination an option to prevent the development of the disease?*

The US-anthrax vaccine is an inactivated cell-free product licensed in 1970. The vaccine is licensed to be given in a 6 dose series and has recently been mandated for all US military active personnel. The current vaccine supply is limited and the US production capacity is modest. Population-wide vaccination at this time would not be recommended given the costs and logistics of a large-scale vaccination program.

*What will I do if I receive an anthrax threat letter?*

First and foremost, DO NOT PANIC! The following are steps (patterned from the CDC Advisory) that you can follow in handling a suspicious letter or package: For anthrax to be effective as covert agent, it must be aerosolized into very small particles. This is difficult to do, and requires a great deal of technical skill and special equipment. If these small particles are inhaled, life-threatening lung infection can occur, but prompt recognition and treatment are effective.

How to handle suspicious letter of package

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Do not shake or empty the contents of any suspicious envelope or package; DO NOT try to clean up powders or fluids. PLACE the envelope or package in a plastic bag or some other type of container to prevent leakage of contents. If you do not have any container, COVER the envelope or package with anything (e.g. clothing, paper, trash can etc) and do not remove the cover.

Then LEAVE the room and CLOSE the door, or section off the area to prevent others from entering.

WASH your hands with soap and water to prevent spreading any powder to your face or skin

If you are at HOME, report the incident to the local police and the Department of Health

If you are at WORK, then report this to the local police, and notify your building security, or an available supervisor.

If possible, LIST all people who were in the room or area when this suspicious letter or package was recognized. Give this list to both the local public health authorities and law enforcement official for follow up investigations and advice

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Shower with soap and water as soon as possible. Do not use bleach or disinfectant on your skin.

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*What constitute a suspicious letter or parcel?*

Some typical characteristics, which ought to trigger suspicion, include letters or parcel that:

1. Have any powdery substance on the outside.
2. Are unexpected or from someone unfamiliar to you.

3. Are addressed to someone no longer with your organization or are otherwise outdated.
4. Have no return address, or have one that can't be verified as legitimate.
5. Are of unusual weight, given their size, or are lopsided or oddly shaped.
6. Have an unusual amount of tape on them.
7. Are marked with restrictive endorsements, such as "Personal" or "Confidential," have strange odors or stains.
8. Show a city or state in the postmark that doesn't match the return address.

## CONCLUSION

Anthrax is just one among the many potential agents that can be used for bio-terrorist attack. Regardless of which agent is used, preparedness is only as good as the local health unit identifying the agent and the system by which immediate response and intervention is carried out.

The recognition of cases is more important than treatment since treatment protocols are readily available for known biological agents. It is therefore recommended that extensive educational campaign be carried among our "frontliners", the local health unit, responding paramedical teams, police department and a strong political will from our local government unit and the national government.

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