



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Deadly viral syndrome mimics

Robert Lowenstein, MD

*Department of Emergency Medicine, Boston Medical Center, Dowling 1 South,
1 Boston Medical Center Place, Boston, MA 02118, USA*

In the United States, it has been reported that more than 3.5 billion in health care costs can be attributed to upper respiratory tract infections (URIs) [1]. URIs (ie, “the common cold”) have several hundred causes, the most common of which include rhinovirus, coronavirus, and respiratory syncytial virus. The clinical presentation varies with symptoms, including any of the following: low-grade fever, malaise, nasal congestion, sore throat, nonproductive cough, rhinorrhea, headache, and generalized myalgias. Every emergency department, no matter what the demographics, cares for patients with this constellation of symptoms. Emergency physicians examine, diagnose, and treat these disorders frequently. With increasing burdens being placed on emergency physicians, it is possible to assume a diagnosis of URI without generating a complete differential diagnosis. The challenge is to identify and recognize the distinctions between an innocuous URI and a life-threatening disease “mimic” or entities. This article discusses some of these life-threatening mimics.

The emergence of new diseases, the reemergence of old diseases, and the development of antimicrobial resistance have created a global problem in public health [2]. Optimism was the prevailing notion with respect to infectious diseases in the early to mid twentieth century with the development of antibiotics and immunizations. That optimism has been challenged with outbreaks, epidemics of new and reemerging infections, and the threat of bioterrorism. Examples of new infections include severe acute respiratory syndrome (SARS), Ebola, human immunodeficiency virus, Hantavirus, and legionnaires’ disease; reemerging infections include malaria, yellow fever, and dengue. Antimicrobial resistance contributes to streptococcal pneumonia and gonorrhea. Many factors influence these changing patterns in infectious disease.

Demographic changes include population and societal changes, such as multifamily homes and increase in day care usage, which result in an

E-mail address: Robert.lowenstein@bmc.org

increase in disease transmission [2]. In addition, there is a susceptibility factor with the aging population and movements of high-risk populations via immigration. Human behavior has contributed to exposure opportunities, examples of which include extreme adventure sports resulting in *Listeria* outbreaks and spelunking associated with histoplasmosis [2]. Air conditioning, a major technologic advancement, has led to outbreaks of legionnaires' disease. Environmental changes involving exposure to the tropical rain forest have resulted in new hemorrhagic fever viruses. Climate changes, including changes in temperature, rainfall, and vegetation, contribute to the emergence of infectious diseases [2]. International travel has facilitated the global transmission of diseases; an example is the introduction of an infected bird or person causing West Nile virus and SARS [3]. A simple, straightforward URI may represent a more complicated, lethal process. The nonspecific symptoms of a URI may represent a kaleidoscope of lethal disease entities.

The generation of a differential diagnosis in a patient with a fever and URI symptoms initially should be broad based and all-inclusive. The history narrows the differential; if it includes recent travel, however, it may pose an unusual challenge to the physician. This challenge might include the identification of an exotic disease, recognition of precautions for infection control, and being in the forefront in establishing an epidemic [4]. Approximately 50 million people travel from the industrialized to the developing world each year, of which 1% to 5% become ill, and 1 in 100,000 die [5]. The development of a differential diagnosis must include the evaluation of the exposure, seasonal and geographic distribution, incubation period, identification of diseases with high mortality, and existence of preventive measures. The evaluation of the exposure includes a travel history with regard to modes of travel, insect exposure, accommodations, activities, animal exposure, and dietary patterns [4]. Risk factors are different for backpackers and executive tourists. The evaluation of preventive measures includes a history of vaccines or medical prophylaxis. Was the patient vaccinated for yellow fever? Was the patient compliant with preventive measures, and did he or she take the appropriate chemoprophylaxis for malaria? Determining an incubation period is essential in prioritizing the differential diagnosis. Malaria and typhoid may present months after exposure compared with dengue and rickettsial viral hemorrhagic fevers, which present within 21 days. Incubation periods are within a few days for most arboviruses.

Seasonal distributions also are helpful in establishing a differential diagnosis. The rainy season attracts mosquitoes, and malaria and dengue are common. In contrast, during the dry season, meningococcemia is seen. Geographic variation includes diseases that may or may not be endemic to various continents.

Finally, after having developed a broad differential diagnosis and taken an extensive travel history, it is important to identify the diseases that

require rapid public health response and have the potential to be rapidly fatal. Diseases that require this response include hemorrhagic fevers, meningococemia, and potential for bioterrorism. The rapidly fatal diseases are the subjects of this article, with particular attention being paid to the diseases that may present in a similar fashion to the innocuous viral URI.

West Nile virus

History and significance

Mosquito-borne illnesses vary depending on the geographic location. With travel so accessible, however, there has been an increase in WNV transmission. WNV is a flavivirus. The first human case in the United States was detected in 1999 in New York City [6], and now it has been reported in 45 states. WNV was found previously in Africa, Europe, Middle East, and Asia. With more than 3500 cases in 2002, there were 200 deaths, often as a result of encephalitis [7].

Clinical presentation

The incubation period is typically 3 to 14 days with the symptoms of an acute nonspecific, flulike illness developing suddenly. These symptoms include high fever, cough, sore throat, headache, malaise, anorexia, nausea, vomiting, rash, and conjunctival injection [8].

Approximately 1 in 150 cases result in severe neurologic disease [9]. Advanced age is the most important risk factor for neurologic sequelae. Peak incidence is late summer. Hospitalized patients with severe disease may present with a change in mental status, profound weakness, cranial nerve abnormalities, myelitis, optic neuritis, seizures, and gastrointestinal symptoms. The weakness can be so severe that some presentations are consistent with Gullain-Barré syndrome; WNV can be distinguished from Gullain-Barré syndrome based on the presence of pleocytosis and nerve conduction studies [10]. In addition to a mosquito, transmission of WNV occurred from an organ donor to four transplant recipients [11]. Zoootic activity of WNV always should raise suspicion.

Diagnosis

The diagnosis is based on a high index of suspicion with sudden onset of febrile illness and change in mental status during the late summer in patients greater than 50 years old. Year-round transmission can occur in patients of all ages, however. Laboratory findings reveal total leukocyte counts in peripheral blood that are normal to elevated. Cerebrospinal fluid typically shows lymphocyte pleocytosis with increase in protein and normal glucose. Hyponatremia may be seen. CT scans of the brain are usually normal, but 50% of MRI studies show enhancement of leptomeninges and

periventricular space. The diagnostic method of choice is detection of IgM antibody to WNV in serum or cerebrospinal fluid via the IgM antibody capture enzyme-linked immunosorbent assay. Previous vaccination or an infection with related flaviviruses, such as yellow fever or St. Louis encephalitis, may lead to false-positive results [9].

Infection control and preventions

Application of diethyltoluamide (DEET) spray in endemic regions and public outreach in education would decrease the risk of being bitten and infected with WNV.

Treatment and prophylaxis

Currently, there is no established antiviral treatment. Interferon alfa, ribavirin, and immunoglobulin have been used. Vaccines for WNV currently are being developed.

Dengue fever

History and significance

Dengue fever is an acute mosquito-borne flavivirus found in most tropical and subtropical areas worldwide. There are four serotypes, all of which cause dengue fever [12]. Infection with one serotype does not provide immunity from another. In addition, infection with another serotype predisposes the patient to the development of dengue hemorrhagic fever or dengue shock syndrome. The annual incidence is more than 50 million with 12,000 deaths [5]. Most fatalities are among children and young adults; this is in contrast to WNV, in which the older adult population is at greatest risk. *Aedes aegypti* feeds on humans and is considered a day biting mosquito. In contrast to malaria and typhoid, dengue has a short incubation period, typically 3 to 8 days from time of exposure [4].

Clinical presentation

Similar to other mosquito-borne pathogens, dengue manifests as a non-specific viral syndrome, which includes fevers, headache, retro-orbital pain, myalgias, arthralgias, cough, sore throat, conjunctival injection, and rash [13]. The fever is of sudden onset and severe, often described as “break bone fever.” A rash occurs in greater than 30% of patients and often is described as a faint macular and erythematous rash. Uncomplicated dengue fever generally resolves within 7 days of illness. Dengue hemorrhagic fever and dengue shock syndrome primarily occur in endemic areas in patients who previously have been infected, not among travelers [13]. The infection is characterized by marked capillary permeability, hemoconcentration,

spontaneous hemorrhagic bleeding, hypotension, and death. Dengue commonly is confused with malaria, typhoid, influenza, and leptospirosis.

Diagnosis

Characteristic laboratory findings include leukopenia and thrombocytopenia. The diagnosis is based on laboratory tests, including the hemagglutination inhibition test and IgG or IgM enzyme immunoassays [14].

Infection control precautions

Dengue is more prevalent now than during any other time, with the number of epidemics increasing [14]. Explanations for this increase include the following: Prevention must focus on the mosquito; however, mosquito control is virtually nonexistent in most endemic areas. Uncontrolled urbanization coupled with population growth predisposes to dengue infection. The public health infrastructure is poorly funded, and increased travel by airplane transports the dengue virus all over the world [12].

Treatment and prophylaxis

No specific therapeutic agent exists for dengue. Although no effective vaccines are available currently, they are being developed. Treatment depends on supportive measures. Prevention must focus on the mosquito—limiting human contact, eradicating larvae from water containers, and using insecticides.

Yellow fever

History and significance

Yellow fever is another mosquito-borne pathogen whose presentation can range from a nonspecific viral syndrome to that of fatal hemorrhagic fever. Even with the development of an effective vaccine, the annual incidence remains 200,000 persons. Traditionally confined to Africa and South America [15], the increase in air travel poses a risk of introduction to North and Central America. Outbreaks generally occur during the rainy season and may be seen in urban locations and isolated villages [16]. Yellow fever remains a continued threat to people who travel to these endemic regions without vaccination. It is the original hemorrhagic fever-causing septicemia and is responsible for 1000-fold greater morbidity and mortality than Ebola. Another distinction is the severity of hepatic injury, resulting in severe jaundice, thus the name *yellow fever*.

Clinical presentation

The incubation period after the bite of an infected mosquito is 3 to 6 days. Fevers usually develop abruptly, accompanied by malaise, headache,

nausea, conjunctival injection, and myalgias, as is seen with other flaviviruses. Jaundice appears 48 to 72 hours from onset of the initial symptoms. After a period of remission of several days, a more severe form develops in 15% to 25% of people, characterized by hepatic and renal failure, sepsis, and hemorrhagic symptoms [15].

Diagnosis

Laboratory analysis reveals elevated transaminases, with serum aspartate aminotransferase often exceeding alanine aminotransferase. Thrombocytopenia, elevated bilirubin, and prolonged prothrombin times are significant. Aside from clinical suspicion, laboratory diagnosis depends on detection of virus or viral antigen in the blood [17].

Infection control precautions

The yellow fever vaccine is a live virus vaccine that provides immunity for 10 years.

Treatment and prophylaxis

There is no specific antiviral treatment for yellow fever aside from supportive care. Prophylaxis includes insect repellent, mosquito netting, and protective clothing.

Ebola hemorrhagic fever

History and significance

Ebola hemorrhagic fever, included in the family of viral hemorrhagic fevers, is another disease that is rapidly fatal. It has been found in the African continent, and it generally presents with transient sporadic outbreaks. There have not been any human cases reported in the United States. It first was diagnosed in 1976 and is caused by infection with Ebola virus [18]. Researchers have failed to identify the origin, location, or natural habitat of the Ebola virus.

Clinical presentation

The symptoms of Ebola hemorrhagic fever are typically acute in onset and range from fever, headache, sore throat, malarias, rash, and weakness [18] to evidence of internal and external bleeding. Physical examination reveals infected conjunctivae and lymphadenopathy followed by a maculopapular rash [19].

Diagnosis

The initial diagnosis is challenging; however, the disease often occurs in clusters of outbreaks, allowing the health care professional to isolate and

notify the proper authorities. Laboratory tests include the antigen-capture, enzyme-linked immunosorbent assay for IgM and IgG reverse transcriptase polymerase chain reaction [19]. Viral isolation also is diagnostic.

Infection control and prevention

Maintaining precautions with mask, gown, and glove is vital because Ebola virus is spread via blood, secretions, and needles. Health care workers commonly are infected.

Treatment and prophylaxis

Supportive therapy is the mainstay of treatment. The best control measure would be a vaccine; however, the research has not reached phase I trials [20,21].

Malaria

History and significance

Malaria is a disease with the potential to be rapidly fatal. It differs from the aforementioned diseases in that there are specific treatments available. Malaria is caused by protozoa of the genus *Plasmodium*. There are four kinds of malaria that can affect humans: *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale*, and *Plasmodium malariae*. Malaria occurs in more than 100 countries. Endemic regions include Central and South America, Haiti, Dominican Republic, Africa, India, and Southwest Asia. The World Health Organization estimates an annual incidence of greater than 300,000 cases with a mortality of greater than 1 million [22]. Mortality is seen primarily in small children who have not developed immunity. The annual incidence is approximately 1200 cases in the United States [15]. *P. falciparum* causes most malaria deaths. It is prudent to maintain a high index of suspicion in any recent traveler with a fever because malaria is one of the most common causes and is missed frequently. It can be rapidly fatal and must be ruled out with peripheral thick and thin smears. Although malaria is found throughout the tropics, various countries are endemic to specific species. *P. falciparum* is the predominant species in Africa, with the presentation of symptoms usually developing within 1 month. In contrast, *P. vivax* is rare in Africa because Africans generally lack an antigen on the surface of the red blood cell (Duffy antigen) necessary for the parasite to penetrate [4]. *P. vivax* predominates in Asia and Latin America; symptoms develop within 1 month only 50% of the time [5].

Clinical presentation

Most patients become symptomatic 10 days to 4 weeks after infection, although patients may present many months later. The clinical presentation

of malaria is nonspecific with fever, cough, sore throat, and flulike illness. Headaches, myalgias, fatigue, and rigors occur. Nausea, vomiting, and diarrhea also may occur. The temperature may not be elevated at the time of presentation, although most patients report fevers at some point during their illness. This situation presents a diagnostic challenge and may account for one of the reasons why patients may make several visits to health care professionals before a diagnosis of malaria is considered [23]. Other reasons include lack of familiarity with tropical disease coupled with the initial presentation occurring weeks to months after travel. It also is uncommon for the classic “cyclical fever” to occur. This is a specific historical finding, but not a sensitive one.

Diagnosis

The diagnosis is confirmed by malarial smears and should be repeated every 8 to 12 hours if clinically suspected. Dip-stick assays, although not commercially available in the United States, have high sensitivity and specificity. On physical examination, splenomegaly may be present. Thrombocytopenia without leukocytosis is a common feature. Total bilirubin and lactate dehydrogenase may be elevated. According to Svenson et al [24], no symptom, sign, or laboratory test predicted malaria with any reliability in a tropical medical hospital. In severe cases, malaria may present with shock, renal failure, hypoglycemia, and pulmonary edema.

Infection control and prevention

In the United States, travelers contribute to most cases of imported malaria, which generally is acquired in Africa. Numerous protective preventive measures can be implemented to decrease the incidence. Prophylactic measures can occur before travel via chemoprophylaxis. Mefloquine has replaced chloroquine as the prophylactic medication of choice in preventing *P. falciparum* secondary to resistance [16]. Alternative medications are available, and it is advisable to contact the US Centers for Disease Control and Prevention malaria hotline before travel [16]. Personal protective measures also are recommended. Recognizing that transmission occurs primarily between dusk and dawn, one can reduce contact with mosquitoes during that time. These measures include insecticide-treated nets when sleeping, remaining in well-screened areas, covering the body with clothes, and applying DEET insect repellants as needed [25].

Treatment and prophylaxis

Treatment of malaria depends on the species and on the severity of symptoms. Traditionally, chloroquine was the drug of choice for all species of malaria. With an increase in chloroquine resistance to *P. falciparum*, quinine and doxycycline may be substituted.

Rocky Mountain spotted fever

History and significance

Tick-borne diseases can be just as deadly as mosquito-borne diseases and can present with respiratory symptoms. Rocky Mountain spotted fever (RMSF), which is caused by *Rickettsiae rickettsii*, is a small pleomorphic obligate intracellular parasite. Aside from Maine and Vermont, RMSF has been found throughout the continental United States [26]. Approximately 1000 cases are reported annually [27]. RMSF is noted to be the most lethal tick-vector illness in the United States. It also has been reported throughout southern Canada and Central and South America. RMSF is an elusive diagnosis to make. Approximately 40% of patients do not report a history of a tick bite. Because of the nonspecific nature of the initial symptoms and the potential severity of disease, therapy often must be initiated without confirmation of disease. RMSF is a misnomer because the disease is located predominantly in the southeastern United States [28]. Although 90% of cases occur during the summer months, there is no seasonal exclusion, and a careful history and physical examination must be performed. The clinician must not wait for the classic petechial rash to develop in the palms and soles to make the diagnosis.

Clinical presentation

Although there is a classic triad of a history of tick exposure, fever, and rash, less than 20% present in this fashion. RMSF is extremely difficult to diagnose in its early stages because the initial presentation is relatively nonspecific and resembles a viral syndrome. The pulmonary manifestations of RMSF include cough (33%), pharyngitis (8%), and pleuritic chest pain (17%) [29]. These nonspecific symptoms last during the first week of the illness, which generally follows a mean incubation time of 7 days [30]. Later manifestations include rash and gastrointestinal symptoms. The rash usually follows the onset of fevers and may not be present for several days after the onset of initial symptoms. Usually the rash begins as macules on the wrists, forearms, and ankles and initially may blanch with pressure. It is not until day 6, however, that the petechial rash develops on the palms and soles. This rash may be seen in only 50% to 80% of patients [30].

Diagnosis

Rickettsia rickettsii is lethal because of its predisposition to infecting endothelial cells, which are the cells lining all major blood vessels and major tissues throughout the body. All organ systems subsequently are affected leading to severe systemic illness. Abnormal laboratory findings include hyponatremia, elevated liver function tests, and thrombocytopenia [30]. The definitive diagnostic test is direct immunofluorescent examination of skin

biopsy samples for *R. rickettsii* antigen [31]. Antibodies are detected 7 to 10 days after the onset of illness.

Infection control and prevention

Careful body inspection after outdoor activities and the application of DEET insect repellent are recommended.

Treatment and prophylaxis

The treatment of choice is doxycycline or tetracycline, even in children. Chloramphenicol is recommended in the setting of severe central nervous system manifestations.

Tularemia

History and significance

Tularemia first was described in the United States in 1911 and has been reported in all states except Hawaii. It is a zoonotic disease caused by the gram-negative coccobacillus *Francisella tularensis*. The most important reservoirs include rabbits, hares, and ticks. Humans may acquire the disease from tick, mosquito, and deer fly bites; direct contact with infected tissues; aerosolized organisms; and ingestion of contaminated foods or water [31]. Approximately 200 to 300 cases are reported annually in the United States [27].

Clinical presentation

Characteristically, tularemia presents as an acute febrile illness; however, it may appear in many forms depending on the route of infection: typhoid I (fevers, chills, and headache), ulceroglandular (ulcer at the site of the bite with lymphadenopathy), glandular (lymphadenopathy), oculoglandular, oropharyngeal, and pneumonia [28]. Tularemia can be a severe illness characterized by sudden onset of high fevers, malaise, and headaches with a 3- to 5-day incubation period and a 1% to 3% mortality [28]. Pneumonia, characterized by respiratory symptoms including chest pain, cough, and pharyngitis, can be seen in 25% of cases [27] and is associated with increased morbidity and mortality. Pleural effusions can be seen in 30% of patients.

Diagnosis

Laboratory testing generally is unremarkable, although mild increases in transaminases and alkaline phosphatase are common. The radiograph may reveal a patchy, ill-defined, multilobar process and is abnormal in 50% of patients [31]. The diagnosis can be confirmed by laboratory cultures of sputum, gastric, and throat specimens. The potential risk of exposure to laboratory workers is significant, however, and cultures should be done only in a biosafety level 3 facility [32]. The diagnosis also can be confirmed

by a fourfold titer change of serum antibodies against *F. tularensis* or by detecting *F. tularensis* antigens with fluorescent assays [33].

Infection control precautions

Patients do not need to be quarantined or isolated. Standard precautions need to be maintained when handling bodily fluids.

Treatment and prophylaxis

Streptomycin is the drug of choice, although gentamicin may be equally effective [30] and provides broader coverage for gram-negative bacteria when the diagnosis is suspected, but not confirmed. Tetracycline and chloramphenicol are alternative agents. Chemoprophylaxis is not recommended for exposed asymptomatic persons.

Legionellosis

History and significance

Several bacterial infections may mimic simple URI. *Legionella pneumophila* causes legionellosis. The severity ranges from a mild illness that resolves spontaneously to a severe illness that results in death. The annual incidence in the United States is 15,000 to 30,000. Legionellosis accounts for 4% of lethal nosocomial pneumonias and approximately 1% to 8% of lethal community-acquired pneumonias [34]. The overall morbidity is 15%. It is thought that cases occur throughout the world. Cases may present in outbreaks or as single cases. Single cases occur year round; however, outbreaks have a predilection for the summer or early fall [35].

Clinical presentation

The signs and symptoms of legionellosis include fevers, chills, cough, and headaches [34]. The cough may or may not be productive. Fevers characteristically are accompanied by a relative bradycardia. Chest x-ray findings vary from patchy segmental infiltrates to a bilateral process with pleural effusions.

Diagnosis

The diagnosis is made via sputum culture, antibody assay from the blood, and urinary antigen [34]. Patients at greatest risk include the elderly, smokers, and chronic obstructive pulmonary disease patients, although any immunocompromised patient is at risk. *Legionella* bacteria are widespread in nature, but are associated more commonly with warm water sources because the bacteria live best in warm water. Outbreaks have been attributed to inhaled aerosols from air conditioning systems and consequently occur during the summer.

Infection control and prevention

Individual cases are not preventable. Outbreaks can be thwarted, however, by identifying and cleaning contaminated water sources.

Treatment and prophylaxis

Antibiotics are the mainstay of treatment. Erythromycin is the drug of choice.

Severe acute respiratory syndrome

History and significance

SARS is an emerging infectious disease and is posing a new global threat. The initial symptoms are consistent with a URI, but eventually manifest into an atypical pneumonia, initially similar to that of any community-acquired pneumonia. SARS is thought to be a novel coronavirus, which has been recovered from wild animals and now has established itself in human hosts [36]. The origin has been traced to the Guangdong province of South China.

The incubation period is 7 to 10 days before the onset of symptoms [37]. This incubation period provides the potential for worldwide exposure because a person harboring the virus can expose the world at large via air travel. There have been more than 7000 cases in 26 countries and 800 deaths throughout the world, and the numbers continue to increase [36]. The United States has seen 300 cases with no fatalities [38]. The World Health Organization reports the overall mortality at 20% for patients admitted with SARS [38]. The extremes of age have the highest morbidity.

Clinical presentation

As mentioned previously, the initial symptoms include those typical of a URI: fever ($>100.4^{\circ}\text{F}$), cough, and headaches. More severe disease progresses to the lower respiratory tract; symptoms include shortness of breath, hypoxia, and dyspnea. With advanced disease, chest x-ray shows evidence of pneumonia or adult respiratory distress syndrome.

Diagnosis

According to the World Health Organization, the diagnosis can be confirmed via positive antibody to SARS, detection via polymerase chain reaction of SARS RNA, and isolation of the SARS virus itself [37,38].

Infection control and prevention

Most cases have been transmitted from person to person via droplet exposure from coughing and sneezing [39]. Most of the outbreaks of SARS have involved health care workers who were in close contact with infected patients. In addition to notifying the public health department, immediate

infectious control precautions must be undertaken after early recognition and isolation [40].

Treatment and prophylaxis

Treatment is supportive, although there has been reported success with steroids and ribavirin. It is up to the emergency physician to suspect SARS in patients with URI symptoms from high-risk regions or potential exposures.

Meningococcal disease

History and significance

Meningococcal disease is the leading cause of bacterial meningitis and sepsis in the United States and a cause of large epidemics in sub-Saharan Africa [41]. The cause is *Neisseria meningitides*, a gram-negative, aerobic diplococcus that contains multiple serogroups. Serogroups that account for most cases of meningococcal disease throughout the world include A, B, C, and Y [41]. The incidence in the United States ranges from 0.5 to 2.9 cases per 100,000 persons, whereas in sub-Saharan Africa the incidence ranges from 10 to 25 cases per 100,000 persons, excluding the major epidemics [42]. Most cases occur in the winter and early spring. Groups at risk include infants and young children, household contacts, military recruits, college freshmen, people exposed to active and passive smoking, and health care professionals. Fatality rates are 10% to 15%, whereas morbidity is comparatively higher [43].

Clinical presentation

Because the symptoms of meningococcemia range from mild illness to serious disease, it is a challenge to diagnose. Mild forms may present as benign infections. Meningeal infection occurs in 50% of patients, who present with sudden fever, headache, and neck stiffness. Severe cases are characterized by rapid change, abrupt onset of fever, petechial or purpuric rash, hemodynamic signs of sepsis, vasomotor collapse, and shock [44].

Diagnosis

The laboratory diagnosis can be confirmed by blood cultures. Sensitivity decreases with the initiation of antibiotic therapy, however. Other modalities include Gram stain of cerebrospinal fluid, Gram stain of peripheral blood buffy-coat specimen, and petechial scraping [44].

Infection control and prevention

Transmission occurs from person to person through direct contact with nose and throat secretions. Close contacts, including household members, child care classmates, and anyone exposed to oral secretions, should receive

prophylactic antibiotic therapy. Isolation of confirmed and suspected cases is required. Routine vaccination of high-risk populations is another cost-effective public health plan. The distribution of serogroups is an important factor in the design of the vaccination program.

Treatment and prophylaxis

Early recognition and treatment with antibiotics are essential. Penicillin G, ampicillin, cefotaxime, and ceftriaxone all treat meningococemia [44]. Studies showed a decline in morbidity with intravenous corticosteroids if initiated before antibiotic administration. Meningococcal vaccine, as an adjunct to prophylactic antibiotics in epidemics and for sporadic cases for close contacts, may be considered [41]. Antibiotic prophylaxis for the close contacts includes single-dose ciprofloxacin, rifampin for 2 days, or ceftriaxone in children.

References

- [1] Jackson JL, Peterson C, Lesho E. A meta-analysis of zinc salt lozenges and the common cold. *Arch Intern Med* 1997;157(20):2373–6.
- [2] Cohen ML. Changing patterns of infectious disease. *Nature* 2000;406:762–7.
- [3] Centers for Disease Control and Prevention. Outbreak of West Nile like viral encephalitis—New York, 1999. *MMWR Morb Mortal Wkly Rep* 1999;48:845–8.
- [4] McLellan SL. Evaluation of fever in the returned traveler. *Prim Care Clin Office Pract* 2002;29:947–69.
- [5] Ryan ET, Wilson ME, Kain KC. Current concepts: illness after international travel. *N Engl J Med* 2002;347:505–16.
- [6] Campbell GL, Marfin AA, Lanciotti RS, Gubler DJ. West Nile virus. *Lancet Infect Dis* 2002;2:519–29.
- [7] Provisional surveillance of the West Nile virus epidemic—US, January–November 2002. *MMWR Morb Mortal Wkly Rep* 2002;51:1129–33.
- [8] Solomon T, Ooi MH, Beaseley DW, Mallewa M. West Nile encephalitis. *BMJ* 2003;326:865–9.
- [9] Centers for Disease Control and Prevention. Fact sheet: West Nile virus (WNV) infection: information for clinicians. Available at: www.cdc.gov/ncidod/dvbid/westnile/resources/fact_sheet_clinician.htm. Accessed: July 17, 2003.
- [10] Pterson LR, Marfin AA. West Nile virus: a primer for the clinician. *Ann Intern Med* 2002;137:173–9.
- [11] Iwamoto M, Jernigan DB, Guasch A, Trepka MJ, Blackmore CG, Hellinger WC. Transmission of West Nile virus from an organ donor to four transplant recipients. *N Engl J Med* 2003;348:2196–203.
- [12] Centers for Disease Control and Prevention. Dengue fever home page. Available at: www.cdc.gov/ncidod/dvbid/dengue/index.htm. Last modified June 19, 2001.
- [13] Gregson A, Edelman R. Dengue virus infection. *Pediatr Infect Dis J* 2003;22:179–81.
- [14] Gibbons RV, Vaughn DW. Dengue: an escalating problem. *BMJ* 2002;324:1563–6.
- [15] Monath T. Yellow fever: an update. *Lancet Infect Dis* 2001;1:11–20.
- [16] Centers for Disease Control and Prevention. Yellow fever—disease and vaccine. Available at: www.cdc.gov/ncidod/dvbid/yellowfever/index.htm. Last modified January 23, 2003.
- [17] Adverse events associated with 17D-derived yellow fever vaccination—US, 2001–2002. *Morb Mortal Wkly Rep* 2002;51:989–93.

- [18] Centers for Disease Control and Prevention. Ebola hemorrhagic fever: special pathogens branch. Available at: www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/ebola.htm. Last modified June 4, 2002.
- [19] Easter A. Ebola: no antiviral compounds are available to treat this hemorrhagic fever. *Am J Nurs* 2002;102:49–52.
- [20] Clarke T, Knight J. Fast vaccine offers hope in battle with Ebola. *Nature* 2003;424:602.
- [21] Thacker P. An Ebola epidemic simmers in Africa: in remote region, outbreak shows staying power. *JAMA* 2003;290:317–9.
- [22] Centers for Disease Control and Prevention. Malaria: general information: travelers' health. Available at: www.cdc.gov/travel/malinfo.htm. Last reviewed July 10, 2000.
- [23] Svenson JE, MacLean JD, Gyorkos TW, Keystone J. Imported malaria: clinical presentation and examination of symptomatic travelers. *Arch Intern Med* 1995; 155:861–8.
- [24] Svenson JE, Gyorkos TW, MacLean JD. Diagnosis of malaria in the febrile traveler. *Am J Trop Med Hyg* 1995;53:518–21.
- [25] Whitty CJ, Rowland M, Sanderson FL, Mutabingwa TK. Malaria. *BMJ* 2002;325:1221–4.
- [26] Abrahamian FM. Consequences of delayed diagnosis of Rocky Mountain spotted fever in children—West Virginia, Michigan, Tennessee, and Oklahoma, May–July 2000. *Ann Emerg Med* 2001;37:537–8.
- [27] Faul JL, Doyle RL, Kao PN, Ruoss SJ. Tick-borne pulmonary disease: update on diagnosis and management. *Chest* 1999;116:222–30.
- [28] Masters EJ, Olsen GS, Weiner SJ, Paddock CD. Rocky Mountain spotted fever: a clinician's dilemma. *Arch Intern Med* 2003;163:769–74.
- [29] Donohue JF. Lower respiratory tract involvement in Rocky Mountain spotted fever. *Arch Intern Med* 1980;140:223–7.
- [30] Centers for Disease Control and Prevention. Rocky Mountain spotted fever: introduction. Available at: www.cdc.gov/ncidod/dvrd/msf.htm Last reviewed August 7, 2000.
- [31] Spach DH, Liles CW, Campbell GL, Quick RE, Anderson DE, Fritsche TR. Medical progress: tick-borne diseases in the United States. *N Engl J Med* 1993;329:936–47.
- [32] Hornick R. An outbreak of primary pneumonic tularemia. *N Engl J Med* 2002;346:1027–9.
- [33] Tularemia—United States, 1990–2000. *MMWR Morb Mortal Wkly Rep* 2002;138:988–9.
- [34] Pneumonia of legionnaires' disease. *The Merck manual of diagnosis and therapy*.
- [35] Centers for Disease and Prevention. Legionellosis: legionnaire's disease and Pontiac fever: disease information. Available at: www.cdc.gov/ncidod/dbmd/diseaseinfo/legionellosis_g.htm. Last Reviewed June 20, 2001.
- [36] Drazen JM. SARS—looking back over the first 100 days. *N Engl J Med* 2003;349:319–20.
- [37] Poutanen SM, Low DE, Henry B, Finkelstein S, Rose D, Green K. Identification of severe acute respiratory syndrome in Canada. *N Engl J Med* 2003;348:1995–2005.
- [38] Ojiaku U. SARS: Emerging infectious diseases and the new global threat. *EMRESIDENT* 2003;30:1–16.
- [39] Cameron PA, Rainer TH. Update on emerging infections: news from the Centers for Disease Control and Prevention. *Ann Emerg Med* 2003;42:110–6.
- [40] Sampathkumar P, Temesen Z, Smith TF, Thompson RL. SARS: epidemiology, clinical presentation, management, and infection control measures. *Mayo Clin Proc* 2003;78: 882–90.
- [41] Rosenstein N, Perkins BA, Stephens DS, Popovic T, Hughes JM. Meningococcal disease. *N Engl J Med* 2001;344:1378–88.
- [42] Diaz PS. The epidemiology and control of invasive meningococcal disease. *Pediatr Infect Dis J* 1999;18:633–4.
- [43] Cohen J. Meningococcal disease as a model to evaluate novel anti-sepsis strategies. *Crit Care Med* 2000;28(suppl):s64–7.
- [44] Meningococemia. In: Falk K, editor. *Rosen's emergency medicine: concepts and clinical practice*. St. Louis, MO, Mosby. p. 1785–811.