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# Article Review: Parasitic Infection of Naegleria Fowleri (Symptoms, Histological Changes on Brain Tissue, Prevention and Treatment)

**Suadad Breesam Khiri**
Department of Biology, College of Education for Pure Science, University of Wasit, Iraq

**Asawer Abdul Jabbar Al- Salman**
Department of Biology, College of Science, University of Wasit, Iraq

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**Annotation:** The small, single-celled creatures known as free-living amoebas do best in freshwater environments. Of the four primary forms that can infect humans, Acanthamoeba species and N. fowleri (Naegleria) are the most troublesome. In order to produce primary amoebic meningoencephalitis (PAM), They are capable of infiltrating the body by the nose then go to the brain, Later they begin to necrotise tissue and induce cerebral oedema. Infections have been connected to breathing in polluted dust, and Naegleria can also live in soil by developing latent "cysts.". Even though there have only been 381 cases of PAM documented throughout the medical literature until 2018, it is incredibly deadly—just seven people out of the 381 cases survived. Because of the low level of medical awareness and the fact that the symptoms resemble bacterial and viral meningitis, which can manifest in certain regions where Naegleria flourishes, it is also possible that many cases go unreported.

Hot and humid regions of the world

record occasional occurrences each year, which are often fatal. Clusters of infections have also been observed connected to tainted water sources, these diseases typically occur in persons who have been swimming in non- chlorinated lakes, rivers, or pools. Although N. fowleri (Naegleria) infections are now uncommon, scientists are worried that as a result of climate change, these and other harmful amoebas may spread their ranges closer to the poles, exposing more people to contaminated water (Linda Geedes , 2024).

A disease-causing flagellate amoeba that is thermophilic and non-parasitic is Naegleria fowleri. Typically found in warm freshwater areas, N. fowleri can withstand temperatures as high as 45% and mostly feeds on bacteria. The trophozoite stage, which is also its reproductive phase, is the most contagious stage. It needs favorable conditions to manifest in this stage.. When water tainted with N. Fowleri is forcefully absorbed during aquatic activities such as swimming and ablution, it enters the body mostly through the olfactory pathway ( Jahangeer et al . , 2020) .

"Brain-eating amoeba Naegleria fowleri is the etiological organism of primary amoebic meningoencephalitis (PAM), a rare yet lethal infection.. Over the past few decades, the number of confirmed PAM cases has increased along with their geographic distribution. The clinical prognosis for PAM is still dire, with a mortality rate exceeding 95%, and there is currently no viable treatment. It is yet unknown how the immune response affects the severity and prevention of disease

(Moseman and Ching, 2022 ).

**Keywords:** Parasitic Infection, Naegleria fowleri, Histological Changes.

**Symptoms**

Fever, excruciating headaches, nausea, vomiting, light sensitivity, seizures, and changed mental state are some of the symptoms. Due to the condition's rapid progression and difficulty in diagnosis, finding appropriate treatments has been somewhat different. Five documented survivors in the United States received treatment using a mix of steroid medications, antibiotics, and antifungals (Linda Geedes , 2024) .

The result of a *N fowleri* infection is amebic meningoencephalitis. The central nervous system become contaminated when exposed to hot freshwater penetrates the nasal cavities and traverses the plate known as the cribriform. Between one and fourteen days may pass during the incubation phase before encephalitis symptoms appear.. PAM symptoms include fever, headache, stiff neck, vomiting, anorexia, and seizures, which resemble the symptoms of bacterial or viral infections. For this reason, *Naegleria fowleri* is often frequently referred to as "brain-eating."amoeba". Because of this resemblance, doctors find it challenging to make an early diagnosis. Within three to seven days of the onset of symptoms, PAM can be fatal (Yoder *et al*., 2010).

**Pathophysiology**

Once freshwater infiltrates the nasal passages under pressure, as occurs When swimming or diving, the amoeba infiltrates the brain and spinal cord , via the nasal passages. People who used antibiotic with tainted water have also contracted the infection. The amoeba infiltrates the olfactory mucosa and respiratory epithelium subsequent to nasal injection. After thatIt enters the central nervous system through the cribriform plate ( Jarolim *et al* ., 2000) . In the brain tissue, *N fowleri* results in tissue necrosis, large cortical hemorrhages and edema . The area most frequently impacted are olfactory bulbs, the cerebellum, , and a basilar section of the frontal cerebri. There is a notable innate immunological response to *N fowleri*. Nitric oxide synthesis, the protein Nfa1 and pore-forming proteins are all necessary for its pathogenicity. Nfa1 facilitates amebic adhesion to designated cells. Its consuming cups, that they use to eat fungus and bacteria from the environment, help the creature directly engulf cerebral cells . Widespread Necrosis is facilitated by the ejection of cytolytic chemicals such as phospholipolytic enzymes, phospholipases and cysteine proteases, and. In primary amebic encephalitis, the virulence and strong immune response of this organism cause a substantial loss of brain parenchymal tissue (Marciano and Cabral , 2007 ).

**Differential Diagnosis**

PAM's clinical manifestation can almost exactly resemble that of any infectious encephalitis. The diagnosis may be difficult due to the absence of pathognomic symptoms on imaging and physical examination, as well as the CSF analysis's resemblance to bacterial encephalitis.. By increasing the suspicion of PAM, a comprehensive history that elicits potential freshwater exposure can help guide the diagnosis (Siddiqui *et al*., 2016).

**Prevention**

People can take certain preventative measures on their own to avoid contracting this amoeba. Before rinsing their nasal passages during ablution, etc., people should avoid using untreated tap water and filter it (using a filter with an absolute particle size of 1 μm or less) or use distilled bottles of water for this purpose (Jahangeer *et al*. , 2020) . People should ensure that swimming pools are adequately chlorinated before engaging in leisure activities like swimming. They should

also avoid getting water in their noses and steer clear of water- related activities during hot weather, such as the summer (Yoder *et al*., 2012) .

### *Naegleria fowleri,* induces infammatory responses in BV-2 microglial cells in vitro

The amoeba could permeate the mucosa of nasal, by olfactory nerves can travel to the brain, and in the central nervous system (CNS) cause deadly pathologic events when its actively reproducing trophozoites infect humans through the nose (Grace *et al*., 2015) . Within seven to ten days of infection, this amoeba can cause severe brain damage that manifests as acute hemorrhagic inflammation and ultimately leads to death. The host's intrinsic immunity is triggered to release mucin during the early stages of *N. fowleri* infection, which can prevent amoeba adherence the host cells and shield host cells (Cervantes *et al*., 2008 ). Massive bleeding and fatal necrosis of leukocytes and cerebral tissues are the results of severe inflammatory reactions that lead to tissue damage when the amoeba enters the brain after surmounting the host's first immune reaction (Cervantes *et al*., 2009).The two main pathogenic mechanisms that the amoeba uses to cause death The inflammatory response and interactions within the host cell occur through both contact-dependent and contact-independent mechanisms (Marciano and Cabral, 2007).

*N. fowleri* trophozoites' aggressive trogocytosis, which destroys host cells after direct contact, is probably the main harmful event that the amoeba causes. Contact-independent mechanisms, on the other hand, are indirect pathogenic events that are mostly brought on by various amoeba-secreted or released proteins and cytolytic agents (Lee *et al*., 2017).

The pathogenic protozoan parasites' cysteine proteases are essential to their life and pathogenicity (McKerrow *et al*., 2006). Through mediation crucial biological phenomena of parasites and regulating host immune responses, they essentially participate in a variety of processes, such as invasion, nourishment, survival of parasitic protozoa , development, and pathogenesis (Rosenthal, 2020 ; Rawat *et al*., 2021). *N. fowleri* secretory proteins called cathepsin B family cysteine proteases are probably implicated in amoeba pathogenicity by promoting amoeba invasion and influencing host immunological responses (Lee *et al*., 2014). Nevertheless, it is still unclear what these enzymes' biological functions are and how they contribute to PAM. To further our comprehension of the biological roles of *N. fowleri* cathepsin B enzymes linked to pathogenic occurrences in PAM, we must look into the fundamental molecular processes of these enzymes concerning the human immune response.

### Current Treatment Protocols

Less than 3 percent of patients in the approximately 60 years of PAM cases linked to *N. fowleri* infection have survived. Because *N. fowleri* infections are uncommon, fast-acting, and nearly lethal, clinical trials are quite challenging. Prior case reports or in vitro research established the therapies, and The Centers for Disease Control and Prevention of the United States (CDC) standard of care (Table 1) is mostly derived from empirical evidence obtained from case reports (CDC, 2024).

**Table 1.** Treatment guidelines for primary amoebic meningoencephalitis

| Compound | Route of Administration and Dosage Information |
|---|---|
| **Amphotericin B** | Intravenous<br>Day 1–3: 1.5 mg/kg/day in 2 divided doses<br>Day 4–14: 1 mg/kg/day once daily<br>OR<br>Intrathecal<br>Day 1–2: 1.5 mg once daily<br>Day 3–0: 1 mg/day every other day |
| **Miltefosine** | Oral<br>Weight < 45 kg, 50 mg twice daily<br>Weight > 45 kg, 50 mg thrice daily<br>Duration: 28 days |
| **Fluconazole** | Intravenous or oral<br>10 mg/kg/day once daily<br>Duration: 28 days |
| **Rifampicin** | Intravenous or oral<br>10 mg/kg/day once daily<br>Duration: 28 days |
| **Azithromycin** | Intravenous or oral<br>10 mg/kg/day once daily<br>Duration: 28 days |
| **Dexamethasone** | Intravenous<br>0.6 mg/kg/day in 4 divided doses<br>Duration: 4 days |

## Nanomateria is Demonstrating Efficacy in Vitro

There are several potential applications for the quickly expanding field of nanomaterials in medicine. When conjugated to a nanomaterial, certain therapeutic agents exhibit improved physicochemical and biological stability and could enable regulated drug release, which is advantageous when trying to restrict the dosing frequency or the concentration of the dosage. It is possible to modify nanomaterials so that they have different surface ligands, like proteins and antibodies, which could attach to a receptor on a specific target . When attempting to convey substantial molecules or proteins through a diminutive aperture , the nanomaterial's surface area can also enable transporting a substantial pharmacological load within a confined volume (ranging from 10 to 1000 nm) . Silver or gold serve as the structural core of the nanoparticles created to

fight *N. fowleri* infections. However, because of their high levels of biocompatibility and biodegradability, organic polymeric nanoparticles like polylactic co-glycolic acid (PLGA) are beneficial (Joseph *et al*., 2022).

**References**


1. **Cervantes-Sandoval, I.; de Jesús Serrano-Luna, J.; García-Latorre, E.; Tsutsumi, V. and Shibayama, M.(2008) :** Mucins in the host defence against *Naegleria fowleri* and mucinolytic activity as a possible means of evasion. Microbiology , 154, 3895–3904 .
2. **Cervantes-Sandoval, I.; Serrano-Luna, J.d.J.; Meza-Cervantes, P.; Arroyo, R.; Tsutsumi, V.and Shibayama, M. ( 2009) :** *Naegleria fowleri* induces MUC5AC and proinflammatory cytokines in human epithelial cells via ROS production and EGFR activation. Microbiology 155, 7373–7373 .
3. Epidemiol Infect ; 138:968-75.
4. **Grace, E.; Asbill, S. and Virga, K. (2015):** *Naegleria fowleri*: Pathogenesis, diagnosis, and treatment options. Antimicrob. Agents Chemother. 59 ,6677-6681.
5. **Jahangeer , M. ; Mahmood , Z. ; Munir ,N. ;Waraich, U.E. ;Tahir, I.M. ; Akram ,M.**; *et al.* (2020): ***Naegleria fowleri*: Sources of infection, pathophysiology, diagnosis, and management; a review. Clin Exp Pharmacol Physiol. 47:199-212.**
6. **Jarolim , K. L.; McCosh, J.K.; Howard , M. J . and John , D. T. (2000) :** A light microscopy study of the migration of *Naegleria fowleri* from the nasal submucosa to the central nervous system during the early stage of primary amebic meningoencephalitis in mice. J Parasitol. ;86(1):50-5.
7. **Joseph, S.K.; Arya, M.A.; Thomas, S.and Nair, S.C.( 2022) :** Nanomedicine as a future therapeutic approach for treating meningitis. J. Drug . Sci. Technol, 67, 102968.
8. **Lee, J.; Kang, J.M.; Kim, T.I.; Kim, J.H.; Sohn, H.J.; Na, B.K.and Shin, H.J.(2017):** Excretory and Secretory Proteins of *Naegleria fowleri* Induce Inflammatory Responses in BV-2 Microglial Cells. J. Eukaryot. Microbiol , 64, 183–192 .
9. **Lee, J.; Kim, J.H.; Sohn, H.J.; Yang, H.J.; Na, B.K.; Chwae, Y.J.; Park, S.; Kim,** K.and Shin, H.J. (2014): **Novel cathepsin B and cathepsin B-like cysteine protease of *Naegleria fowleri* excretory-secretory proteins and their biochemical properties. Parasitol. Res , 113, 2776-2765.**
10. **Linda Geedes .( 2024) :** Everything you need to know about the brain-eating amoeba that's killed three children in Kerala, Health Journalist Network Uganda .
11. **Marciano-Cabral ,F .and Cabral ,G. A. (2007) :** The immune response to *Naegleria fowleri* amebae and pathogenesis of infection. FEMS Immunol Med Microbiol ;51(2):243-59.
12. **McKerrow, J.H.; Caffrey, C.; Kelly, B.; Loke, P. and Sajid, M. (2006):** Proteases in parasitic diseases. Annu. Rev. Pathol. 2006, 1, 497–536 .
13. **Moseman ,E.A. and Ching ,W.C.( 2022) :** Pro-inflammatory cytokine responses to *Naegleria fowleri* infection , National library of Medicine , 3:1082334.
14. **Rawat, A.; Roy, M.; Jyoti, A.; Kaushik, S.; Verma, K.;and Srivastava, V.K. ( 2021) :** Cysteine proteases: Battling pathogenic parasitic protozoans with omnipresent enzymes. Microbiol. Res , 249, 126784 .
15. **Rosenthal, P.J. ( 2020) :** Falcipain cysteine proteases of malaria parasites: An update. Biochim. Biophys. Acta-Proteins Proteom , 1868, 140362 .
16. **Siddiqui, R.; Ali, I.K.M.; Cope, J.R. and Khan, N.A.( 2016) :** Biology and pathogenesis of *Naegleria fowleri.* Acta Trop , 164, 375–394 .

17. **Yoder ,J .; Eddy ,B.; Visvesvara, G.; Capewell ,L. and Beach, M.( 2010):** The epidemiology of primary amoebic meningoencephalitis in the USA, 1962–2008.

18. **Yoder, J. S.; Straif-Bourgeois, S.; Roy ,S. L.; Moore, T.A.; Visvesvara ,G.S.; Ratard, R.C. *et al*. ( 2012) :** Primary amebic meningoencephalitis deaths associated with sinus irrigation using contaminated tap water. Clin Infect Dis. 55:79-85.