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COMMENTARY/POLICY

Primary Amoebic Meningoencephalitis and the *Naegleria fowleri* Freshwater Amoeba: A New Concern for Northern Climates

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ABSTRACT

Naegleria fowleri (N fowleri), the freshwater amoeba known to cause primary amoebic meningoencephalitis (PAM), is historically found in the southern United States and Central America. Increased incidence of this rare, deadly, and often misdiagnosed illness in northern states causes concern that *N fowleri* is expanding northward due to climate change, posing a greater threat to human health in new regions where PAM has not yet been documented. This case study provides an example of public health nurses incorporating environmental health data into communicable disease investigations, demonstrating how public health professionals, health care providers, and individuals living in northern climates can work together to prevent, detect, and treat *N fowleri* infection.

INTRODUCTION

Communicable Disease Investigation Case Study

During a recent summer, a public health nurse (PHN) working at a local public health department in the northern midwest United States received notice from the infection control nurse (ICN) at the local hospital of a suspected bacterial meningitis case. A female in her mid-30s, and mother of a young child, was unconscious upon arrival to the local emergency department via emergency medical services transport, having recently developed neurological symptoms including severe headache, photosensitivity, nausea, and confusion. Her long-term personal medical history included a bicycle accident 10 years prior that caused facial trauma and septum deviation.

The PHN immediately opened a communicable disease investigation under the case classification suspect bacterial meningitis. The PHN interviewed the patient's spouse via phone regarding potential sources of exposure. Responses to investigative questions (including close contact with other symptomatic individuals prior to and since symptom onset and contact tracing based upon bacterial meningitis communicability guidelines) were unremarkable. However, the spouse and child had experienced confirmed or potential direct contact with the mother's oral secretions that would merit medication to prevent the development of illness. As the PHN broadened questions to capture other activities occurring in the 2 weeks prior to symptoms, the spouse stated that 4 days ago the family had traveled to a public-access beach at a freshwater lake in a neighboring county where the patient swam and submerged her head. The PHN coordinated the prescription of post-exposure medication to prevent the development of illness in household contacts via their primary care providers, educated the family to watch for signs and symptoms of bacterial meningitis, and instructed them to report symptoms immediately for rapid treatment should they occur.

Diagnostic Test Results

Cerebrospinal fluid (CSF) cultures yielded no bacterial growth, and CSF findings were also inconsistent with bacterial infection. No viral infection was detected in CSF; however, conventional laboratory techniques may fail to detect infectious agents, leaving up to 60% of presumed viral encephalitis cases unexplained.[1] The case classification in the communicable disease reporting system was then updated to suspect viral (aseptic) meningitis (Table 1). The

Table 1. Epidemiological Comparison of Primary Amoebic Meningoencephalitis, Bacterial Meningitis, and Viral (Aseptic) Meningitis

	Primary amoebic meningoencephalitis[2,3,4]	Bacterial meningitis[5,6]	Viral (aseptic) meningitis[7,8]
Organism	*N fowleri* amoeba (protozoan)	Most common: Neisseria meningitidis, Streptococcus pneumoniae, and Haemophilus influenza Group B	Most common: Non-polio enteroviruses; may also be caused by measles, mumps, varicella-zoster, Epstein-Barr, influenza, and other viruses
Source/ Reservoir	Warm, untreated freshwater/soil	Humans	Humans
Mode of transmission	Contact of contaminated water to nasal membrane; not infectious via ingestion	Spread by respiratory droplet or direct contact with respiratory secretions; sharing cups or utensils, kissing, coughing	Transmission varies by virus; infection may occur in contacts but is unlikely to cause meningitis.
Incubation period	Range 1-9 days (median 5 days) after exposure	Range 1-10 days (median 3-4 days) after exposure	Varies by virus
Period of communicability	Not contagious from person to person	Immediately following symptom onset until at least 24 hours after treatment with appropriate antibiotics	Varies by virus
Signs/Symptoms	Stage 1: Severe frontal headache, fever, nausea/vomiting Stage 2: Stiff neck, seizures, altered mental status, hallucinations, coma	Fever, headache, and stiff neck in meningococcal meningitis cases, (sepsis and rash in meningococcemia)	Fever, headache, stiff neck, photophobia, somnolence, nausea, irritability, vomiting, anorexia, lethargy
Prognosis	Usually fatal (94.6-97%); postmortem diagnosis	10-15% mortality; up to 20% of survivors experience long-term disability including loss of limb(s), deafness, nervous system problems, or brain damage	Usually resolves spontaneously in 7-10 days

ICN reported to the PHN that the patient's condition was worsening, increasingly inconsistent with viral meningitis, and the infectious disease team used the working diagnosis of meningoencephalitis, but diagnostic testing remained inconclusive.

Public Health Nursing Actions

As the infectious disease team manages aspects of direct patient care and treatment of communicable disease, the public health department is responsible for considerations of disease transmissibility and outbreak prevention. In this case, given the absence of detectable pathogens, the patient's deteriorating condition, no known symptomatic contacts, and the continued search for noninfectious causes, the PHN has a set of expected interventions. These include prophylaxis coordination for close contacts, symptom education for the family, preparations for rapid close-contact treatment response and outbreak case management, community surveillance of other potential cases, and follow-up with the ICN for confirmatory updates as details emerge.

The PHN was faced with 3 possible outcomes impacting case reporting and management. If symptoms resolve spontaneously, leading the infectious disease team to conclude the cause was likely viral, the patient will recover and the case may be closed under the classification confirmed viral (aseptic) meningitis. If a noninfectious cause is identified, the case may be closed under the classification viral (aseptic) meningitis—not a case regardless of patient outcome. However, if the PHN were to leverage the interdisciplinary nature of public health practice to pursue the patient's environmental exposure as a potential cause of meningoencephalitis, an effective treatment method may be found for the patient. With support from the medical director, the PHN chose to consult the Bureau of Infectious Diseases at the state department of health for expertise related to potential meningoencephalitis cases of unknown etiology in humans related to exposure to fresh water.

Possible Cause

The state department of health contacted the Centers for Disease Control and Prevention (CDC). The CDC offered the state department of health a small number of collected case reports from the southern United States and Central America describing patients with similar neurological symptoms who had a recent history of swimming in warm freshwater ecosystems. Case reports indicated the cause of infection was the amoeba *Naegleria fowleri* (*N fowleri*).

Naegleria fowleri and Primary Amoebic Meningoencephalitis

N fowleri is a thermophilic amoeba occurring in warm, untreated freshwater, soil, and dust that is known to cause primary amoebic meningoencephalitis (PAM) in humans. Primary amoebic meningoencephalitis is a necrotizing, hemorrhagic, and often fatal meningoencephalitis occurring most frequently in healthy children and young adults with a history of recent contact with untreated fresh water.[9]

Not infectious through oral ingestion, water vapor, or human-to-human transmission,[10] *N fowleri* infects by entering the nose via contaminated water, crossing the nasal membrane, and following the olfactory nerve through the cribriform plate to the brain.[9,11] The incubation period typically ranges from 1 to 9 days (median 5 days) after exposure.[2] The rapid onset of neurological symptoms may be categorized as early (flu-like symptoms including headache, fever, nausea, and vomiting) or late (central nervous system signs including stiff neck, seizures, altered mental status, hallucinations, and coma).[2,3] Cerebrospinal fluid analysis may resemble

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bacterial meningitis (high opening pressures, elevated white blood cell counts, and elevated protein levels). Abnormal imaging results are present in most cases but are not diagnostic for amoebic infection.[2] Disease progression is often too rapid for premortem diagnosis and intervention, leading to case fatality in 1 to 18 days (median 5 days) after symptom onset.[2] While a treatment regimen including the current gold standard medication for free-living amoeba infections, miltefosine, and therapeutic hypothermia have been successful in some cases, PAM is usually fatal (94.6% to 97%) and often diagnosed postmortem.[9,11-13]

Naegleria fowleri Life Cycle and Transmission

N fowleri has 3 stages: cyst, trophozoite, and ameboflagellate.

The thermophilic *N fowleri* is most prolific in water temperatures up to 115 °F (46 °C) but is tolerant of even higher temperatures for short periods, making it able to easily withstand human fever. If environmental conditions become cold, nutrient depleted, or dry, the trophozoite can revert to a non-feeding form for protection from freezing water temperatures.[14]

Because *N fowleri* infects via the nasal membrane, activities that push contaminated water into the nasal cavity are epidemiologically associated with infection. This includes swimming, splashing, and submersion in naturally occurring bodies of freshwater, such as lakes, ponds, hot springs, and reservoirs[15] (Figure 1). In addition to geographical changes in recent years, novel routes of transmission have been documented, including warm hose water, lawn water slide and splash pad use, and exposure of the nasal membrane to tap water from private well systems, which has been known to occur when using a nasal irrigation device at home.[16,17]

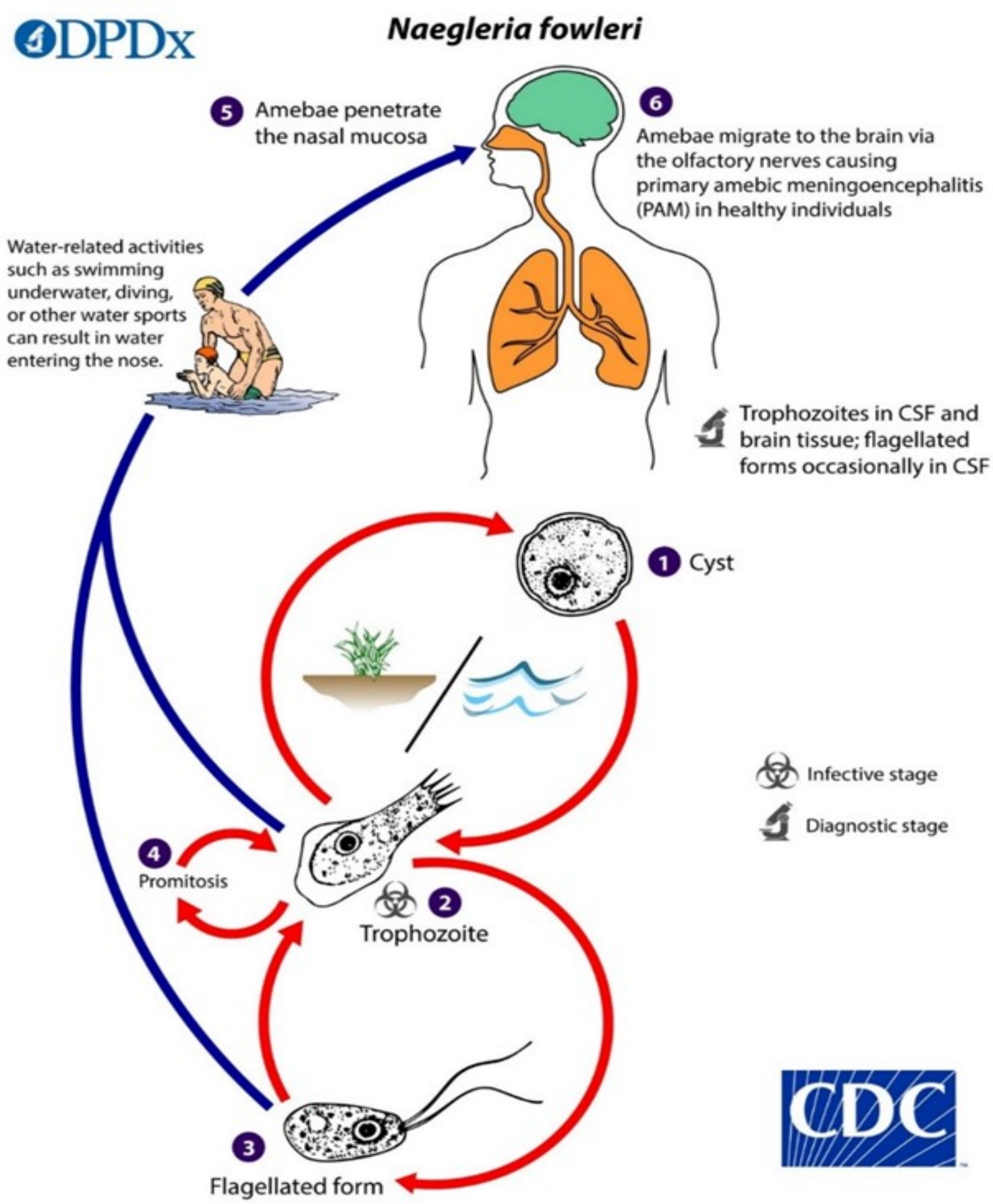

Figure 1. Transmission of *Naegleria fowleri* to a Human Host

Naegleria fowleri Incidence and Climate Change

Historically, *N fowleri* cases in the US have been known to occur in southern states, but recent data indicate an increased incidence since 2010 in northern states such as Minnesota, Indiana, and Missouri.[2,16,19,20] The incidence of *N fowleri* infections is historically rare; 138 PAM cases were reported in the US from 1962 to 2015 with a range of 0 to 8 cases annually.[16] Patients have been predominantly male (76%) and less than or equal to 18 years of age (83%, N = 142).[2]

Climate change data indicate consistent increases in surface water temperatures, increasing the likelihood that *N fowleri* will pose a greater threat to human health in regions with a history of occurrence and new regions where PAM has not yet been documented.[13,19-22] Despite its rarity, the severity of illness and poor patient outcomes make the increased incidence of PAM in northern climates an emerging health concern. Combined with increased incidence in northern climates, untrained and unaware public health professionals and health care providers may exacerbate prolonged diagnostic periods and delay time-sensitive treatment in what is ultimately a quick decline for PAM patients.

Case Study Outcome

Acting in the role of liaison between direct care personnel and state/national public health entities, the PHN obtained and relayed evidence pertinent to the case for health care provider review. Information regarding miltefosine availability and dosage were communicated from the CDC team (this product has since become commercially available). The patient responded favorably to the medication. Two weeks after symptom onset, she recovered with minimal neurological damage and was able to resume a high quality of life with her family.

Primary Amoebic Meningoencephalitis Prevention

Effective treatment is essential when confronting PAM, but tertiary prevention is only one aspect of proactive care. When confronting any condition of public health importance, be it a reportable communicable disease, rare illness of environmental etiology, or chronic disease impacting a substantial portion of the population, interventions focused on secondary and primary prevention are crucial. Below are recommendations for public health professionals, health care providers, and individuals to take regarding *N fowleri* in northern regions.

Public health professionals: In northern climates, consider monitoring warm, freshwater recreational sites for presence of *N fowleri* amoebae.[9] As repeated cases have been documented in the same freshwater lake over years, perform public education and outreach to inform visitors to freshwater recreational sites.[16] Integrate environmental exposure screening into meningitis case investigation protocols; if PAM is suspected, immediately contact the Centers for Disease Control and Prevention at (800) 232-4636 in concert with the health care provider.

Health care providers: Incorporate environmental exposure screening into initial patient assessment for suspect meningitis cases. Regardless of geography, consider PAM in the differential diagnosis for meningitis[16] and, if suspected, immediately contact the public health department.

Individuals: When swimming in freshwater, do not splash or submerge your head. Maintain adequate chlorine concentrations in water distribution systems, especially those with elevated temperatures, to inactivate *N fowleri* cysts and trophozoites.[16] If neurological symptoms occur, seek care quickly and report environmental exposures if applicable.

PUBLIC HEALTH IMPLICATIONS

Within the last century, Ohio temperatures have increased approximately 1 °F and up to 2.35 °F in the northeastern portion of the state.[23] The popularity of Ohio's state parks, of which 71% offer freshwater swimming access and 97% allow fishing,[24] increased due to the COVID-19 pandemic. Ohio public health professionals should take note of the incidence of *N fowleri* infections in northern states including Indiana, Iowa, and Minnesota, as well as common vacation destinations for Ohioans where *N fowleri* infection has been reported, such as Virginia, North Carolina, South Carolina, Georgia, and Florida.[10]

Increased incidence of *N fowleri* in northern climates is but one of many ways climate change threatens human health and merits novel education of health care providers. Health care providers, especially those working in northern climates, should be prepared for increases in waterborne and vector-borne diseases, air quality issues, extreme weather events, impacts on food production, and temperature-related death and illness.[25] It is crucial for nurses in public health and direct care settings to seamlessly collaborate when providing patient care for those with reportable communicable diseases and their contacts, especially those with suspected environmental exposures.

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