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REVIEW

Infectious Disease & Wilderness Medicine

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Abstract

Purpose of Review The recognition, treatment, and management of infectious processes is critical for individuals traveling into the wilderness. Particularly in a resource- limited environment, individuals exposed to infectious disease in the wilderness can experience sequalae not commonly observed in the hospital-based urban clinical environment. In the United States, several infectious pathogens are well known to contribute to the development of infection in the wilderness setting. The purpose of this review is to discuss the treatable infectious diseases encountered by individuals venturing into the wilderness of the United States of America. Diligent preparation stands as the cornerstone for safe and rewarding outdoor adventures. By performing critical analysis of current literature, we seek to offer a comprehensive guide on the identification and management of infectious agents that pose a risk to the outdoors people of the United States.

Recent Findings Current literature regarding infectious disease in the wilderness consistently highlights the diversity of pathogens encountered in the wild. However, the most common clinical manifestation acquired in the wilderness is diarrhea (Auerbach in Wilderness Medicine (7th ed.). Elsevier, 2017 [1], Victora et al. in Bull. World Health Organ. 78:(10), 1246, 2000 [2]). Frequently transmitted through fecal–oral route, contaminated water sources are frequently implicated in these cases (Auerbach in Wilderness Medicine (5th ed). Elsevier, 2018 [3], https://www.cdc.gov/healthywater/drinking/travel/backcountry_water_treatment.html, www.cdc.gov/eid). Tick-borne illnesses also represent a major avenue by which wilderness explorers become infected (Openshaw et al. in Am J Trop Med Hyg. 83(1), 174–182, 2010 [5]). Lyme disease and Rocky Mountain Spotted Fever are two of the most common diseases wilderness travelers face (Rosenberg et al. in Morbidity and Mortality Weekly Report, 68(9), 1–11, 2019 [6], https://www.cdc.gov/rmsf/index.html). Zoonotic infections are spread when an infectious pathogen is introduced to a human via an animal host. Individuals can become infected by direct contact with the animal host, their bodily fluids, or their environment. Some ticks and mosquitoes are considered "vectors" and directly transmit the infectious agent (Auerbach in Wilderness Medicine (7th ed.). Elsevier, 2017 [1], Harms et al. in J Infect. 82(1), 98–104, 2021 [7], https://www.cdc.gov/rmsf/index.html, Openshaw et al. in Am J Trop Med Hyg. 83(1), 174–182, 2010 [5]).

Summary Certain infections are prevalent in people travelling to rural United States. This review concentrates on the management of common treatable infections acquired in wilderness areas within the United States.

Keywords Emergency medicine · Infectious disease · Wilderness medicine · Water purification · Tick born illness · Water borne illness · Lyme disease · Rocky mountain spotted fever · Giardiasis · E. Coli · Travelers diarrhea · Cryptosporidium · Leptospirosis

Introduction

Water Purification

Water purification in the wilderness is crucial for ensuring safe drinking water and preventing spread of waterborne illnesses. It is important to try collecting water from the cleanest source available such as a spring, flowing river, rainwater, or melted snow. Next, allowing sediment to settle will increase the effectiveness of any purification method.

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If possible, utilizing a combination of the following methods provides the best protection against waterborne illness [4, 9]. Water purification can be summarized to 3 primary methods; boiling, filtration, and disinfection.

Boiling water is the most effective method for killing the various bacteria, viruses, and protozoa responsible for waterborne illness. Water should be brought to a boil for at least 1 min. At altitude greater than 6,500 feet, water should be boiled for a total of 3 min [4, 9].

Filtration involves passing the water through a physical barrier that removes most bacteria and protozoa. However, filtration has limited effectiveness against viruses as they are typically small enough to pass through the filter. Only filters with a chemical disinfectant matrix will be effective against some viruses [4, 9].

Disinfection utilizes chemical agents or ultraviolet light to kill or inactive microorganisms. Chemical agents such as chlorine, iodine, and chlorine dioxide are commonly used. These agents are mixed in the water source, creating a reaction which kills microorganisms. These chemicals can leave behind an unpleasant taste and require longer wait time for safe drinking. Ultraviolet light works by damaging the DNA of these organisms rendering them innocuous. Ultraviolet light works almost immediately and doesn't leave behind a foul taste; however it can be limited by the clarity of the water [4, 9].

Lyme Disease

Lyme disease is the most common vector borne zoonotic infection in the United States [6]. Lyme disease is caused by the spirochete bacteria, *Borrelia Burgdorferi.* This bacteria is transmitted to humans by the *Ixodes scapularis* tick, also known as the deer tick or the black legged tick. Because the disease is spread via this host, peak transmission occurs during the warmer months; (May through August) [6].

The disease takes its name from Old Lyme, Connecticut. This is the town from which a group of cases were initially investigated during the 1970's by researchers from Yale. Since that time, Lyme disease has been reported internationally. However, it has been reported that 96% of cases are localized to just 14 states in the northeast United States [6, 11]. Therefore, geographic location and recent travel are crucial to making the diagnosis.

The clinical manifestations of Lyme disease begin 3–30 days following the tick bite. The initial symptoms to be aware of are fevers, chills, myalgia, arthralgia, lymphadenopathy, and the characteristic "bull's eye" rash. This rash known as Erythema migrans (EM) is a red circular rash that develops around the site of the tick bite. The rash will gradually expand over a few days and then develop central clearing giving the characteristic appearance. EM is present in 70–80% of Lyme disease cases [6, 12]. Delayed disseminated manifestations occur weeks to months after a tick bite and include dermatologic, neurologic, cardiac, and rheumatologic pathologies [6, 12]. These latter manifestations are unlikely to be encountered by the wilderness explorer within the acute timeframe. That said, it is not uncommon for patients to present with findings such as facial palsy or heart block who do not recall a specific tick bite.

The most effective means of protection against Lyme disease is preventing tick contact in the first place. Physical barriers such as long clothing and insect repellant such as DEET (N,N-diethyl-meta-toluamide) are effective measures [13, 14]. DEET is a chemical originally created by the US military, became commercially available in 1956 and is considered among the most broad spectrum and efficacious insect repellants. The US Centers for Disease Control and Prevention recommend the use of DEET in prevention of Lyme disease. The safety and efficacy of DEET has been reviewed on several occasions by the US environmental protection agency [13]. With proper use and application,the safety profile of DEET is promising with mild skin reactions being most common. The US Food and Drug Administration has deemed DEET safe for use in 2nd and 3rd trimester pregnant women [15]. The American Academy of Pediatrics does not recommend use of DEET in children < 2 years of age. Children > 2 years of age should use products with a maximum DEET concentration of 33% [13].

Prompt treatment of Lyme disease often leads to rapid and complete resolution [6, 7]. If a tick is attached to the skin, removal of the tick is advised as soon as possible. Using a pair of fine tipped tweezers, grasp the tick as close to the surface of skin as possible and gently pull upward. Attempt to remove all parts of the tick from the skin. After tick removal, thoroughly clean the bite area with rubbing alcohol or soap and water.

If EM develops, antibiotic therapy is advised [7]. Dosage may be adjusted depending on patient's age, medical history, pregnancy, and allergies. Doxycycline, amoxicillin, or cefuroxime axetil are recommended by the CDC as first-line agents. Doxycycline dosing is 100 mg orally twice daily for adults; 4.4 mg/kg per day in two divided doses (maximum 100 mg per dose) for children. The duration of therapy is 10 days [6–8].

Prophylactic antibiotic therapy should be considered on a case-by-case basis [7, 10]. One resource advises use of a single dose of doxycycline for nonpregnant adults and children who meet a set criteria; these include attached tick identified as a deer tick, attachment for > 36 h, prophylaxis within 72 h of tick removal, bite occurring within a highly endemic area, and doxycycline not being contraindicated [10]. This prophylactic dose of doxycycline is 200 mg for adults and 4.4 mg/kg up to maximum dose of 200 mg for children given as a single dose. For those who cannot take doxycycline, an alternative antibiotic is not recommended.

Rocky Mountain Spotted Fever

Rocky Mountain Spotted Fever (RMSF) is caused by the bacterium Rickettsia rickettsii, a coccobacillary, obligate, intracellular organism [16]. This bacterium is spread by three tick species: the American dog tick in the eastern United States, the Rocky Mountain wood tick in the central mountain states, and the brown dog tick in the Southwestern United States [17]. Although cases have been reported in each of the lower 48 states, more than 60% of cases have been reported in North Carolina, Oklahoma, Arkansas, Tennessee, and Missouri. Peak transmission occurs between May and August [5].

RMSF is a rapidly progressive disease and can be deadly without early administration of antibiotics. Most people report sudden onset fever and headache approximately 3–12 days following a bite from an infected tick [18]. A characteristic rash will develop in approximately 90% of patients during their illness. The rash is described as small, flat, pink macules on the extremities, which may progress to include the trunk, palms of the hands and soles of the feet [18]. Development of a petechial rash is an ominous finding and is associated with severe disease. Delayed treatment can progress to more severe illness, including neurological deficits, respiratory compromise, necrosis of tissue surrounding the bite, and multiorgan system dysfunction [17, 18].

Once diagnosis of RMSF is suspected, prompt treatment with doxycycline 100 mg twice daily for adults and 2.2 mg/kg/dose twice per day (max 200 mg) for children should be initiated [10]. Doxycycline is most effective at preventing severe complications if started within the first 5 days of illness. The minimum course of treatment is 5–7 days; however, the CDC recommends treating with doxycycline for at least 3 days after the fever subsides and there is evidence of clinical improvement [7, 17].

Giardiasis

Giardia is the most common protozoal intestinal parasite worldwide and is more prevalent in developing areas with poor sanitation [19]. Giardiasis is also known as "backpacker's diarrhea" because of the common association with hikers exposed to contaminated water [20]. Giardia is transmitted via the fecal–oral route and all age groups may be affected [21]. Most cases occur during the summer months, as this coincides with increased outdoor activity and potential exposures, such as camping or the use of communal water sources. Water is a primary source of infection in community outbreaks, usually in small water systems that use untreated or inadequately treated surface water [28].

Clinical symptoms consist of diarrhea, abdominal cramping, and bloating. Stools have a characteristic foul smell and greasy appearance. Limited cases can go onto develop chronic symptoms including worsening abdominal symptoms, malnutrition, and weight loss [19, 20].

Disease prevention is critical and is promoted by implementation of strict handwashing and avoidance of ingesting contaminated water. Treatment of symptomatic patients includes the use of nitroimidazoles such as tinidazole (2 g once), metronidazole (250 mg three times per day for 5 days), or nitazoxanide (500 mg twice daily for 5 days) [19].

Escherichia Coli

Overall, the most common cause of traveler's diarrhea is Enterotoxigenic Escherichia coli (ETEC) [2]. E. coli are normal inhabitants of the human gastrointestinal tract. However, when they acquire additional genetic material they can become pathogenic [22]. ETEC specifically express fimbriae which allow for intestinal attachment. ETEC also produces secretory toxins which manifest clinically as watery diarrhea, which is the hallmark symptom of this bacterium [23]. ETEC outbreaks are associated with unsafe preparations and storage of food and water. ETEC has a relatively short incubation period of 1 – 3 days. The illness is self limited, lasting 1 – 5 days [24].

The treatment of this acute diarrhea focuses on the correction of fluid and electrolyte losses. The majority of these cases can be treated with oral rehydration salts [25]. The World Health Organization and United Nations Children's Fund recommends a reduced osmolarity solution containing 2.6 g sodium chloride, 2.9 g sodium citrate, 1.5 g potassium citrate, and 13.5 g glucose per one liter of clean water [26]. For those individuals exhibiting signs of severe volume loss (lethargy, inability to drink, weak radial pulses) IV fluid replacement with a balanced crystalloid solution (ex. Lactated Ringer's) is advised [27]. Antimicrobial therapy is not recommended for acute watery diarrhea, as most cases resolve spontaneously [9, 26].

Cryptosporidium

Cryptosporidiosis, caused by C parvum and C hominis, are common intestinal parasites. Reporting is infrequent because patients may be asymptomatic and symptoms when present typically resolve within two weeks in immunocompetent patients. Cryptosporidium infections occur typically in summer and fall, related to drinking water contamination, animal contact, use of recreational water facilities and travel. Ammonia or formalin have been proposed to purify drinking water. Cryptosporidiosis, as with other waterborne infections, has been associated with non-wilderness exposures. It has been reported that 43 million US residents are served by private wells or domestic water systems that are not regulated by the Environmental Protection Agency Safe Drinking Water Act [9]. For our purposes, enteric pathogens from

ingesting untreated water can be introduced via stormwater runoff, animal waste, sewage or septic system malfunction, or swimming in lakes and rivers. Infectious Cryptosporidium oocysts have tough outer shells which confer extreme chlorine tolerance [9]. Cryptosporidium infections have been reported to cause of the order of 211,000 exposures annually in the United States resulting in approximately 750 hospitalizations. As a classical waterborne pathogen, Cryptosporidium is predominantly sourced from animals such as cattle, with high prevalence rates in wastewater and higher detection rates and concentrations during warmer seasons [28].

Symptoms ranging from mild watery diarrhea to severe enteritis with possible biliary tract involvement may occur. The latter may be manifest by elevated alkaline phosphatase, or an enlarged gall bladder with a thickened wall, and dilated biliary ducts on ultrasound. Joint pain, weight loss, abdominal pain and fatigue may be presenting complaints [19].

Diagnosis is most reliably made by microscopy/immunofluorescence, enzyme immunoassays or polymerase chain reaction. Routine stool ova and parasite examinations may not detect the oocysts so, if suspected, the laboratory should be notified in order to use the correct staining techniques [21].

Treatment is, for the most part, supportive with hydration. Antidiarrheal agents such as loperamide or even tincture of opium have been advocated. Spontaneous recovery typically occurs within one week. Parasitic cure also occurs within a few weeks to months [19]. If symptoms persist beyond two weeks, Nitazoxanide is approved by the US Food and Drug Administration for treatment. A typical dosage for an adult is 500 mg twice daily for three days [29]. Patients should be warned that the drug may cause nausea, headache, and bright yellow urine. Patients should avoid public pools for two weeks following diarrhea.

Patients with advanced HIV, for example CD4 counts of less than 50 cells/microliter, may need immune restoration with antiretroviral therapy (ART) before symptoms can be eradicated and may require nitazoxanide therapy for many weeks. While nitazoxanide is the only FDA approved therapy for treatment of cryptosporidiosis, other agents have been proposed for treatment, notably paromomycin [29]. ART and management of infections in immunocompromised patients is beyond the scope of this review.

Leptospirosis

Leptospirosis is a zoonotic waterborne disease caused by spirochetes of the genus *Leptospira*. Adolph Weil described it in 1886 from kidney tissues, and the lethal disseminated disease has been known as Weil's Disease [30]. In Weil's description, patients had icterus, renal failure, conjunctivitis, and an enlarged spleen [31]. It is highly prevalent in the tropics, and particularly in Southeast Asia, and may be the most widely spread zoonotic infection in the world [32]. Flooding from hurricanes or monsoons increase the risk of infection from contaminated water.

While rats are the major carriers of leptospires, leptospirosis has been well-documented in dogs, cattle, swine, and horses, among others. Rats excrete very high concentrations of organisms. It is endemic in countries with humid or subtropical climate, but now is also seen in temperate regions due to climate change, human migration, and poor sanitation or waste disposal. There are at least nine species of pathogens associated with human leptospirosis, with many more serotypes and hundreds of serovars of strains. While unusual in recreational travelers within the United States, leptospirosis accounts for over 1 million infections and approximately 60,000 deaths annually worldwide [33].

Transmission of Leptospira is generally via direct transmission by contaminated water or soil/carrier mammals. Therefore in tropical regions farmers, agricultural workers, rodent catchers, animal caretakers, fishermen, gardeners and health care professionals are at risk. For the wilderness traveler in the US, skin abrasions and cuts or entry through mucous membranes or conjunctivae are common exposure risks from ponds, rivers, lakes, puddles, or water dams contaminated with rat urine. This applies especially to people who participate in surfing, caving, canoeing, or any freshwater sport. The bacterium has been reportedly able to enter through intact skin as well [32].

Leptospirosis shows two phases of infection. There is a mild anicteric phase, which generally is self-limiting without treatment. The incubation period is approximately 1–2 weeks. Approximately 90% recovery from anicteric leptospirosis has been reported [30]. Leptospirosis can present with protean manifestations: weakness, cough, fever, vomiting, chills, shortness of breath, vomiting and headache. There may be conjunctivitis and uveitis, myalgias, and prostration.

One problem with the diagnosis of leptospirosis is that the signs and symptoms of the disease overlap with those of other diseases which occur in warm humid climates. As well, there may be co-infection with dengue, malaria, chikungunya, hepatitis, or typhus. Patients diagnosed with leptospirosis must have these illnesses considered as well, although some are rare for the wilderness traveler within the US [33].

Recovery takes place in the majority of people. However, in some cases, the infection will re-appear after 2–3 days and cause severe infection with involvement of the kidney, liver, lungs, myocarditis, uveitis and meningitis. There may be myocarditis, encephalomyelitis, intracranial bleeding, or transverse myelitis, and pancreatitis [31]. The icteric phase or Weil's disease ensues when the leptospires infect hepatocytes, causing anuria and oliguria. Leptocytes can be found in the urine from 7–30 days of infection [30]. Pulmonary hemorrhage may occur with or without renal failure or jaundice. Anemia, thrombocytopenia, elevated transaminases, rhabdomyolysis CSF pleocytosis may be present.

Diagnosis may be suspected in some one with a history of risk exposure, perhaps with prostration, jaundice, conjunctivitis, oliguria recently arrived from a camping trip to Hawaii. Blood, urine, and cerebrospinal fluid are typical body fluids used for the diagnosis of leptospiral infection. Leptospires can be found in the blood initially (within the first week), and later in the urine.

Leptospira may be seen under dark-field microscopy (DFM) without staining. DFM can demonstrate leptospires in the blood and CSF in the early bacteremic phase [33].

Blood culture for leptospirosis requires samples during the first week of illness. Culture of leptospires can be performed using a special medium, but takes time for growth.

There are several serological techniques available to check for antibodies against Leptospira. The gold standard is the microscopic agglutination test (MAT), but there are commercially available ELISA-based test kits to detect IgG and IgM antibodies. MAT is very sensitive in the early stages of infection, with a titer value of > 400 considered a positive test. ELISA is used to detect IgM antibody in the early stage of infection [30]. ELISA tests become positive after the 6th day of disease onset [32].

Polymerase chain reaction (PCR) has been deemed to be a rapid diagnostic tool on admission, and may be positive even with very low levels of leptospiral DNA [32, 34]. One drawback of serologic testing Is the inability to differentiate earlier or past infections. It is suggested to coordinate testing with one's laboratory capabilities.

Prevention includes avoiding contacts with water bodies which are likely to contain urine from rodents, cattle, pigs, or other domesticated animals. Chemoprophylaxis with penicillin or doxycycline has been proposed [30].

As noted above, many cases of leptospirosis are subclinical or resolve spontaneously. Cephalosporins such as ceftriaxone, penicillin, doxycycline, or azithromycin have proven effective. Mild outpatient cases can be managed with doxycycline or azithromycin. Pregnant women can be treated with amoxicillin or azithromycin. For mild disease and no evidence of organ involvement, doxycycline 100 mg twice daily for 7 days is suggested [31].

Patients with severe disease (Weil's) will require more intensive care and supportive therapy. Penicillin G 1.5 million units every 6 h or ceftriaxone 1 g twice daily may be used, with azithromycin or doxycycline for patients allergic to penicillin.

No vaccine is currently available [31]. Vaccine development has been difficult due to the high number of strains- literally in the hundreds. As well, the renal carrier state can last for months or even years, and leptospiral cells can survive in distilled water for months, making the disease difficult to eradicate [30].

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Data Availability No datasets were generated or analysed during the current study.

Declarations

Conflict of Interest The authors declare that they have no conflict of interests.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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