

Review

Naegleria fowleri, the “brain-eating amoeba”: an invisible enemy in nasal irrigation with untreated water

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SUMMARY

In a world where the search for natural and simple solutions for everyday health problems is increasingly widespread, practices such as nasal irrigation with tap water have gained popularity for relief from conditions such as rhinosinusitis. However, this seemingly harmless practice hides an invisible and potentially fatal risk: infection by *Naegleria fowleri*. Known as the “brain-eating amoeba”, this microscopic threat turns a personal care gesture into a potential deadly danger. This review emphasizes the implications of using untreated water for nasal irrigation, highlighting the critical importance of water choice as a means of prevention against primary amoebic meningoencephalitis (PAM).

KEYWORDS: *Naegleria fowleri*, nasal irrigation, infection

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INTRODUCTION

Naegleria fowleri, a thermophilic free-living amoeba, is the etiological agent of primary amoebic meningoencephalitis (PAM), a rare but almost universally fatal condition ¹. *Naegleria fowleri* exists in three stages: cysts, trophozoites, and flagellates, with the trophozoites being the infective form for humans. This amoeba prefers warm environments (27-37°C) and feeds on Gram-positive and Gram-negative bacteria, yeasts, and algae ². Transmission occurs when water containing *Naegleria fowleri* enters the human body through the nasal cavities ³, typically during activities that involve submerging the head in water or through the practice of nasal irrigation with contaminated water ^{1,4,5}. Once in the nasal environment, *Naegleria fowleri* migrates to the brain through the olfactory nerve, penetrating the cribriform plate, a thin perforated bone barrier that separates the nasal cavity from the brain. This direct pathway to the central nervous system is what makes the pathogen particularly dangerous ^{1,2,4}. Once in the brain, the amoeba begins to destroy brain tissue, causing inflammation and edema. The symptoms of PAM develop rapidly and can include severe headache, fever, nausea, vomiting, neck stiffness, confusion, loss of balance, seizures, and, in many cases, rapidly leads to coma and death. The rapid progression of the disease, from a few days to about a week from the onset of symptoms to death, makes prevention essential and, in the case of suspected infection, immediate medical intervention ¹.

PAM is characterized by a high mortality rate, about 98%, and death typically occurs less than two weeks after the onset of symptoms, making it the world's most lethal parasitic infection. Treatment options are limited, as drugs have difficulty crossing the blood-brain barrier (BBB) to eliminate the parasite, contributing to its high mortality rate ².

TABLE I. Some of the antibiotics used for treatment of PAM.

Antibiotic	Dosage	Mode of Administration	Duration	Notes	Reference
Amphotericin B	Intravenous: 0.25 to 1.5 mg/kg/die Intrathecal: 1.5 mg/die for 2 days then 1 mg/die	Intravenous and Intrathecal	IV: 10-14 days IT: 10 days	Cornerstone of therapy, used with or without therapies	9, 10
Miltefosine	50 mg orally two to three times daily, with a max dose of 1.5 mg/kg/die	Oral	28 days	Showed promise when early diagnosis is made; part of successful treatment in survivor cases	10
Fluconazole	10 mg/kg/day once daily (max 600 mg/day)	Intravenous	28 days	Considered an add-on therapy to amphotericin B; penetrates into CNS	10
Azithromycin	10 mg/kg/day once daily (max 500 mg daily dose)	Intravenous	28 days	Tested in vitro; growth at concentration of 10 and 100 µg/ml	10

IV: intravenous; IT: intrathecal.

Initial symptoms can be vague and mimic other conditions, such as bacterial meningitis. Confirmatory diagnostic tests include direct visualization of the amoeba or the use of the polymerase chain reaction (PCR) method⁶⁻⁸. Treatment for PAM caused by *Naegleria fowleri* includes the use of monotherapy with miltefosine or combined therapy with amphotericin B, rifampicin, miconazole, fluconazole, and doxycycline (Tab. I), depending on the patient's conditions^{9,10}.

To conduct the literature review, a systematic search was performed using scientific databases such as PubMed and Google Scholar with keywords like '*Naegleria fowleri*', 'nasal irrigation infection', and 'primary amoebic meningoencephalitis'. The selected articles were analyzed for relevance and scientific validity, including case studies, reviews, and epidemiological research published in the last 30 years. The reviewed articles^{11,13} highlight the growing importance of recognizing the risk factors associated with the use of unsafe water for nasal irrigation.

Research shows that *Naegleria fowleri* can survive and multiply in wells^{14,15}, cisterns¹⁶, in domestic water systems¹⁷⁻¹⁹, including drinking water distribution networks, and that the practice of nasal irrigation, especially when performed with untreated or insufficiently treated tap water, can increase the risk of PAM^{11-13,20}.

EPIDEMIOLOGY

Considering all transmission routes, cases of PAM have been reported in more than 20 countries across all continents except Antarctica. There is a higher incidence of cases in the United States, particularly in the southern states where temperatures are higher⁶.

Extensive research has revealed about 260 cases of PAM worldwide from 1962 to 2014 (Fig. 1), with 17 cases in Pakistan, 132 in the United States, 7 in Venezuela, 9 in Mexico, 19 in Australia, 9 in New Zealand, 11 in India, 4 in Nigeria, and one case each in Namibia, Iran, Costa Rica, Papua New Guinea, South Africa, and Madagascar. There have been 5

cases reported in Thailand and Belgium, 16 in the Czech Republic, and 2 in the United Kingdom. This condition is almost always fatal, with a mortality rate of over 95% and only 11 survivors worldwide⁹. In Europe, most cases of infection occurred in France. This distribution pattern underlines the presence of *Naegleria fowleri* in different climatic regions, extending from temperate to tropical and subtropical climates, implying that various environmental, cultural, and recreational practices contribute to the spread of this pathogenic amoeba²¹ and that the disease can occur in any area where environmental conditions are favorable.

Cogo et al.²² reported the first case of PAM in Italy, diagnosed post-mortem in a 9-year-old immunocompetent child in 2003. The child had swum in a polluted water hole in the Po River 10 days before symptom onset. The diagnosis was confirmed through histopathological examination of the brain. Genetic typing by PCR identified the amoeba as *Naegleria fowleri* genotype I, a strain previously identified also in France, Hong Kong, and the United States. A systematic review⁶ explores the global distribution of *Naegleria fowleri*. Cases vary in age from infancy up to 75 years, demonstrating that the infection can affect a broad demographic spectrum. Most infections occurred following exposures to freshwater sources, such as recreational activities in lakes, rivers, or water parks, or from the habit of irrigating the nostrils⁶.

DISCUSSION

Sazzad et al.¹³ presented the first recognized case of primary amoebic meningoencephalitis (PAM) caused by *Naegleria fowleri* in Bangladesh, affecting a 15-year-old boy. The patient practiced daily nasal washes with untreated well water. The disease led to the boy's death within 6 days from the onset of symptoms.

In 2012, in St. Thomas, in the US Virgin Islands, the first documented case of death from PAM in the territory was caused by *Naegleria*

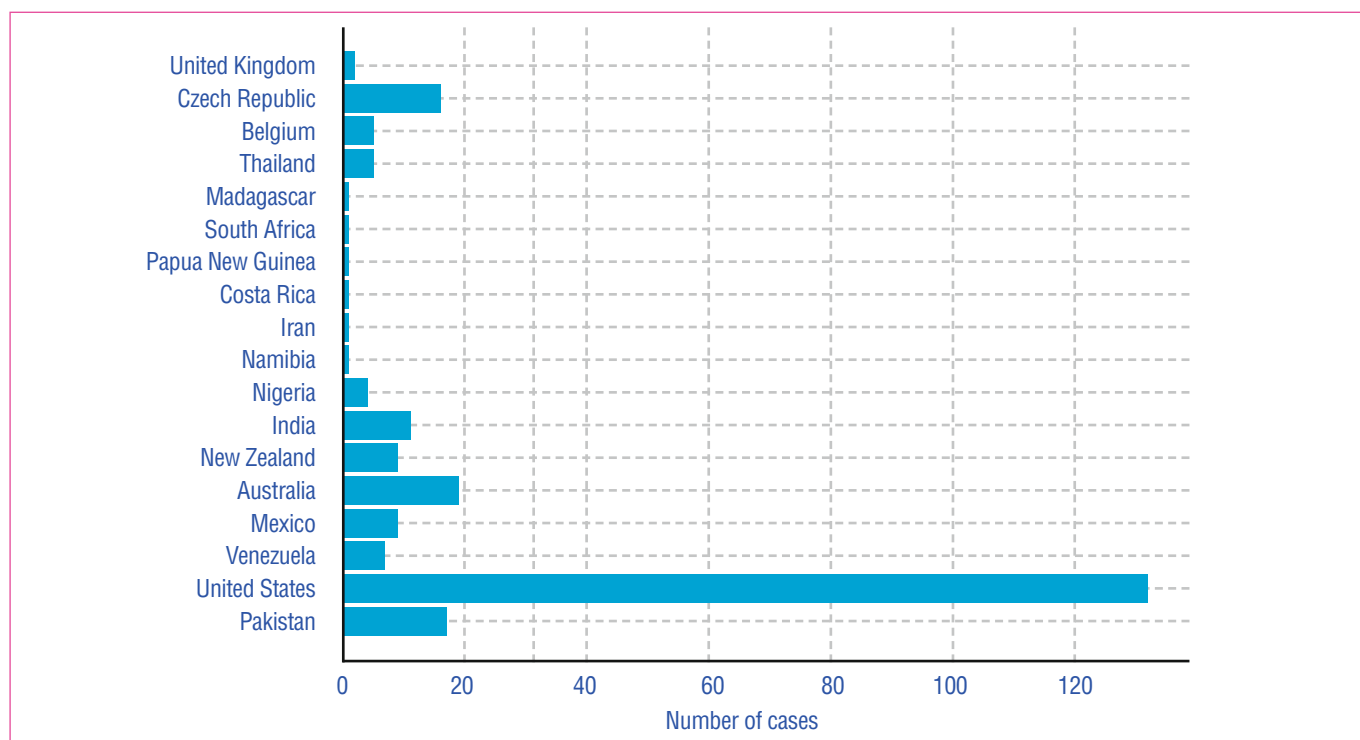


FIGURE 1. PAM cases worldwide between 1962-2014.

*fowleri*¹². The patient was a 47-year-old man who had no known exposures to recreational fresh water, but used tap water for daily household activities and ablution, a ritual cleansing practiced several times a day in preparation for prayer, which included nasal rinsing. A subsequent environmental investigation revealed that the patient's household water sources were untreated groundwater from a well and untreated rainwater from a cistern, both connected to the home's plumbing system, with no connections to municipal water. This case highlighted how exposure to *Naegleria fowleri* and the subsequent development of PAM can also occur through practices such as ablution that include nasal rinsing, in addition to more common recreational exposures in fresh waters.

Yoder et al.¹¹ examined two fatal cases of PAM associated with the use of nasal irrigations with tap water contaminated by *Naegleria fowleri* in Louisiana in 2011. These are the first reported cases in the United States associated with the presence of *Naegleria fowleri* in home plumbing served by treated municipal water supplies and potentially linked to the use of nasal irrigation devices, such as neti pots. Both patients regularly practiced nasal irrigation with tap water, and environmental investigations confirmed the presence of *Naegleria fowleri* in their homes. These cases draw attention to the expanding geography of PAM beyond the southern states of the USA, with recent cases also reported in Minnesota, Kansas, and Virginia. The case highlights the need to implement and maintain stringent water treatment and disinfection protocols in public infrastructure,

including adequate chlorination, to reduce the risk of PAM. Najia et al.²⁰ illustrated the case in 2014, in Karachi, Pakistan, of a 34-year-old man with no previous exposure to recreational waters, who died from PAM caused by *Naegleria fowleri*. This case led to investigations on the presence of *Naegleria fowleri* in household and municipal water sources. Twenty-three samples were collected from two water treatment plants and their distribution areas. Plant A, which had not received a chlorine boost, supplied water to the patient's residence. Plant B had received a chlorine boost following previous PAM cases. Results confirmed the presence of *Naegleria fowleri* in water distributed by Plant A, but not in that of Plant B. The lack of residual chlorine and water temperatures above 30°C in household sources might have provided favorable conditions for the proliferation of *Naegleria fowleri*. These findings underline the importance of maintaining adequate levels of residual chlorine in drinking water and distribution networks to prevent *Naegleria fowleri* contamination. Infection could have been contracted through domestic water use, including potentially ablution or other practices involving water contact with the nostrils.

In Canada, a cross-sectional survey²³ revealed that despite recommendations to use distilled, bottled, or boiled water for nasal irrigation, 48% of patients used tap water, primarily for convenience. This study highlights the challenges in following preventive recommendations and the importance of raising awareness about safe water use.

Some of these reports describe cases of PAM following the use of nasal irrigation devices, such as neti pots, with tap water contaminated by *Naegleria fowleri*, highlighting the need for precise guidelines for safe water use in nasal irrigation practices. Current recommendations suggest the use of distilled, sterilized (boiled for at least 1 minute and then cooled), or filtered water through filters with pores small enough to remove the amoeba as preventive measures against infection^{10,24,25}. In particular:

1. Water Chlorination: a case illustrated that even though the water came from a water system that supposedly received chlorinated treatment, the amoeba was found in home plumbing, indicating that the treatment was not sufficient or that residual chlorine was absent or inadequate in the farthest parts of the distribution system. This suggests the importance of ensuring an adequate level of residual chlorine throughout the water network to prevent the survival and proliferation of the amoeba^{20,24,25};
2. Prevention Measures: to reduce the risk of exposure to *Naegleria fowleri*, the use of distilled, sterilized (boiled for at least 1 minute and then cooled), or filtered water through filters with pores small enough to remove the amoeba is recommended^{20,24-27};
3. Maintenance and Cleaning of Water Tanks: some cases have highlighted that storage tanks for untreated or insufficiently treated water can serve as habitats for *Naegleria fowleri*. It is important that domestic water tanks are regularly cleaned and disinfected to eliminate contaminants and prevent the growth of amoebae^{24,28}.

Four genera of amoebae are known to be associated with human diseases: *Acanthamoeba* spp., *Balamuthia mandrillaris*, *Naegleria fowleri*, and *Sappinia diploidea*²⁴.

While tap and drinking water in the United States is extremely safe, thanks to techniques such as coagulation, flocculation, sedimentation, filtration, and disinfection, water sources can become contaminated. Research on public drinking water distribution systems using methods such as nucleic acid sequencing has shown that amoebae and various bacteria are present in drinking water in the United States²⁴. The greatest challenge in controlling *Naegleria fowleri* lies in home plumbing systems, where conditions are largely outside the control of utilities, chlorine residuals might be low or nonexistent, and water temperatures may be high enough to support rapid growth of amoebae. It is crucial to maintain adequate levels of residual chlorine and control water temperature in distribution systems to prevent the growth of *Naegleria fowleri*^{29,30}.

The FDA and CDC have both outlined recommendations for nasal irrigation to mitigate the possibility of *Naegleria fowleri* infection, which include the use of distilled or boiled then cooled water, filtered using specific devices, or disinfected with chlorine bleach²⁴.

CONCLUSIONS

PAM from nasal and sinus irrigation is an extremely rare but deadly disease. Although there are few reported cases, PAM is preventable

if appropriate guidelines are followed. The safest water sources for nasal and sinus irrigation are distilled water and boiled tap water that has been allowed to cool, as no cases have been reported following these types of water preparation^{24,26,27}.

Water analysis by health authorities, particularly in regions with known cases of PAM, along with public awareness about the risk associated with the use of unsafe water for nasal washing, are crucial in preventing this lethal disease. Educating patients on the correct preparation and hygiene practices for nasal irrigation devices can significantly reduce the risk of exposure to *Naegleria fowleri*. A thorough understanding of the transmission mechanisms of *Naegleria fowleri* and the implementation of prevention strategies based on scientific evidence are essential to protect public health. Collaboration among healthcare professionals, researchers, and public authorities is crucial to increase awareness and promote safe water use practices for nasal washings in order to minimize the risk of potentially fatal infections like PAM.

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Conflicts of interest statement

The authors declare no conflict of interest.

Ethical considerations

Not applicable.

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Authors' contribution

CI, SC, GM: conceptualized the project. CI, SC, GM, AP, VT: wrote the first draft. All authors revised the manuscript and approved the final version.

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