

# Terrorism and Disaster

WHAT  
CLINICIANS  
NEED TO  
KNOW



## Anthrax

 RUSH UNIVERSITY  
MEDICAL CENTER



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## SERIES EDITORS

**Rush University  
Medical Center  
Chicago, Illinois**

Stephanie R. Black, MD\*  
Assistant Professor of Medicine  
Section of Infectious Diseases  
Department of Internal Medicine

Daniel Levin, MD\*  
Assistant Professor  
General Psychiatry Residency Director  
Department of Psychiatry

Gillian S. Gibbs, MPH\*  
Project Coordinator  
Center of Excellence for Bioterrorism  
Preparedness

Linnea S. Hauge, PhD\*  
Assistant Professor  
Educational Specialist  
Department of General Surgery

**AUTHORS  
Rush University  
Medical Center  
Chicago, Illinois**

Stephanie R. Black, MD\*  
Assistant Professor of Medicine  
Section of Infectious Diseases  
Department of Internal Medicine

Daniel Levin, MD\*  
Assistant Professor  
General Psychiatry Residency Director  
Department of Psychiatry

**Uniformed Services University  
Health Sciences  
Bethesda, Maryland**

David M. Benedek, MD, LTC, MC, USA\*  
Associate Professor of Psychiatry

Steven J. Durning, MD, Maj, USAF, MC\*  
Associate Professor of Medicine

Thomas A. Grieger, MD, CAPT, MC, USN\*  
Associate Professor of Psychiatry  
Associate Professor of Military &  
Emergency Medicine  
Assistant Chair of Psychiatry for Graduate  
& Continuing Education

Molly J. Hall, MD, Col, USAF, MC, FS\*  
Assistant Chair & Associate Professor  
Department of Psychiatry

Derrick Hamaoka, MD, Capt, USAF, MC, FS\*  
Director, Third Year Clerkship  
Instructor of Psychiatry

Paul A. Hemmer, MD, MPH, Lt Col, USAF, MC\*  
Associate Professor of Medicine

Benjamin W. Jordan, MD, CDR, MC, USNR, FS\*  
Assistant Professor of Psychiatry

James M. Madsen, MD, MPH, COL, MC-FS, USA\*  
Associate Professor of Preventive Medicine  
and Biometrics  
Scientific Advisor, Chemical Casualty Care  
Division, US Army Medical Research Institute  
of Clinical Defense (USAMRICD), APG-EA

Deborah Omori, MD, MPH, FACP, COL, MC, USA\*  
Associate Professor of Medicine

Michael J. Roy, MD, MPH, FACP, LTC, MC\*  
Associate Professor of Medicine  
Director, Division of Internal Medicine

Jamie Waselenko, MD, FACP\*\*  
Assistant Professor of Medicine  
Assistant Chief, Hematology/Oncology  
Walter Reed Army Medical Center  
Washington, DC

## Guest Faculty

Ronald E. Goans, PhD, MD, MPH\*  
Clinical Associate Professor  
Tulane University School of Public Health &  
Tropical Medicine  
New Orleans, LA

Sunita Hanjura, MD\*  
Rockville Internal Medicine Group  
Rockville, MD

Niranjan Kanesa-Thasan, MD, MTMH\*  
Director, Medical Affairs & Pharmacovigilance  
Acambis  
Cambridge, MA

Jennifer C. Thompson, MD, MPH, FACP\*  
Chief, Department of Clinical Investigation  
William Beaumont Army Medical Center  
El Paso, TX

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# Anthrax

**CASE AUTHORS:** Michael J. Roy, MD, MPH, FACP, LTC, MC  
Steven J. Durning, MD, Maj, USAF, MC  
Molly Hall, MD, Col, USAF, MC, FS

## DISCLAIMER

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## INSTRUCTIONS

The questions that appear throughout this case are intended as a self-assessment tool. For each question, select or provide the answer that you think is most appropriate and compare your answers to the key at the back of this booklet. The correct answer and a discussion of the answer choices are included in the answer key.

In addition, a sign is provided in the back of this booklet for posting in your office or clinic. Complete the sign by adding your local health department's phone number.

# Anthrax

CASE AUTHORS: Michael J. Roy, MD, MPH, FACP, LTC, MC  
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## INTENDED AUDIENCE

Internal medicine, family medicine, and emergency medicine clinicians, and mental health care professionals, including psychiatrists, psychologists, and social workers who will provide evaluation and care in the aftermath of a terrorist attack or other public health disaster

## EDUCATIONAL OBJECTIVES

Upon completion of this case, participants will be able to:

- Identify key clinical findings that facilitate differentiation of inhalational anthrax from common respiratory infections such as influenza, influenza-like illnesses, and community-acquired pneumonia.
- List the most useful methods for the rapid diagnosis of anthrax.
- Describe the initial on-site management of potential exposure to anthrax or other biological agents, including large numbers of individuals who fear they were exposed.
- Summarize the most effective treatment regimens for clinical anthrax infection.
- Outline common persistent somatic and psychological effects in survivors of inhalational anthrax.
- Describe recommended methods of communicating with the media and public during a disaster.

## CASE HISTORY

Albert Brown, a 33-year-old news editor at a national cable news station's Washington office, reports feeling well until yesterday when he awoke feeling feverish, sweaty, and fatigued despite having had a good night's sleep. He took acetaminophen and called in sick to work yesterday, but the fever, fatigue, and generally ill feeling have persisted, with nausea and decreased appetite. He feels like he has the flu, but did receive a flu shot this year. This morning, he developed a dry cough, along with some chest discomfort, difficulty breathing, and the feeling that he "couldn't get enough air," all of which prompted him to present for evaluation at your primary care facility. His joints are not painful, but he has a diffuse throbbing headache, and generalized myalgias. He does not have a runny nose or a sore throat. No household contacts are ill. In the past 2 months he had an uneventful business trip to Europe and a vacation to Jamaica.

## QUESTION 1

What presenting symptom should lead you to seriously consider a diagnosis other than influenza or influenza-like illness?

- a. cough
- b. dyspnea
- c. fatigue
- d. chest discomfort
- e. fever

**Reminder:** You can find the Answer Key & Discussion on page 11.

**COMMENT:** Drenching sweats were prominent (70%) in the inhalational anthrax (IA) cases of 2001 though they have been rarely seen in occupation-related IA cases, influenza, or influenza-like illnesses (ILI).<sup>1,2</sup> As illustrated in the table, symptoms that are less frequent in IA than in laboratory confirmed influenza or ILI include headache, myalgias, and especially sore throat and rhinorrhea. The presence of nausea or vomiting may also be helpful as it was reported in 9 of 11 cases of IA in 2001, but is only seen in about one-third of patients with influenza or ILI. Among exam and laboratory findings, tachycardia, elevated hematocrit, hypoalbuminemia, and hyponatremia are all more frequent in IA than with influenza, ILI, or community-acquired pneumonia (CAP). The presence of dyspnea and chest discomfort should heighten concern for something other than influenza or ILI, and warrants immediate careful evaluation.

**Table. Comparison of Presenting Signs and Symptoms and Laboratory Findings in 11 Cases of Inhalational Anthrax (IA)\* Versus Patients With Influenza-like Illness (ILI) and Hospitalized Patients With Community-Acquired Pneumonia (CAP)†**

Signs or Symptom	IA	ILI	P Value‡§	CAP	P Value‡
Tachycardia	9/11 (82%)	58/422 (14%)	.0001	320/649 (49%)	.04
Presence of:					
Nausea or vomiting	9/11 (82%)	227/649 (35%)	.002		
Chest pain	7/11 (64%)	202/650 (31%)	.04		
Dyspnea¶	8/10 (80%)	6%			
Lack of: #					
Sore throat	9/11 (82%)	166/684 (24%)	.0001		
Nasal symptoms	8/11 (73%)	131/684 (19%)	.0002		
Headache	6/11 (55%)	97/684 (14%)	.002		
Myalgias	4/11 (36%)	60/684 (9%)	.01		
Lab findings**					
Leukocytosis	3/11 (27%)	47/697 (7%)	.04	393/645 (61%)	.03
High AST	8/9 (89%)	122/687 (18%)	<.0001	77/269 (29%)	.0004
High ALT	8/9 (89%)	219/687 (32%)	.0008	54/185 (29%)	.0005
Hyponatremia	8/10 (80%)	63/687 (9%)	<.0001	222/636 (35%)	.005
High BUN	4/8 (50%)	23/630 (4%)	<.0002		
Low platelet count	2/9 (22%)	26/660 (4%)	.05		
High hemoglobin	4/11 (36%)	40/670 (6%)	.004		
High bilirubin	3/8 (38%)	38/682 (6%)	.009		
Hypoalbuminemia	6/9 (67%)	12/686 (2%)	<.0001		
Hypocalcemia	8/8 (100%)	303/687 (44%)	.002		

\* Cases from the 2001 US Postal Service outbreak.

† Table modified from Kuehnert, et al, with ILI and CAP data based on retrospective review of symptomatic clinical trial participants who had confirmatory diagnostic tests.<sup>2</sup>

‡ Only findings with p value <.05 are shown.

§ IA vs. ILI

|| IA vs. CAP

¶ Dyspnea was not included in Kuehnert's model, but others have noted its discriminatory value, including the CDC, which provided these percentages without further analysis.<sup>1</sup>

# Presence of abdominal pain, diarrhea, dyspnea, and chills not available for patients with ILI.

\*\*Creatinine, platelet count, hemoglobin, bilirubin, potassium, albumin, and calcium levels not available for patients with CAP.

The following multivariate models<sup>2</sup> can be used to distinguish IA from other acute respiratory illnesses:

*Variables to discriminate IA from ILI*

(2 points each): tachycardia, hypoalbuminemia, lack of nasal symptoms

(1 point each): hyponatremia, high hematocrit, lack of headache, no myalgias

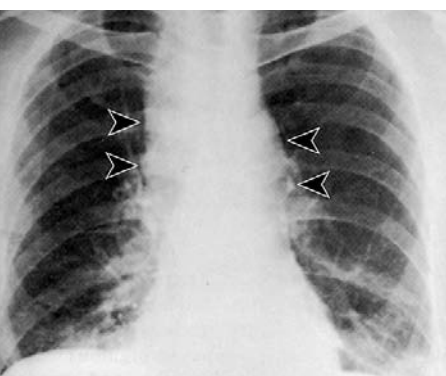
A cut-off score of 4 captured all 11 patients with IA for 100% sensitivity with 96% specificity.<sup>2</sup>

*Variables to discriminate IA from CAP*

(1 point each): nausea or vomiting, tachycardia, elevated transaminases, hyponatremia, normal white blood cell count

A cut-off score of 2 had 100% sensitivity for IA with 48% specificity.<sup>2</sup>

These models may assist in differentiating IA from ILI and CAP, but they are based on a retrospective review of only 11 cases of IA and have not yet been validated in another population.



**FIGURE.** A chest radiograph with inhalational anthrax infection. Reprinted from *JAMA* 1999;281:1735-1745.<sup>3</sup>

Mr. Brown reports that 1 hour after eating a light breakfast he experienced increased nausea and abdominal discomfort without emesis. His temperature at home was 102.4°F last night, and 101.3°F this morning. Mr. Brown lives with his wife and 6-year-old son. Mr. Brown rarely drinks alcohol, does not smoke or use recreational drugs, and takes no prescription or alternative medications. He has no allergies and no significant past medical or surgical history. Mr. Brown works at a computer, frequently uses a telephone and a fax, manages files, and processes mail for the station's news anchors. He is unaware of any ill colleagues.

On physical exam, Mr. Brown appears tired and ill at ease, with labored breathing. His temperature is 101.5°F, with a respiratory rate of 22, blood pressure of 102/60, and heart rate of 118. Lung exam reveals slight dullness at both bases, with crackles throughout the lower left lung field. The remainder of his exam is notable only for a regular tachycardia and mild diffuse abdominal tenderness without rebound.

At this point you decide to admit Mr. Brown for further evaluation. Laboratory studies show a white blood cell count of 12.4 with 80% polymorphonuclear leukocytes (PMNs) and 12% band forms, hematocrit 42%, and platelets 105,000. Chemistries are notable for: sodium 132 mmol/L, potassium 5.4 mmol/L, and glucose 47 mg/dL. Liver function tests show mild elevations of aspartate aminotransferase (AST, 60 U/L) and alanine aminotransferase (ALT, 58 U/L), with a moderate depression of the serum albumin to 3.0 gm/dL. His chest X-ray is displayed in the figure.

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## QUESTION 2

What findings can be seen on a chest radiograph with inhalational anthrax infection?

- a. parenchymal infiltrate
- b. pleural effusion
- c. mediastinal widening
- d. perihilar fullness
- e. all of the above

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**COMMENT:** In IA, spores enter the tracheobronchial tree and are ingested by alveolar macrophages, which transport some spores to regional lymph nodes, where they germinate to vegetative forms that produce virulence factors. Germination may be delayed for as much as 2-3 months, but in the 2001 US mail-related outbreak, the incubation period was only 4-6 days for the 9 cases with a known time of exposure.<sup>4</sup> Exotoxin production within tracheobronchial lymph nodes leads to massive edema, hemorrhage, and necrotizing lymphadenitis and mediastinitis, resulting in the pathognomonic

widened mediastinum on chest radiograph as seen in the photograph. Infection is within the lymph nodes; anthrax does not classically cause a true pneumonia, though there may be the appearance of an infiltrate on a chest X-ray.

Of the eleven cases of IA spread by the US mail in 2001, the initial chest X-ray was interpreted as normal in three cases, but more careful review by radiologists identified abnormalities in every case.<sup>4</sup> Two patients had pulmonary infiltrates without mediastinal widening, while the others had at least hilar or paratracheal fullness, but more commonly frank mediastinal widening consistent with lymphadenopathy. Further, all eleven cases had pleural effusions. Hemorrhagic pleural effusions were also prominent in other case series, including victims of an accidental release of spores from a military research facility in Sverdlovsk, Russia in 1979, which resulted in at least 66 deaths, the largest epidemic of IA in the past century.<sup>5</sup>

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### QUESTION 3

**Which of the following characteristics make anthrax a likely and effective bioterrorist weapon?**

- a. easily obtained and easily transmitted from person-to-person
- b. easily disseminated and easily obtained
- c. easily transmitted from person-to-person and highly lethal

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**COMMENT:** Anthrax is the first disease to be deliberately disseminated through the US mail. There were 11 cases each of IA and cutaneous anthrax in the fall of 2001. At least 20 of the 22 cases were linked to 5 letters contaminated with a single strain of anthrax that were mailed from Trenton, New Jersey. Five of 11 cases of IA resulted in death and thousands of people received prophylactic antibiotics for possible exposure to anthrax spores.

Fortunately, many experts believe that the manufacture of uniform, finely milled, highly lethal spores such as those spread in this case may be beyond the financial or technological capacity of many terrorist groups. For example, Aum Shinrikyo (the Japanese cult that staged the lethal sarin attacks in the Tokyo and Matsumoto subway systems) attempted to use anthrax on several occasions, largely without success. However, a large-scale IA bioterrorist attack has horrific potential. A 1993 report by the US Congressional Office of Technology Assessment estimated that up to 3 million deaths would follow the aerosolized release of 100kg of weapons grade anthrax spores over the Washington, DC, area — a lethality on the order of a hydrogen bomb.<sup>6</sup> Evaluation of the US Postal Service cases indicates as few as 1-3 spores may be sufficient to cause IA, with lowered immunity in the very young and very old rendering them particularly vulnerable.<sup>7</sup>

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### QUESTION 4

**A diagnostic study needs to be ordered. What is the best test for confirming the diagnosis of inhalational anthrax in a symptomatic patient?**

- a. nasal swab
  - b. sputum gram stain and culture
  - c. blood culture
  - d. fiber optic bronchoscopy with transbronchial biopsy
  - e. serology
-



**COMMENT:** Although the initial phase of IA can be easily mistaken for a viral ILI, if treatment is not initiated during this phase, the infection will almost certainly be fatal. Therefore, physicians must have a high index of suspicion, based upon suggestive clinical signs and symptoms, as previously discussed, as well as epidemiologic indicators. Epidemiologic circumstances that should lead to consideration of IA, in addition to plague and other biological warfare agents, include:

- a potential exposure history (eg, mail handler)
- other recent case(s) of confirmed inhalational or cutaneous anthrax
- the sudden appearance of multiple cases of severe flu-like illness with high mortality, unexplained respiratory failure, unexplained sepsis or death following acute febrile illness
- ILI in summer months.<sup>8</sup>

Diagnostic evaluation should be expedited, but if clinical suspicion for IA is high, directed therapy should be implemented immediately, since test results will not be altered by recently initiated treatment, whereas delay in treatment can be fatal. A reliable laboratory test to rapidly confirm the diagnosis of anthrax is most important. A rapid handheld instrument utilizing PCR or enzyme-linked immunosorbent assay (ELISA) technology can be used to test an environment where there is concern that spores may have been released. The availability of rapid field testing has increased in recent years.<sup>8</sup>

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## QUESTION 5

**Antibiotic therapy needs to be initiated. Which of the following is the best choice for initial treatment of suspected inhalational anthrax infection?**

- intravenous ciprofloxacin
- intravenous doxycycline
- intravenous ceftriaxone
- intravenous ciprofloxacin or doxycycline, and ampicillin
- oral ciprofloxacin and doxycycline

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**COMMENT:** Inhalational anthrax is a Category A agent. The Centers for Disease Control and Prevention (CDC) classifies Category A agents as those considered to have the greatest potential for adverse public health impact with mass casualties. Most require broad-based public health preparedness efforts (eg, improved surveillance and laboratory diagnosis and stockpiling of specific medications). Category A agents also have a moderate to high potential for large-scale dissemination or a heightened general public awareness that could cause mass public fear and civil disruption.<sup>11</sup>

Inhalational anthrax is unique among potential bioterrorist agents in combining the following features:

- effective treatment is readily available
- it is imperative to initiate treatment immediately

There are no clinical studies of the treatment of IA in humans. Treatment guidelines are largely the result of limited case series of IA in humans, extrapolation from animal data, in-vitro studies, and expert opinion.

At the time of the 1990-91 Gulf War, US military planners were concerned that Iraq might genetically engineer anthrax strains resistant to common antibiotics such as penicillin and doxycycline. This concern led to the selection of ciprofloxacin as the treatment of choice against anthrax, since it was a new, highly effective antibiotic, with little chance of resistance having been engineered against it. The anthrax disseminated by mail in 2001 was sensitive to multiple antibiotics, including penicillin, doxycycline, rifampin, and ciprofloxacin. However, anthrax produces an inducible beta-lactamase, potentially reducing sensitivity to beta-lactamase inhibitors if a high volume of bacteria is present, so penicillin



alone is not advisable (in fact, in a symptomatic patient, monotherapy with any agent is considered inadequate).<sup>8</sup> Doxycycline is inexpensive, well-tolerated, and effective. The mortality rate from IA is exceedingly high if therapy is delayed until pathognomonic findings (eg, widened mediastinum on chest radiograph) develop. Delaying antibiotic therapy by a few hours can substantially reduce survival.<sup>12</sup> Therefore, in an area where anthrax cases are occurring, all patients with fever or systemic illness should be treated for anthrax until it can be ruled out.<sup>8,9</sup>

Patients may be transitioned to an oral antibiotic, preferably ciprofloxacin or doxycycline, after stabilization. The duration of therapy remains controversial. Options suggested by the CDC, based primarily on studies of monkeys, range from 60 days of antibiotics with close clinical follow-up, to as much as 100 days of antibiotics in conjunction with vaccination against anthrax.<sup>10</sup> Unvaccinated monkeys did not develop protective antibodies and succumbed to re-challenge with spores, but survival rates were markedly improved after vaccination.<sup>11</sup> Given the long duration of treatment required, after antibiotic susceptibility of the index case has been determined, the most widely available, efficacious, tolerable, and inexpensive oral antibiotic should be chosen.

Prior to the 2001 US Postal Service anthrax outbreak, the mortality rate of IA was exceedingly high: 16/18 (89%) of US occupational cases and 68/79 (86%) of Sverdlovsk cases resulted in death. However, only 5/11 (45%) died in 2001,<sup>9</sup> with multiple factors likely contributing to survival. Prompt presumptive diagnosis and treatment were key, with death resulting in all 4 patients who demonstrated late stage signs prior to antibiotic initiation.<sup>4</sup> Other factors which may have influenced outcome include critical care units, improved ventilator support, and multi-drug antibiotic regimens.

Asymptomatic patients who have a credible exposure should receive at least 60, and as much as 100, days of antibiotics, and should be offered anthrax vaccination.<sup>10</sup> While awaiting nasal swab results, patients with a likely exposure history should initiate antibiotic prophylaxis with either ciprofloxacin or doxycycline. A negative nasal swab does not rule out anthrax exposure since swabs are almost universally negative greater than 24 hours after IA exposure; in fact, one fatal case in the 2001 US Postal Service-related series was a patient with a negative nasal swab.<sup>12</sup>

The anthrax vaccine currently used by the US military is an inactivated cell-free product made from a filtrate of an attenuated strain of *B. anthracis*. Hundreds of thousands of military service members have received the vaccine. Minor reactions at the site of inoculation have been common, but serious side effects to the vaccine, such as allergic reactions requiring hospitalization, have been rare.

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## QUESTION 6

You receive a call from a concerned colleague of Mr. Brown's at the station. She would like to know whether they should take any precautions at the studio. What public health measures should be taken when a case of anthrax is suspected?

- a. Notify public health authorities.
- b. Quarantine infected individuals.
- c. Wash clothing and body surfaces with 5% bleach solutions.
- d. Use high-speed fans to clear spores out of an area of suspected infection.

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Having learned lessons from the anthrax mail attacks in 2001, the media, government leaders, and scientific experts in this instance move rapidly to provide timely, accurate information to the public. The CDC media relations office fields hundreds of inquiries daily.

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Given the lethality of IA, antibiotic recommendations are similar for children, pregnant women, and the immunocompromised, despite a greater risk of side effects.

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Nasal swabs of each nostril should be collected from asymptomatic patients.

Nasal swabs are not useful in symptomatic patients.

A negative nasal swab for *B. anthracis* does not rule out anthrax.

Ideally, blood cultures should be collected immediately prior to administering antibiotics.

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## QUESTION 7

How should the medical community respond in order to manage the public's emotional and behavioral response to this bioterrorist event?

- a. Proactively reassure the public that there is no cause for alarm and to go about life as usual, because anthrax is not contagious.
- b. Appear authoritative and offer definitive opinions, because people need to feel that the situation is being handled.
- c. Set realistic expectations and update the media frequently using layman's terms to explain the emerging science.
- d. Avoid talking to the media.

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**COMMENT:** The effectiveness of public officials and the medical community in containing the outbreak plays a determining role in how the public responds. Authorities should place a high priority on working with the media to provide frequent updates on the health crisis in an open and honest fashion. Rumors and misinformation quickly establish public mistrust and, coupled with a response that is perceived to be slow or ineffective or one that appears to protect some but not others, may lead to desperate people taking matters into their own hands. The risk of panic is heightened when people believe that there is a small chance of escape, that they are likely to become infected, and that there are limited resources available on a first come, first served basis.

Biological agents are especially effective at causing terror. As is the case with radiation, biological agents are invisible, odorless, and imperceptible to humans. Their effects are not immediate, but delayed and often protracted. Dormant biological agents such as anthrax spores can persist undetected for years in the environment. Ongoing risk of exposure or contracting the illness is difficult to assess, which heightens a sense of vulnerability, loss of control, and anxiety. Biological agents that cause disfigurement, deformity, or are contagious are even more terrifying.<sup>13,14</sup>

The medical community must set realistic expectations about the process of diagnosis, treatment, and containment plans. Simply stating "we don't have the answers yet; we may not know now, but here's what we're doing to find out" is better than having to go back and undo an inaccurate assertion. In the period unfolding around a crisis, the medical community must keep the press updated and engaged to avoid uninformed speculation and worst-case horror stories. During the 2001 anthrax mail attacks it would have been helpful to the public if the media had clarified medical terms and recommendations, such as the difference between sensitivity and specificity as well as false positives and false negatives, the basis of changing antibiotic recommendations, different laboratory tests used, and the role of nasal swabs in determining how far the spores might have traveled versus confirming infection.<sup>14</sup>

The role of accurate information and clear rationale for decisions in sustaining public trust and compliance cannot be underestimated. The perception of a double standard can fracture social fault lines of race, socioeconomic status, religion, and ethnicity. The rapid response at the US Capitol including evacuation of buildings, nasal swabbing, and distribution of ciprofloxacin to employees contrasted dramatically with the later recognition that Brentwood postal workers who were at risk of exposure continued to work in a contaminated building, and appeared to be treated less urgently.

Although media reporting, public education, and leadership response were well organized and largely effective following this incident of contaminated mail addressed to the station's lead anchor, one emergency room in the heart of the station's postal district continued to see a surge of patients fearing that they had been exposed.

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## QUESTION 8

In the wake of a bioterrorism event, emergency departments may see considerable numbers of patients with somatic complaints who believe they have been infected. Guidelines for appropriate evaluation and management would include which of the following?

- a. Any patient thought to have minimal risk of exposure should be referred to a mental health provider.
  - b. Patients described as “the worried well” will be reassured once they understand that they couldn’t possibly have been exposed.
  - c. Every patient should be seen by a mental health provider first so as to minimize unnecessary physical exams and laboratory tests.
  - d. Every patient needs a history, focused physical exam and medical work-up.
- 

**COMMENT:** Triage of patients who are primarily distressed and may have somatic symptoms from those who may have been exposed or injured is a critical and challenging first step in emergency care. The term “worried well” is disparaging and should not be used. The patient may feel that their health concerns have not been taken seriously and that they have been told “it’s all in your head.” A non-stigmatizing triage labeling system such as high risk, moderate risk, and minimal risk conveys concern and promises continued monitoring, which is reassuring to patients. Ideally, psychiatrists and other mental health professionals should be an integral part of the teams performing initial screening and triage to maintain mental health care in conjunction with other medical assessment and treatment. In an acute event, patients who remain fearful and are not reassured by negative findings may be best cared for in a separate area near the emergency department. This allows for continued evaluation and easy return to the emergency department, if necessary. Establishing a clinical registry to follow up patients who are distressed is a sound public health intervention as well as a psychological intervention, assuring patients that their concerns are being taken seriously.

Mr. Brown was treated with intravenous ciprofloxacin, doxycycline, and clindamycin for 2 weeks. He required intubation and mechanical ventilation for 3 days, but subsequently did well, and was transitioned to oral doxycycline for an additional 86 days. Spores were identified in an envelope addressed to a lead anchor, and nasal swabs were positive for another 6 workers at the station’s Washington office as well as for 8 postal workers. Two developed cutaneous anthrax that was successfully treated, and the others were provided with prophylactic treatment.

A year after Mr. Brown recovered from life threatening IA he had not returned to his job full-time and was now considering applying for disability benefits. He continued to complain of poor appetite, frequent nausea, muscle and joint pain, and exercise intolerance. Climbing a flight of stairs resulted in difficulty breathing and dizziness. Medical work-up, including pulmonary function tests, joint X-rays, chest CT scans, thyroid, ESR, C-reactive protein, antinuclear antibodies, was negative.

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## QUESTION 9

A constellation of unresolved physical symptoms following a life-threatening event may be understood as which of the following?

- a. The clinical syndrome known as post inhalation anthrax deconditioning.
- b. Medically Unexplained Physical Symptoms (MUPS) described in patients following traumatic and terrorist experiences.
- c. Malingering to avoid work and receive compensation.
- d. A hysterical reaction to a near-death experience.

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**COMMENT:** A recent study of survivors of the 2001 bioterrorist attacks found many had continuing significant health problems, psychological distress, and loss of functional capacity.<sup>15</sup> Physical symptom complaints may arise as part of a number of physical and mental disorders and psychosocial distress. Some postulate that posttraumatic stress mediates this presentation through increased cardiovascular reactivity, disturbed sleep physiology, and adrenergic dysregulation.<sup>16</sup> MUPS pose a clinical and management challenge.

Standard assessment of terrorism survivors should include physical health complaints as well as other symptoms of depression, posttraumatic stress, anxiety, and substance abuse disorders. As these patients are more likely to present to primary care settings, primary care clinics should routinely assess the degree of concern about exposure-related illness regardless of whether a known exposure occurred. A helpful screening question might be to ask whether or not the patient's visit is related to terrorism or bioterrorism concerns. If the answer is positive, extra time could be devoted to exploring the nature of these concerns in order to develop recommendations for additional testing, clinic visits, and patient education. Scheduled follow-up visits in conjunction with the development of a clinical contact registry communicates compassion and concern. Early triage into this level of follow-up care may mitigate the later development of persistent medically unexplained syndromes such as Gulf War syndrome.<sup>13,16</sup> Gulf War syndrome is a set of poorly defined, heterogeneous ailments that consists mainly of chronic pain, fatigue, depression, and other idiopathic symptoms that have afflicted veterans of the 1991 Gulf War for which no definitive cause has been found.

## SUMMARY

Anthrax is a rare infection in humans. The physician should assume IA is due to bioterrorism until proven otherwise. Consideration of bioterrorism should also be entertained in patients presenting with cutaneous anthrax. This clinical vignette demonstrates clinical and epidemiologic features which should immediately lead to the suspicion of a bioterrorism incident, and of anthrax in particular. An anthrax exposure constitutes a medical emergency, necessitating rapid diagnostic and therapeutic interventions, with prompt notification of public health authorities and hospital laboratory workers.

## ANSWER KEY & DISCUSSION

### QUESTION 1

What presenting symptom should lead you to seriously consider a diagnosis other than influenza or influenza-like illness?

- a. cough
- b. dyspnea
- c. fatigue
- d. chest discomfort
- e. fever

**ANSWER:** The correct answer is b. Cough (70-80%), fatigue (75-94%), and fever or chills (80-90%) are all quite common in individuals with influenza or influenza-like illnesses (ILI).<sup>1,2</sup> Chest pain or discomfort is less common (23-35%), but not rare. However, dyspnea, or shortness of breath, has been reported in only 6% of those with influenza or ILI, whereas it was present in the majority (81%) of the 2001 mail-borne cases of inhalational anthrax (IA). In the IA case series, fatigue and fever or chills were universally present, cough was present in 90% of the cases, and chest pain or discomfort was present in 63% of the cases. Each symptom was more common in IA than with influenza or ILI, but none has the strong association of dyspnea.

### QUESTION 2

What findings can be seen on a chest radiograph with inhalational anthrax infection?

- a. parenchymal infiltrate
- b. pleural effusion
- c. mediastinal widening
- d. perihilar fullness
- e. all of the above

**ANSWER:** The correct answer is e. Although mediastinal widening and pleural effusion are classically associated with inhalation anthrax, any of these findings may frequently be seen.

### QUESTION 3

Which of the following characteristics make anthrax a likely and effective bioterrorist weapon?

- a. easily obtained and easily transmitted from person-to-person
- b. easily disseminated and easily obtained
- c. easily transmitted from person-to-person and highly lethal

**ANSWER:** The correct answer is b. Inhalational anthrax represents a leading bioterrorism threat due to ready access (high prevalence in soil throughout the world), high infectivity (eg, transmitted by opening spore-containing mail), high lethality, and the ability to form an odorless and invisible aerosol, which can then be easily disseminated. However, anthrax does not pose a risk for person-to-person transmission.

## QUESTION 4

A diagnostic study needs to be ordered. What is the best test for confirming the diagnosis of inhalational anthrax in a symptomatic patient?

- a. nasal swab
- b. sputum gram stain and culture
- c. blood culture
- d. fiber optic bronchoscopy with transbronchial biopsy
- e. serology

**ANSWER:** The correct answer is c. Blood cultures for *B. anthracis* almost universally provide preliminary positive results within 24 hours in patients with IA and should be promptly obtained. Nasal swabs of each nostril should be collected from asymptomatic patients with a credible exposure history, for epidemiological investigation only; polymerase chain reaction (PCR) can identify spores after as little as 30 minutes of incubation. Positive nasal swabs confirm exposure, not infection with *B. anthracis*. Nasal swabs are not useful in symptomatic patients, as the spores are usually cleared from the nares by the time symptoms develop. A negative nasal swab for *B. anthracis* does not rule out anthrax. Sputum gram stains and culture are unlikely to be positive, since the bacteria are within the lymph nodes rather than the lung parenchyma. Ideally, blood cultures should be collected immediately prior to administering antibiotics, though cultures were positive in Sverdlovsk in patients who had received antibiotics for less than 21 hours, whereas greater than 24 hours of antibiotics rendered virtually all cultures negative.<sup>8</sup> Patients with IA are often too ill to undergo bronchoscopy, and in the absence of a compelling reason to consider another diagnosis that can be more reliably made in this manner (eg, *Pneumocystis carinii* pneumonia), blood culture is preferable. Serology is generally useful only for making a retrospective diagnosis.

## QUESTION 5

Antibiotic therapy needs to be initiated. Which of the following is the best choice for initial treatment of suspected inhalational anthrax infection?

- a. intravenous ciprofloxacin
- b. intravenous doxycycline
- c. intravenous ceftriaxone
- d. intravenous ciprofloxacin or doxycycline, and ampicillin
- e. oral ciprofloxacin and doxycycline

**ANSWER:** The correct answer is d. Patients with suspected IA should be admitted to a hospital and started on multiple intravenous antibiotics — any single agent is considered inadequate.<sup>8,9</sup> The CDC recommends ciprofloxacin or doxycycline plus 1-2 other IV antibiotics.<sup>10</sup> Clindamycin may be a particularly valuable component of the treatment regimen since it has been shown to inhibit toxin production in static culture.<sup>8</sup> Some authorities recommend combination therapy with penicillin or chloramphenicol for anthrax meningitis, due to uncertain CNS penetration of ciprofloxacin and doxycycline. Other antibiotics with *in vitro* efficacy include macrolides, aminoglycosides, vancomycin, and other quinolones in addition to ciprofloxacin. Cephalosporins, often used to treat CAP, are ineffective against anthrax, because *B. anthracis* produces a cephalosporinase.

## QUESTION 6

You receive a call from a concerned colleague of Mr. Brown's at the station. She would like to know whether they should take any precautions at the studio. What public health measures should be taken when a case of anthrax is suspected?

- a. Notify public health authorities.
- b. Quarantine infected individuals.
- c. Wash clothing and body surfaces with 5% bleach solutions.
- d. Use high-speed fans to clear spores out of an area of suspected infection.

**ANSWER:** The correct answer is a. Rapid notification of public health and/or law enforcement agencies upon diagnosing a case of anthrax is vital. Further, the laboratory should be notified when suspected cases of anthrax are encountered so that *Bacillus* species can be properly identified on culture results (except in bioterrorism circumstances, many laboratories do not routinely speciate *Bacillus* since it is usually a contaminant) and to ensure that laboratories institute proper safety precautions. It is also important to immediately isolate potential sources or locations of anthrax spores, including clothing or other items that might have been exposed. Hand washing followed by showering with soap and water is advised for anyone coming in direct physical contact with a substance alleged to contain *B. anthracis* spores.<sup>9</sup> There is no evidence that bleach has added efficacy, and its use is not felt to be necessary. Moreover, there is no evidence of person-to-person transmission of anthrax, so that quarantine is not necessary. Standard barrier isolation precautions are recommended for hospitalized patients. The greatest risk to human health occurs following initial aerosolization of anthrax spores, which is known as primary aerosolization. The risk of clinical disease with secondary aerosolization from movement of spores after their initial settling is uncertain, but the use of fans or other devices that would further disperse spores is not advisable.

## QUESTION 7

How should the medical community respond in order to manage the public's emotional and behavioral response to this bioterrorist event?

- a. Proactively reassure the public that there is no cause for alarm and to go about life as usual, because anthrax is not contagious.
- b. Appear authoritative and offer definitive opinions, because people need to feel that the situation is being handled.
- c. Set realistic expectations and update the media frequently using layman's terms to explain the emerging science.
- d. Avoid talking to the media.

**ANSWER:** The correct answer is c. The media is the public's primary source of information and recommendations in the event of a natural disaster or terrorist event. Medical professionals are in the unique and critical position of providing credible, understandable information to government leadership and media sources to ensure the most effective public response.



## QUESTION 8

In the wake of a bioterrorism event, emergency departments may see considerable numbers of patients with somatic complaints who believe they have been infected. Guidelines for appropriate evaluation and management would include which of the following?

- a. Any patient thought to have minimal risk of exposure should be referred to a mental health provider.
- b. Patients described as “the worried well” will be reassured once they understand that they couldn’t possibly have been exposed.
- c. Every patient should be seen by a mental health provider first so as to minimize unnecessary physical exams and laboratory tests.
- d. Every patient needs a history, focused physical exam and medical work-up.

**ANSWER:** The correct answer is d. Every patient must be evaluated according to a medical protocol appropriate to the scenario. The most important element of psychological first aid is good medical care.

## QUESTION 9

A constellation of unresolved physical symptoms following a life-threatening event may be understood as which of the following?

- a. The clinical syndrome known as post inhalation anthrax deconditioning.
- b. Medically Unexplained Physical Symptoms (MUPS) described in patients following traumatic and terrorist experiences.
- c. Malingering to avoid work and receive compensation.
- d. A hysterical reaction to a near-death experience.

**ANSWER:** The correct answer is b. Medically Unexplained Physical Symptoms (MUPS) is a syndrome presentation that has been described following a variety of traumatic experiences including terrorism and war.

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## SUGGESTED READING

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