Staphylococcal Enterotoxin B

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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.

Note: These self-assessment questions are not intended for CME credit. To apply for CME credit, you must complete the CME Test at the back of this booklet and submit it according to the directions provided.

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.

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INTENDED AUDIENCE

Internal medicine, family medicine, and emergency medicine physicians, and other clinicians who will provide evaluation and care in the aftermath of a terrorist attack or other public health disaster

LEARNING OBJECTIVES

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

- Discuss the initial presentation of acute gastrointestinal illness due to Staphylococcal enterotoxin B (SEB), and contrast this with other common agents that occur naturally or that may be the result of intentional poisoning.
- Describe the natural and intentional sources of transmission and spread of SEB and other common biologic agents.
- List treatment options for patients with SEB.
- Summarize information that patients need to know about toxin-mediated illness.

CASE PRESENTATION

You receive a phone call that one of your patients, a 45-year-old male, has presented to the Emergency Department (ED) late in the morning with complaints of recurring episodes of vomiting over the past 3 hours. You are informed by the ED attending that your patient's symptoms began with a sudden onset of intense nausea, some abdominal cramping, followed quickly by repeated emesis. You are told that your patient believes he has vomited 10 times in the past 3 hours and cannot tolerate anything by mouth. He reports having had 1 loose bowel movement. He denies witnessing blood in his emesis or stool, and there has been no coffee ground emesis. There is no history of fever. He was well upon waking this morning and until the onset of symptoms. He has been attending a local political convention for the past 3 days. Shortly after his arrival in the ED, 3 fellow convention attendees present with similar symptoms.

QUESTION 1

At this time, likely etiologies of your patient's symptoms could include:

a. Ingestion of Staphylococcal enterotoxin B (SEB), or *Bacillus cereus*
b. Ingestion of *Bacillus anthracis*, or *Clostridium botulinum toxin*
c. Fish or shellfish poisoning

Reminder: You can find the Answer Key & Discussion on page 9.

COMMENT: Acute gastrointestinal illness due to ingestion of contaminated food is a very common problem, with estimates as high as 81,000,000 cases annually.[1] **The diagnosis of foodborne disease should be considered when acute illness with gastrointestinal or neurologic symptoms affects 2 or more people who have shared a meal within the past 72 hours.**[2] While such illness is commonly acquired naturally, intentional contamination of food and water supplies as a weapon of bioterrorism is an increasing area of concern. Many of the common bacterial agents that cause acute gastrointestinal disease are listed by the Centers for Disease Control and Prevention (CDC) as Category B biologic agents for bioterrorism.[3] These Category B agents include: Staphylococcal enterotoxin B (SEB), *Salmonella* species, *Shigella* dysenteriae, *Escherichia coli* O157:H7, *Vibrio cholerae*, and *Cryptosporidium parvum*. Furthermore, two Category A agents may also cause acute gastrointestinal illness if ingested: *Bacillus anthracis* (anthrax), and *Clostridium botulinum* toxin (botulism). Because use of such agents is likely to be covert, people affected will be unaware of their exposure and will first come to attention when they seek medical care.[3] Thus, familiarity with the basic presenting clinical features is essential for early recognition, diagnosis, and treatment of infection with these agents.

The initial presentation of your patient with an acute vomiting syndrome should raise the suspicion of acute foodborne disease, particularly in light of 3 fellow convention attendees presenting with similar symptoms. In the initial approach to such patients, key historical information would include the symptom complex and trying to identify the incubation period of the illness (see Table 1). Illness due to the ingestion of preformed bacterial toxin will have the shortest incubation period, often on the order of a few hours. The most common bacterial agents to cause such illness are *Staphylococcus aureus* and *Bacillus cereus*. Both are likely to present with symptoms of nausea, repeated episodes of vomiting, and abdominal cramps within 1-6 hours of ingesting contaminated food. Diarrhea may be present. *S. aureus* may elaborate five distinct heat-stable toxins (A, B, C, D, and E), and the clinical manifestations of illness are similar.[2] SEB has relevance as a bioterrorism agent as it has already been isolated and produced.[6] **Fever is an uncommon manifestation of gastrointestinal illness with *S. aureus*.**

CDC CLASSIFICATION OF BIOTERRORISM AGENTS

Category A Agents

- Can be easily disseminated or transmitted person-to-person
- Cause high mortality with a potential large public health impact
- Might cause panic and social disruption
- Require special attention for public health preparedness

Category B Agents

- Moderately easy to disseminate
- Cause moderate morbidity and low mortality
- Require enhancements to CDC's diagnostic and surveillance abilities

Table 1. Category A and B Bioterrorism Agents* Capable of Causing Acute Gastrointestinal Illness

Agent [CDC Category]		Incubation Period, Range	Clinical Manifestations
Staphylococcus aureus	[B]	1-6 hours	Vomiting, nausea, crampy abdominal pain, diarrhea, fever (~25%)
Bacillus cereus	[B]	1-16 hours	Vomiting, crampy abdominal pain, diarrhea (~33%) Emetic syndrome: nausea, vomiting, 1-6 hours Diarrheal syndrome: abdominal cramping and diarrhea, 8-16 hours
Clostridium Botulinum	[A]	18-36 hours†	Vomiting and nausea (~50%), diarrhea (~25%), descending paralysis
Bacillus anthracis (anthrax)	[A]	3-7 days†	Gastrointestinal disease: Initial: vomiting, nausea, abdominal pain, fever Later: severe abdominal pain, bloody diarrhea, toxemia, and intestinal perforation Oropharyngeal disease: neck swelling, lymphadenitis
Salmonella species	[B]	16-72 hours†	Diarrhea, crampy abdominal pain, nausea, vomiting, fever, headache, rarely bloody diarrhea
Shigella dysenteriae	[B]	16-72 hours†	Crampy abdominal pain, fever, diarrhea, bloody diarrhea, headache, nausea, vomiting
Escherichia coli O157:H7	[B]	72-120 hours†	Crampy abdominal pain, bloody diarrhea, fever (rare unless complicated by hemolytic-uremic syndrome), thrombotic thrombocytopenic purpura (developing 5-10 days after diarrhea) †
Vibrio cholerae	[B]	16-72 hours†	Profound watery diarrhea, dehydration, fever (rare)‡
Cryptosporidium parvum	[B]	5-28 days§	Diarrhea, may also have low grade fever, malaise, nausea, vomiting‖

* As defined by the Centers for Disease Control and Prevention[3]
† Data from Tauxe, Swerdlow, and Hughes.[2]
‡ Data from Seas and Gotuzzo.[4]
§ Mean incubation period is 7-10 days
‖ Data from Unger.[5]

Bacillus cereus produces a toxin that may lead to a short-incubation syndrome or emetic syndrome with an incubation period of 1-6 hours, nausea, abdominal cramps, vomiting, and less commonly diarrhea. *B. cereus* may also produce a diarrheal syndrome characterized by a longer incubation period of 8-16 hours, diarrhea and abdominal cramps. Vomiting is uncommon with the diarrheal syndrome, and fever is uncommon with both the emetic and diarrheal syndomes.[2]

Clostridium botulinum (botulism) also produces illness through a preformed toxin. Initial manifestations may include nausea and vomiting in up to 50% of affected people.[2] However, the incubation period may be longer, up to 18-36 hours. It is also characterized by the onset of a descending paralysis, typically causing bulbar palsies before descending to involve the extremities and respiratory musculature.[7]

Ingestion of *Bacillus anthracis* (anthrax) leads to nausea, vomiting, abdominal pain, and fever approximately 1-7 days after ingestion.[7] Symptoms rapidly worsen to include bloody diarrhea, severe abdominal pain with peritoneal signs, and occasionally hematemesis. Ascites may develop, as may bacteremia, gastrointestinal hemorrhage, or intestinal perforation.[7] Ingestion may also cause an oropharyngeal disease with neck swelling, lymphadenitis, and pharyngeal ulcers with a pseudomembrane.[7]

The other Category B agents listed by the CDC[3] will also cause an acute gastrointestinal illness. However, as summarized in Table 1, they tend to have a longer incubation period and often have diarrhea and fever as prominent clinical manifestations. Shigella and *E. coli* O157:H7 are common causes of bloody diarrhea.

Briefly, ingestion of heavy metals (copper, zinc, tin, and cadmium) may cause nausea, vomiting, and abdominal cramps within one hour of ingestion.[2] The presence of paresthesias along with abdominal symptoms should prompt consideration of various types of fish or shellfish poisoning, or ingestion of monosodium glutamate or niacin.

Approximately 4 hours before presenting to the ED, your patient had breakfast at a special interest group meeting involving several hundred delegates. The food was served in a buffet. He recalled having eggs, bacon, coffee, milk, and a small cream-filled pastry. His symptoms began approximately 2 hours after eating. The 3 other patients reported they had also been present at the morning meetings and had eaten similar foods, including eggs, bacon, sausage, cereal, milk, coffee, pastries, and a series of cold cut meats.

On examination, the patient's vital signs included: Blood Pressure: 115/65, with no orthostatic changes; Pulse 90 and regular; Respirations 14; Temperature 37.2°C. He is in mild distress, holding his abdomen, and vomits once during the examination. His abdomen is soft, non-tender, and there are diffusely increased bowel sounds.

QUESTION 2

Foods commonly associated with the "natural" transmission of SEB include all of the following except:

a. Fried rice

b. Cream-filled pastries

c. Ham

d. Poultry

e. Potato salads

COMMENT: The additional history, as well as the corroboration with others who are ill, suggest a causative organism with a short incubation period — likely *S. aureus* or *B. cereus*. Staphylococcal food poisoning has been associated with foods with a high salt or sugar content[7] such as ham, pork, canned beef, egg and potato salads, and cream-filled pastries.[2] In some cases, a food handler with a purulent skin infection can be identified as the source, but this is often not the case.[2] *B. cereus* is classically associated with fried rice, where the rice has been cooked and then held warm for a prolonged time.[2] The most commonly associated foods with transmission of the other Category A and B agents are listed in Table 2.

Table 2. Foods Commonly Associated with Natural Transmission of CDC Category A and B Bioterrorism Agents*

Agent [CDC category]		Common food sources
Bacillus anthracis (anthrax)	[A]	Contaminated beef
Clostridium Botulinum	[A]	Improperly home-canned vegetables, fruit, fish; honey (infant botulism)
Salmonella species	[B]	Beef, poultry, eggs, dairy, produce
Shigella dysenteriae	[B]	Milk, salads (egg, potato, tuna, turkey), lettuce
Staphylococcus aureus	[B]	Ham, Pork, Canned Beef, Egg and Potato salads, cream filled pastries
Escherichia coli O157:H7	[B]	Salads, beef
Vibrio cholerae	[B]	Contaminated water, shellfish
Cryptosporidium parvum	[B]	Contaminated water

*Data from Tauxe, Swerdlow, and Hughes,[2] Centers for Disease Control and Prevention,[3] and Hamer and Gorbach.[7]

QUESTION 3

SEB may be chosen as an agent of bioterrorism because:

a. It can be an effective lethal agent.

b. It can be an effective incapacitating agent.

c. It is spread effectively from person to person.

d. It has a prolonged incubation period.

COMMENT: The use of any of these bacterial agents as a bioterrorism weapon may nullify these "classic" associations with specific food groups. Specifically, if the agents are to be deliberately used, they could be disseminated onto the most readily available food products. Thus, distribution of the agent on food served to large numbers of people (meetings, troop meals, grocery stores) would have the greatest impact.[8] Although such deliberate use of these agents seems difficult to consider, recent history points to their successful use. In 1984, 751 people in The Dalles, Oregon became ill following ingestion of Salmonella species deliberately placed on food supplies at local restaurants by a local religious faction hoping to influence election results.[9] There was also a case reported in 1997, in which 12 laboratory employees became ill after ingesting food contaminated with Shigella species; the investigation failed to identify a responsible party.[10]

The patient's laboratory report demonstrated the following: normal complete blood count. Chemistries: Na 143, K 3.5, Cl 100, CO2 27, BUN 15, Creatinine 1.2, Glucose 104 mg/dL. Stool negative for occult blood, no fecal leukocytes.

QUESTION 4

In patients whose illness is due to ingestion of SEB, what is the most likely acid-base disturbance to develop?

a. Metabolic acidosis

b. Metabolic alkalosis

c. Respiratory acidosis

d. Respiratory alkalosis

COMMENT: Because vomiting tends to be the most common and recurrent symptom, patients may develop a metabolic alkalosis.[7] In severe cases, volume depletion and prostration may occur[7] and may result in hemoconcentration and elevation in the BUN.

The diagnostic approach to patients with acute gastrointestinal illness, particularly when it appears to be associated with an outbreak, is aimed at attempting to isolate the causative organism. In the case of SEB, the diagnosis is made primarily on clinical and epidemiological grounds, as it is difficult to test for the toxin.[11] The diagnosis might also be confirmed by isolating *S. aureus* from the vomitus or feces of ill people and matching it to a sufficient amount of organism isolated from contaminated food or food handler's lesion.[2]

In general, the specimens to collect for laboratory analysis would include feces, vomitus, serum, and blood.[2] Cultures and samples of the food, the food preparation areas, and food handlers might also be warranted. Finally, it is important to notify and work with the laboratory so that any special collection or laboratory techniques that may not be readily known by practitioners can be used to identify all possible organisms.[2]

The patient was hydrated with intravenous normal saline and reported feeling better. He was discharged home with instructions to return if he developed a fever, bloody diarrhea, or was unable to tolerate oral intake. Subsequent investigation recovered *S. aureus* from the breakfast buffets used at all of the interest group meetings. Contaminated foods included the eggs, breakfast meats, and pastries. In all, 850 people became ill, and all voting at the convention had to be postponed. Although no arrests were made, authorities received a message from a terrorist cell within the US claiming responsibility and warning that this successful act was just the first of many planned attempts to poison the US food supply.

QUESTION 5

Reasonable treatment options for patients suspected of having illness due to ingestion of SEB would include all of the following <u>except</u>:

a. Hydration

b. Anti-emetics

c. Anti-diarrheal

d. Dicloxacillin

COMMENT: Patients frequently request antibiotics because they do not know that antibiotics are not an effective treatment for toxin-related illnesses, such as SEB. Patients should be educated about toxin-related illnesses and the appropriate treatment options. See page 11 of this case booklet for an example of a patient education handout on ingestion of toxins. *You may detach this page and freely photocopy it for your patients.*

It is important to note that SEB has been isolated and produced as a powder, making it possible to disseminate the agent via aerosol. Thus, it has the potential to infect many more people, even miles from the delivery point, depending on prevailing winds.[8] The incubation period following inhalation of SEB is 3-12 hours.[8] Initial symptoms include severe headache, chills, myaligias, non-productive cough, and a high fever up to 41.1° Celsius (106° Fahrenheit).[8] While fever is not a common symptom of gastrointestinal SEB, it is typical of inhalational SEB. Dyspnea and chest pain may be present. Although diarrhea is unusual following inhalation, it may develop if patients were to swallow, as well as inhale, the agent.[8] The fever may last up to one week, and the cough up to one month.[8]

Physical exam findings may be nonspecific, including high fever and crackles on lung exam, and the chest x-ray is often normal except in severe cases where there may be increased interstitial markings, pulmonary edema, or adult respiratory distress syndrome.[6,8] The differential diagnosis of inhaled SEB would include flu-like illnesses, but there would likely be far more people presenting for evaluation following SEB inhalation than for a naturally occurring epidemic.[8] SEB differs from anthrax or pneumonic plague in that it does not rapidly progress to death, and differs from tularemia and plague due to lack of infiltrates on chest x-ray.[8]

Treatment of inhaled SEB is supportive, including oxygenation, fluid replacement, and ventilator support, if necessary.[6] Antibiotics are not indicated. Recovery is the rule, although patients may be incapacitated for days or weeks.[8]

CASE SUMMARY

A microorganism that could be effective as a bioterrorism weapon should be:

- Able to cause illness in most who are exposed to the agent.
- Easily disseminated.
- Capable of causing infection despite different environmental exposures (eg, being distributed on a variety of foods).
- Available for production in sufficient quantity.[11]

The goal of a bioterrorist is to cause fear, uncertainty, a sense of vulnerability, and lack of control. These goals may be met by using agents that kill. However, the goals may also be accomplished by incapacitating large numbers of people, and this may, at times, be more effective than a lethal agent. Microorganism agents are likely to be used in a covert manner, so that the initial presentation of the attack will be patients who are ill, and presenting to their physicians or other health care providers.[3] For example, many of the Category B agents listed by the CDC[3] are capable of causing acute gastrointestinal illness, and some have already been used in a limited way.[9,10]

SEB meets many of the criteria for use as a bioterrorism weapon. Its primary use would be as an incapacitating agent, rather than a lethal agent.[6] The toxin has been isolated and produced, and the toxin is heat-stable. It has a high attack rate — most who are exposed through ingestion will become clinically ill.[7] The presenting symptoms following ingestion are non-specific and include nausea, repeated emesis, abdominal cramps, followed by onset of diarrhea. Fever is an uncommon manifestation of gastrointestinal illness from SEB. The short incubation period from exposure to onset of symptoms is characteristic of ingesting a preformed toxin, but such a history may not be immediately evident. While specific foods have been associated with SEB and other agents,[2,7] if used as a bioterrorism agent, such associations may not be valid. Laboratory studies that may help distinguish SEB from other agents would include the presence of fecal leukocytes and bloody stools in patients with invasive organisms. Although the toxin is difficult to test for, bodily fluids (vomitus, stool, blood, serum) should be collected to test for a causative organism, and samples from suspected food should also be collected. Antibiotics have a limited role in treating acute gastrointestinal illness, and have no role in the treatment of SEB. Supportive care and hydration therapy are indicated for SEB.

While it may seem a remote possibility that biologic agents will be used intentionally to contaminate food or water supplies, health care providers must remain vigilant to this possibility. Early identification of a potential outbreak may help speed the identification of the causative organism, improve intervention, and limit the psychological

impact (eg, fear, sense of vulnerability) of such an event. **Therefore, it is imperative that health care providers contact their local health departments if a toxin-related illness, such as SEB, is suspected.**

ANSWER KEY & DISCUSSION

QUESTION 1

At this time, likely etiologies of your patient's symptoms could include:

a. Ingestion of Staphylococcal enterotoxin B (SEB), or *Bacillus cereus*
b. Ingestion of *Bacillus anthracis*, or *Clostridium botulinum* toxin
c. Fish or shellfish poisoning

ANSWER: The correct answer is a. Ingestion of preformed toxin such as Staphylococcal enterotoxin B (SEB) or *Bacillus cereus* leads to the abrupt onset of nausea, vomiting, and abdominal symptoms. *Bacillus anthracis* and *Clostridium botulinum* toxin also have abdominal symptoms, but they are associated with longer incubation periods and are associated with bloody diarrhea in the former and descending paralysis in the latter. While fish or shellfish poisoning is possible, the lack of paresthesias makes this less likely at this point.

QUESTION 2

Foods commonly associated with the "natural" transmission of SEB include all of the following except:

a. Fried rice
b. Cream-filled pastries
c. Ham
d. Poultry
e. Potato salads

ANSWER: The correct answer is a. *Bacillus cereus* is classically associated with ingestion of fried rice, where the rice has been cooked and then held warm for a prolonged time.[2] All of the other listed foods are associated with transmission of SEB; cream-filled pastries and potato salads are commonly thought of foods associated with SEB.

QUESTION 3

SEB may be chosen as an agent of bioterrorism because:

a. It can be an effective lethal agent.
b. It can be an effective incapacitating agent.
c. It is spread effectively from person to person.
d. It has a prolonged incubation period.

ANSWER: The correct answer is b. SEB has a high attack rate — most who are exposed through ingestion will become clinically ill[5] and incapacitated. SEB is not generally a lethal agent nor is it effectively transmitted from person to person, and it has a short incubation period of 1-6 hours.

QUESTION 4

In patients whose illness is due to ingestion of SEB, what is the most likely acid-base disturbance to develop?

a. **Metabolic acidosis**

b. **Metabolic alkalosis**

c. **Respiratory acidosis**

d. **Respiratory alkalosis**

ANSWER: The correct answer is b. There are no specific laboratory findings associated with gastrointestinal illness due to SEB. Because vomiting tends to be the most common and recurrent symptom, patients may develop a metabolic alkalosis.[5] In severe cases, volume depletion and prostration may occur[5] and one may see laboratory evidence such as hemoconcentration, and elevation in the BUN.

QUESTION 5

Reasonable treatment options for patients suspected of having illness due to ingestion of SEB would include all of the following except:

a. **Hydration**

b. **Anti-emetics**

c. **Anti-diarrheal**

d. **Dicloxacillin**

ANSWER: The correct answer is d. Antibiotics are not indicated in the treatment of SEB or *B. cereus*. Antibiotics are lifesaving in the treatment of salmonellosis and typhoid fever, but should not be used in nontyphoidal salmonella infections.[2] Treatment of many cases of food or water borne illness is focused on supportive measures, including hydration and anti-emetics. While anti-diarrheal agents may be used for some patients, they are to be avoided in patients with high fever, bloody stools, or fecal leucocytes (signifying invasive infection).[2]

PATIENT EDUCATION

Your acute illness of vomiting, nausea, and diarrhea is likely due to a chemical (a toxin) naturally produced by bacteria in the food that you ate.

For most people, the illness will last about 12 hours. You should drink liquids and eat what you can tolerate without vomiting. Although your illness is most likely caused by a bacterial toxin, antibiotics will not help the problem. Your body will be able to clear the toxin in a matter of hours.

You should contact your doctor or seek medical attention if any of the following occur:

1. High fever (greater than 101.5°F)
2. Dizziness when standing (this may mean you haven't been able to drink enough fluids).
3. You cannot eat or drink anything for more than 12-24 hours.
4. There is blood in your stool or bloody diarrhea.

As a general rule, good hand washing, especially after using the restroom, will help prevent the spread of gastrointestinal illness to other people.

Patient education material developed by Paul A. Hemmer, MD, MPH, Lt Col, USAF, MC, Associate Professor of Medicine, Uniformed Services University of the Health Sciences, Bethesda, Maryland.

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SUGGESTED READING

1. Blazes DL, Lawler JV, Lazarus AA. When biotoxins are tools of terror. *Postgrad Med.* 2002;112:89-95.

2. Moran GJ. Threats in bioterrorism II: CDC category B and C agents. *Emerg Med Clin North Am.* 2002;20:311-330.