Chapter Four

BACTERIAL DISEASES (OTHER THAN MYCOPLASMA)

TYPHOID FEVER

Introduction

Typhoid fever is a life-threatening illness caused by the bacterium *Salmonella typhi*. The infection is common throughout the world except in the United States, Canada, Australia, Japan, and Western Europe. There are about 400 cases per year in the United States. *S. typhi* colonizes only humans, so spread of the disease requires close contact with an infected individual, either somebody with an active infection or a chronic carrier. The infection is transmitted via the fecal-oral route, and the most common method by which infection is acquired is through consumption of contaminated food and water. Infected individuals have the bacteria in the blood and digestive tract. A small percentage of individuals recover from the acute infection but become carriers and continue to shed the bacteria and therefore remain infectious. The classical case is that of “Typhoid Mary” Mallon who infected many individuals for whom she prepared food as a professional cook.

What Infected Patients Experience

The incubation period for typhoid fever depends on the amount of organism ingested and the immune status of the patient, with a range from a few days to one or two months. Then the patient experiences the insidious onset of a sustained fever with temperatures up to 103°F–104°F accompanied by headache, malaise, anorexia, relative bradycardia (out of proportion to what would be expected with high fever), chills, constipation or diarrhea, and a nonproductive cough (Keusch, 1991; Centers for Disease Control and Prevention, 1990). With rapid treatment, patients usually feel better within a few days.

The spectrum of illness ranges from a brief illness to an acute severe infection with central nervous system involvement and circulatory collapse. With severe
infections, patient may have altered mental status, hepatitis, meningitis (Abuekteish et al., 1996), myocarditis (du Plessis et al., 1997; Hewage et al., 1994), pneumonia, arthritis (Fule and Chidgupkar, 1994), chorioamnionitis (Hedriana et al., 1995), and hemorrhage or perforation (Keusch, 1991). Untreated, up to 20 percent of patients may die from the above or other complications. About 3–5 percent of patients become long-term carriers if they remain untreated. Many of these individuals never realize they were infected.

Diagnosis

A probable diagnosis can be made when a patient has a clinically compatible illness associated with a confirmed outbreak. Confirmed diagnoses require isolation of *S. typhi* from blood, stool, or another clinical specimen (Centers for Disease Control and Prevention, 1990).

Prevention

The main preventative measures for typhoid fever include avoiding potentially infectious foods and drinks and vaccination against infection. Individuals who travel to areas where typhoid is common should be vaccinated. Both oral and injectable vaccines are available (Hone et al., 1994; Klugman et al., 1996; Kollaritsch et al., 1997; Levine et al., 1996). Even those vaccinated against typhoid fever should be careful about what they eat, since the vaccine is not 100 percent effective.

Correlation with Gulf War Illnesses

Serologic markers exist to identify patients infected, either at present or in the past, with *S. typhi*. Investigation of Gulf War veterans has not detected increased antibody levels to this organism. Furthermore, in most patients this disease is either self-limited or results in severe symptoms that would precipitate immediate treatment.

Summary

Typhoid fever is caused by the bacteria *S. typhi*. This bacteria is found in most parts of the world, although it is not common in the United States, except in individuals returning from international destinations where infection is more common. Because this disease is easily diagnosed and generally lasts only a

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relatively short period of time, particularly with treatment, it is not a likely cause of unexplained Gulf War illnesses.

**MYCOBACTERIA TUBERCULOSIS**

**Introduction**

*Mycobacterium tuberculosis* is the primary bacterium responsible for causing the disease commonly known as tuberculosis (TB). The disease is present worldwide and is responsible for considerable morbidity and mortality. Tuberculosis usually exists in the form of a lung infection; however, the organism may cause disease in any organ or tissue throughout the body. The tubercule bacillus responsible for the disease is usually transmitted by the infected individual through coughing or sneezing. Although a single casual contact may transmit disease, most infections result from sustained exposures.

**Epidemiologic Information**

*Tuberculosis* has remained endemic in developing countries; however, it has reemerged as a major threat to both developing and industrialized countries over the last decade (Porter and Adams, 1994). Around the world, there are almost nine million new cases annually with more than 7,000 deaths per day attributable to TB (Rattan et al., 1998). The emergence of HIV and AIDS as a global disease has further aggravated the issue because tuberculosis flourishes in immunosuppressed patients (Daley, 1997; Co, 1994).

**What Infected Patients Experience**

Clinical signs and symptoms of tuberculosis vary considerably, ranging from a silent disease to severe systemic infection. For most individuals who contract the infection, the disease process is almost always silent, being detected only through familiar TB skin tests or x-ray findings. Occasionally, individuals with a primary TB infection may have a low-grade fever and mild anorexia. TB may remain dormant for years or even for a lifetime (Parrish et al., 1998).

Secondary tuberculosis—the phase of the disease that arises in a previously exposed individual—may also be asymptomatic although more commonly it is accompanied by insidious onset of fever, night sweats, weakness, fatigability, anorexia, and weight loss. Usually, secondary tuberculosis represents reactivation of a dormant primary infection, although exposure from exogenous sources may also occur. When the infection invades and destroys the bronchi, patients develop a productive cough, often with blood-tinged sputum and oc-
casionally frank hemoptysis. When the disease disseminates, patients may experience differing symptoms and a fever without a clear origin.

**Diagnosis**

A definitive diagnosis of tuberculosis requires the identification of the tubercule bacillus. However, most individuals have been tested for *tuberculosis* using common TB skin tests (e.g., purified protein derivative, PPD) where the patient develops an infiltration (swelling) around the sight of antigen injection within 24 hours. A negative skin test, however, does not exclude the possibility of infection and patients with a past history of exposure to TB may have a positive test without an active infection. Detecting the bacillus by sputum or other culture is not always simple.

**Treatment and Prevention**

Preventing TB requires prompt identification and treatment of infected patients. Family members and close contacts of those found to be infected should be tested and also treated if they are shown to be positive, even if the infection is an asymptomatic primary one. A major risk factor for spread of TB is crowded living conditions and a depressed socioeconomic status.

**Correlation with Gulf War Illnesses**

The spectrum of disease caused by tuberculosis has been well known for centuries. The disease is recognized throughout the world, including in the Persian Gulf. It would be almost impossible to not identify some Gulf War veterans with tuberculosis given the prevalence of the disease in the population. However, the mechanism of spread, the ability to detect the infection in most individuals through simple, routinely used skin tests, and the epidemiology of the disease all suggest that tuberculosis is not the cause of undiagnosed Gulf War illnesses.

**Summary**

Tuberculosis is a common pulmonary infection commonly caused by repeated close contact with infected individuals. Primary infection is usually asymptomatic. However, disease reactivation occurs and the seriousness of infection is much greater in individuals with impaired immune systems (e.g., patients with HIV and those undergoing immunosuppressive treatments). Although some Gulf War veterans will undoubtedly be found to have tuberculosis, tuberculosis does not appear to be the etiology for the many individuals with undiagnosed Gulf War illnesses.
ENTERIC AGENTS: ENTEROTOXIGENIC *E. coli*, *CAMPYLOBACTER*, *SHIGELLA*, AND OTHER *SALMONELLA*

Introduction

Infectious diarrhea continues to be a major source of international disease and death (Murray and Lopez, 1996). Although many of these infections are self-limited, some are more problematic, causing disability and even death (Frost et al., 1998). There were a number of outbreaks of diarrhea during Operation Desert Shield (Hyams et al., 1991). Such outbreaks can be particularly disabling during periods of deployment because of both the disability they inflict on the individual and the potential for spread to other individuals.

Epidemiologic Information

Hyams and colleagues collected data from U.S. troops stationed in northeastern Saudi Arabia between September and December 1990. They cultured stool from 432 individuals presenting with diarrhea, cramps, vomiting, or hematochezia. They also surveyed 2,022 soldiers in regions throughout Saudi Arabia. Researchers were able to identify a bacterial enteric pathogen in 49.5 percent of the troops with gastroenteritis. The most common bacteria were enterotoxigenic *Escherichia coli* and *Shigella sonnei*.

What Infected Patients Experience

Individuals may experience self-limited mild-to-moderate abdominal cramps with these infections, or disabling symptoms including diarrhea, cramps, vomiting, and hematochezia. Common organisms include enterotoxigenic *E. coli*, *Campylobacter*, *Shigella*, and other *Salmonella*. Each of these is slightly different.

*Enterotoxigenic E. coli* has an incubation period of from one to three days. Following incubation, the illness can be mild to fulminant. Most commonly patients experience mild, watery diarrhea with abdominal cramps. Vomiting is present in about half of infected individuals although it rarely is responsible for major disability. This organism is responsible for what is commonly recognized as traveler’s diarrhea. The disease resolves with or without treatment; however, in the most extreme cases, fluid replacement may be necessary.

*Campylobacter jejuni* is second only to *Giardia* in the frequency with which it causes waterborne diarrheal diseases in the United States. After an incubation period of from two to six days, patients develop fever, cramping, abdominal pain, and diarrhea that is at first watery but later contains blood and mucus.
The diarrhea is usually mild, but not always, and lasts for a few days without therapy. Sometimes the infection can persist and patients may develop a reactive arthritis that is most commonly associated with patients carrying the HLA-B27 antigen (Altekruse, 1999).

*Shigella* produces an acute infectious colitis that is commonly referred to as “bacillary dysentery.” The spectrum of disease is variable from mild watery diarrhea to the fatal dysentery that is more common in less-developed regions. The incubation period is from one to two days, following which some patients develop fever, some diarrhea, and some both. Patients with dysentery experience small-volume frequent stools (several per hour) consisting of blood, mucus, and pus, with abdominal cramps and tenesmus. Most patients recover over the period of up to a week, although with severe disease, they can suffer colonic perforation that can prove fatal. Very rarely patients may experience broader persistent systemic symptoms (e.g., hemolytic uremic syndrome, arthritis, seizures).

*Salmonella* are responsible for a number of diseases in humans. In addition to causing typhoid fever, infection can present as acute diarrhea or in more severe cases as septicemia, meningitis, reactive arthritis, osteomyelitis, and endocarditis. With respect to the gastroenteritis, the incubation period is generally from one to two days. Diarrhea (sometimes with the presence of blood) may be accompanied by nausea, vomiting, and abdominal cramps. Generally the illness is mild and self-limited, although immunosuppressed, elderly, and young patients are particularly at risk for more severe disease.

*Reactive arthritis* is a term used to describe joint pain and inflammation following exposure to bacterial infections, generally through either the gastrointestinal tract (most commonly following exposure to *Yersinia, Salmonella*, or *Campylobacter* species) or the genitourinary tract (most commonly associated with chlamydia infections) (Ebringer and Wilson, 2000). Many Gulf War Veterans reporting illness describe joint pain among their findings (Table 1.2).

Typical reactive arthritis patients give a history of infection within three weeks followed by arthritis in one or several joints. Some cases are accompanied by other, nonarthritic manifestations. Sometimes the diagnosis is problematic because of coexisting inflammatory processes and because in about one of four cases no infectious agent is identified (Nordstrom, 1996). Although sometimes infectious organisms may be found in the joints, laboratory findings are usually nonspecific (Beutler and Schumacher, 1997). The disease is usually self limited and resolves within six months (Nordstrom, 1996). Although some patients develop chronic arthritis, the incidence is believed to be fairly uncommon (Nordstrom, 1996; Burmester et al., 1995).
There is an extremely strong correlation between the risk of reactive arthritis and the presence of human leukocyte antigen B27 (HLA-B27) (Ebringer and Wilson, 2000; Beutler and Schumacher, 1997; al-Khonizy and Reveille, 1998; Braun and Sieper, 1996; Keat, 1999). The HLA-B27 antigen is present in approximately 8 percent of the general population (Ebringer and Wilson, 2000) with a range of 3 percent to 13 percent in the European population (Olivieri, 1998). The strength of the association between HLA-B27 can be expressed as the relative risk (of developing reactive arthritis) given the exposure (the HLA-B27 antigen). The relative risk for this association is 18, an extremely strong association.

**Diagnosis**

Diagnosis generally requires isolation of the organism from stool. Common laboratory techniques exist to distinguish known bacterial pathogens that infect the gastrointestinal tract.

**Treatment and Prevention**

Treatment depends on identifying the infecting organism and its antibiotic resistance pattern. In reality, most diseases are self-limited, particularly in healthy infected hosts. Once the bacterial resistance pattern is known, an appropriate antibiotic may be selected for those patients needing more aggressive therapy. For patients with severe diarrhea, fluid and electrolyte replacement may be indicated.

Because these are contagious, infectious diseases, prevention centers around isolation of infected individuals until the disease resolves. Furthermore, good hygiene contributes considerably to reducing the likelihood of infection.

**Correlation with Gulf War Illnesses**

Clearly, enteric infections occurred during the Gulf War (Hyams et al., 1991, 1995). This is not surprising given that these diseases are ubiquitous. The most common organisms identified were enterotoxigenic *E. coli* and *Shigella*. The particular strains were frequently resistant to commonly dispensed antibiotics. Although these infections occurred in the Gulf and were clearly a major problem during deployment (Hyams et al., 1991), findings were not unlike those experienced by civilians and therefore could not account for unexplained Gulf War illnesses. Some veterans likely suffer from chronic manifestations of reactive arthritis given the number of individuals who served in the Gulf and the frequency of predisposing genetic risk factors (i.e., HLA-B27). However, most patients who develop reactive arthritis achieve resolution within months.
Summary

Enteric pathogens are ubiquitous organisms known to cause diarrhea, abdominal pain, and fever. They were clearly present during service in the Persian Gulf and, in fact, accounted for a major portion of the infectious morbidity soldiers experienced during service. Most cases were mild. Except in rare cases, infections with these pathogens were self-limited. They are also easily diagnosed through common laboratory tests. Therefore, enteric pathogens could not account for the extended chronic symptoms experienced by those with unexplained Gulf War illnesses.

MENINGOCOCCUS

Introduction

*Neisseria meningitidis* is a gram-negative bacteria that normally populates the oropharynx (upper respiratory tract) but has the potential to cause a number of diseases, most importantly meningitis (for which it is named) and bacteremia in susceptible hosts. Healthy individuals may be carriers of the infection, and sporadic epidemiologic outbreaks continue to occur in both industrialized and developing countries.

Epidemiologic Information

Despite what has been learned about the biology and pathogenicity of *Neisseria meningitidis*, infection remains a major worldwide public health problem. The highest percentage of disease is in infants and children. In fact, *N. meningitidis* has become the leading cause of bacterial meningitis in this age group (Centers for Disease Control and Prevention, 1997a). The risk of death from disease depends on a number of factors, including the prevalence of disease, the type of infection, and the sociodemographic characteristics of the area where infection occurs (Apicella, 1995). In the United States, an 8–13 percent case-fatality rate has been reported (Centers for Disease Control and Prevention, 1997a; “Analysis of endemic meningococcal disease . . .,” 1976). In some underdeveloped countries, fatality can exceed 50 percent among septic patients (Apicella, 1995).

What Infected Patients Experience

The clinical manifestations of *N. meningitidis* infections are quite variable, ranging from a transient episode of fever to an overwhelming infection that results in death. Irrespective of the presentation, the nasopharyngeal infection that precipitates disseminated disease usually goes unrecognized or is mistaken
for a mild respiratory infection. Apicella (1995) reviews the four common clinical scenarios:

- **Bacteremia without sepsis**—The patient has a nonspecific upper respiratory infection or rash. Although the diagnosis may be made by blood culture, the disease often resolves before the diagnosis is made.

- **Meningococcemia without meningitis**—The individual shows signs of sepsis (elevated white cell count, skin rashes, malaise, weakness, headache, hypotension) but without meningeal signs.

- **Meningitis with or without meningococcemia**—These patients have headache, fever, and accompanying meningeal signs. Cerebrospinal fluid examination suggests infection.

- **Meningoencephalitis**—These individuals are septic, obtunded, with meningeal signs.

With active disease, the signs a patient expresses vary widely. Petechial rashes measuring from 1–2 mm may be present, particularly on the lower half of the body. These spots may coalesce to form what appear to be ecchymoses.

Cardiovascular involvement is also well recognized with this infection, with accompanying arrhythmias, congestive heart failure, decreased tissue perfusion, and pulmonary edema. The most devastating findings are septic shock and diffuse intravascular coagulation (DIC).

**Diagnosis**

Because the organism commonly colonizes the oropharynx, the mere isolation of *N. meningitidis* is insufficient to confirm an infection. In fact, many healthy individuals harbor this organism. Therefore, diagnosis depends on isolation of the bacteria from what is otherwise a sterile body environment (e.g., blood, cerebrospinal fluid (CSF), pleural fluid, pericardial fluid). Bacterial culture is the standard for diagnosis, although gram-negative diplococci can be seen with abundant infections on initial Gram’s stain. However, diagnosis is conventionally done by serologic measures through detection of antigens from body fluids (e.g., blood, joints, CSF). These tests (e.g., latex agglutination, counter-immunoelectrophoresis) offer accurate rapid diagnosis. These tests also enable demonstration of the specific serogroup responsible for infection. More recently, use of the polymerase chain reaction has emerged as an additional powerful diagnostic technique for meningococcal infection (Newcombe et al., 1996; Ni et al., 1992a, 1992b).
Treatment and Prevention

Particularly with the development of antibiotic resistant strains of *N. meningitidis*, efforts have been undertaken to develop vaccines using the bacterial antigens as targets for the vaccine (Oppenheim, 1997; Peltola, 1998; Saez Nieto and Vazquez, 1997; “Vaccines against meningococcal meningitis . . . ,” 1994; Al- Aldeen and Cartwright, 1996). In large populations, achieving a sufficient number of protected individuals creates what is known as “herd immunity” whereby the risk of epidemics is reduced because the number of individuals harboring the infection is low, and there are no clusters of infectious individuals. In the health care setting, it is important to avoid direct contact with potentially infectious individuals, particularly those with a respiratory infection, by adhering to droplet precautions (Bolyard et al., 1998).

Secondary prevention includes chemoprophylaxis in those with known exposures. Treatment for meningococcal disease has dramatically altered the course of epidemics. Penicillin, administered either intravenously or intramuscularly, remains the first-line treatment.

Correlation with Gulf War Illnesses

Richards and colleagues (1991) confirmed four cases of *N. meningitidis* infection during Operation Desert Storm. The clinical manifestations of this disease, other than the carrier state, are generally quite dramatic, and if a significant additional population of service personnel was infected, manifestations would have been apparent and readily diagnosed. The rate of infection among those serving in the Gulf War is consistent with the rate of infection for adults in the general population. Service members were vaccinated to provide immunity, likely contributing to the low rate of infection (Lashof et al., 1996).

Summary

*Neisseria meningitidis* is a common bacteria that has the potential to cause serious disseminated disease in both an endemic and an epidemic fashion. Diagnostic tests exist to detect infection, and four cases were identified during the Persian Gulf occupation. Although many more individuals who served in the Persian Gulf could be found to carry the infection in the “carrier state,” the mere presence of the bacteria does not imply disease. Given the dramatic clinical manifestations of disease (meningitis and sepsis), *N. meningitidis* could not account for the unexplained illnesses in Gulf War veterans.
BRUCELLA

Introduction

Brucellosis, also known as undulant fever, is a systemic bacterial infection that in humans results from contact with infected animals or ingestion of infected animal products, including milk. The disease was first recognized over a century ago during the Crimean War as causing “Mediterranean gastric remittent fever.” Four recognized species result in human disease, including *B. melitensis* (the usual animal hosts are sheep and goats), *B. abortus* (the usual animal hosts are cattle), *B. canis* (the usual animal hosts are dogs), and *B. suis* (the usual animal hosts are swine). The bacteria is a small, nonmotile, nonencapsulated, gram-negative coccobacillus. Brucellosis is an enteric fever that produces primarily systemic complaints often with associated gastrointestinal manifestations. Because of the way the bacterium is spread and its worldwide distribution, it has been responsible for considerable morbidity among humans and animals.

Epidemiologic Information

Brucellosis continues to be a major source of disease among humans and domestic animals. Incidence and prevalence vary from country to country, although bovine brucellosis, caused mainly by *B. abortus*, is still the most widespread infection. In humans, ovine/caprine brucellosis caused by *B. melitensis* is the most important clinically apparent disease, particularly in the Mediterranean, western Asia, and parts of Africa and Latin America (Corbell, 1997). For example, in the southern region of Saudi Arabia, a recent study found that 19 percent of the population had serologic evidence of exposure to Brucella antigen, and 2.3 percent of individuals had active disease (Alballa, 1995).

The reported incidence of brucellosis varies from less than 0.01 per 100,000 to over 200 per 100,000 population (Corbell, 1997). Incidence of infection is high in some areas, such as Kuwait and Saudi Arabia. Areas where rates appear low may reflect underreporting rather than actual low incidence of disease. Differences in various countries may also reflect food preparation customs, public health measures, including pasteurization of dairy products, and the extent of contact with potentially infected animals.

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What Infected Patients Experience

Symptom onset, generally starting about two to eight weeks following exposure, can be either acute or insidious, with equal likelihood. Patient symptoms are generally nonspecific and include fever, sweats, malaise, anorexia, headache, and back pain. These nonspecific findings can be misinterpreted as being a benign viral illness. Without treatment, patients experience an undulating febrile pattern, hence its common name “undulant fever.” Patients may have other complaints including depression and an unusual taste in the mouth. Reports of physical findings vary and are more elusive with about 10 percent experiencing lymphadenopathy, 20–30 percent having splenomegaly, and 10–60 percent with hepatomegaly (Young, 1995a, 1995b; Kaye, 1991).

Gastrointestinal symptoms are usually present but may or may not be severe even though brucellosis is an enteric infection. Usually the generalized findings predominate. Up to 60 percent of patients report joint problems (Young, 1995a), particularly the hips, knees, and ankles. Bone scans may show inflammation, although definitive radiological evidence of damage is a late finding. Neurologic manifestations of the disease include meningitis, encephalitis, peripheral neuropathy, and psychosis. Central nervous system involvement is less common. A small fraction (2 percent) of patients experience endocarditis although this is the most worrisome manifestation and can be fatal because of valvular destruction, if not recognized soon enough. Myocarditis and pericarditis can also occur. About a quarter of patients have some respiratory symptoms ranging from those commonly associated with nonspecific viral illness to bronchopneumonia, lung abscesses, and pleural effusions. Genitourinary findings are unusual but can occur.

A chronic form of brucellosis is recognized when a patient has ill health for a period of at least 12 months. These individuals have relapsing illness and most have persisting focal infection, such as in bone, spleen or liver (Young, 1995a).

Diagnosis

Because the clinical presentation is not specific, laboratory confirmation must be made to arrive at a definitive diagnosis. Routine laboratory tests (e.g., white cell count) generally do not suggest the presence of a bacterial infection. For patients with acute disease, blood (or tissue) culture remains the diagnostic standard (Corbell, 1997; Gad El-Rab and Kambal, 1998; Gaviria-Ruiz and Cardona-Castro, 1995). Because the presence of Brucella cannot be demonstrated through standard culture techniques, serologic tests can be used to establish a presumptive diagnosis (Gad El-Rab and Kambal, 1998; Barbuddhe et al., 1994; Barbuddhe and Yadava, 1997; Young, 1991).
Prevention

The key to elimination of brucellosis in humans is the eradication, or at least the control, of the disease in animals. The greater risk is the consumption of infected animal products, rather than the handling of animals (Cooper, 1992). Individuals working in higher risk venues, such as farmers, veterinarians, and other animal health professionals, should receive specific education on hygienic precautions to avoid infection and training to recognize the possibility that findings might be secondary to *Brucella*. A safe and effective human vaccine is not available at present and those that have been developed have been fraught with problems (Corbell, 1997).

Correlation with Gulf War Illnesses

Brucellosis is a bacterial infection with a worldwide distribution. Infection occurs by consuming or handling infected animals or animal products such as dairy products. The CDC reports a fairly high incidence of brucellosis in areas involved with Operation Desert Storm and Operation Desert Shield. However, brucellosis is a bacterial disease with a known cause that can be diagnosed by currently available techniques. Clearly, many of the nonspecific findings associated with brucellosis have similarities with undiagnosed Gulf War illnesses; however, because diagnostic tests exist for brucellosis and veterans have not shown evidence of infection, brucellosis is not likely to explain the undiagnosed illnesses in Gulf War veterans. Given the natural prevalence of brucellosis, some individuals may actually have a chronic infection unrelated to their service in the Gulf.

Summary

Brucellosis is a zoonotic bacterial disease that infects humans through contact with infected animals and animal products, particularly dairy products. The bacteria have a worldwide distribution, and some species are prominent in the Middle East. Patients may either present with an acute infection or experience a more insidious course. Infection usually manifests with a number of nondiagnostic findings, including GI, orthopedic, neurologic, cardiovascular, and pulmonary symptoms. Many of these findings have some similarity to reported symptoms in patients with undiagnosed Gulf War illnesses. However, brucellosis is diagnosable through culture, serologic (presumptive), and molecular methods. Investigation of ill individuals following Gulf War service has not revealed evidence of infection with this bacterium.
CHOLERA

Introduction

*Vibrio cholerae* is a gram-negative comma-shaped bacterium that has been known for many years to cause diarrheal illness secondary to intestinal infection. The infection is frequently mild or asymptomatic, but it can be severe. Approximately 5 percent of infected persons have severe disease (cholera) characterized by profuse watery diarrhea, vomiting, and leg cramps. In these individuals, rapid loss of body fluids leads to dehydration and shock; without aggressive treatment, death can occur within hours.

Epidemiologic Information

In the United States, cholera was common during the 1800s. The disease has been virtually eliminated by modern sewage and water treatment systems. However, travelers to areas with epidemic cholera may be exposed to the cholera bacterium.

During epidemics, many individuals excrete large volumes of stool containing abundant vibrio organisms. This excrement can contaminate the water supply that is used for washing, drinking, cooking, and swimming.

What Infected Patients Experience

The pathogenicity of cholera results from an enterotoxin that the bacteria produces. The organism itself does not result in patient illness. The enterotoxin activates enzymes in the small bowel that result in massive secretion of fluid into the bowel, overwhelming the normal reabsorptive capacity of the colon. Patients produce large volumes of dilute, relatively clear diarrhea. Untreated, patients experience signs of dehydration with dry mouth, recessed eyes, a thready pulse, lethargy, and anuria. With adequate therapy in the form of fluid replacement, almost all patients survive. With inadequate treatment, death rates may approach 50 percent, mostly from dehydration and its consequences.

Diagnosis

When cholera is suspected, definitive diagnosis can be made through microbiologic examination of the stool. The organism can be identified by trained microbiologists on examination of fresh stool, and the bacterium can be cultured using readily available media. Newer immunologic and molecular mechanisms now exist to aid in the diagnosis of this disease (Hoshino et al., 1998; Varela et al., 1994; Hasan et al., 1994; Qadri et al., 1994).
Treatment and Prevention

A short-acting vaccine is available for individuals exposed to cholera; however, the vaccine is not usually recommended for individuals traveling to areas (e.g., Latin America) where cholera is commonly found.

Treatment for cholera is supportive, with replacement of fluids and electrolytes through intravenous and oral therapy. When recognized and treated, patients recover from their infection without long-term consequences.

Correlation with Gulf War Illnesses

Cholera produces an acute, devastating diarrheal illness that would be hard to miss. The findings (or lack thereof) in patients with undiagnosed Gulf War illnesses are not consistent with cholera.

Summary

Cholera is an acute diarrheal illness that places the patient at serious threat of mortality from dehydration if the fluids lost are not properly replaced. However, with timely treatment, patients recover from the infection without long-term sequelae. Given the acute nature of the disease, cholera is not consistent with undiagnosed Gulf War illnesses.