WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.453
Volume 14, Issue 21, 1312-1320. Review Article ISSN 2277–7105

AMOEBIC MENINGOENCEPHALITIS: A COMPREHENSIVE REVIEW OF PATHOGENESIS, DIAGNOSIS & MANAGEMENT

Arun G. Krishnan*, Amala Alex[1], Navya Elsa Thomas[2], Princy P.[3]

*Associate Professor, Dr. Joseph Marthoma Institute of Pharmaceutical Science and Research, Alappuzha, India.

Article Received on 07 October 2025,
Article Revised on 27 October 2025,
Article Published on 01 Nov. 2025,

https://doi.org/10.5281/zenodo.17539601

***Corresponding Author**

Arun G. Krishnan

Associate Professor, Dr. Joseph Marthoma Institute of Pharmaceutical Science and Research, Alappuzha, India.

How to Cite This Article: Arun G. Krishnan*, Amala Alex, Navya Elsa Thomas, Princy P. (2025). Amoebic Meningoencephalitis: A Comprehensive Review of Pathogenesis, Diagnosis & Management. World Journal of Pharmaceutical Research, 14(21), 1312–1320.

ABSTRACT

Amoebic meningoencephalitis is a rare but highly fatal infection of the central nervous system caused by free-living amoeba Naegleria fowleri. This pathogenic organism is commonly found in warm fresh water, soil and poorly chlorinated water sources. Infection typically occurs when contaminated water enters the nasal passages allowing the amoeba to migrate along the olfactory nerves into the brain. The disease progresses rapidly, resulting in extensive brain inflammation, necrosis and hemorrhage. Clinical manifestation include fever, headache, vomiting, altered mental status and seizures, often resembling bacterial meningitis, leading to frequent misdiagnosis. Diagnosis is challenging and usually confirmed through cerebrospinal fluid examination, imaging techniques or molecular assays like polymerase chain reaction (PCR). Despite aggressive therapy with amphotericin B, miltefosine, azole antifungals, mortality rates remain exceedingly high due to delayed recognition and limited treatment efficacy. Preventive measures focus on avoiding exposures to contaminated water and maintaining proper chlorination in recreational facilities. This review summarizes the epidemiology, pathogenesis, clinical features, diagnostic advancements and therapeutic strategies of amoebic meningoencephalitis, highlighting the urgent need for early diagnosis and effective treatment to improve survival outcomes.

KEYWORDS: Amoebic meningoencephalitis, Naegleria fowleri, Central nervous system infection, diagnosis, treatment.

INTRODUCTION

Amoebic encephalitis is a rare but lethal central nervous system infection caused by free-living amoebae found in freshwater, lakes, and rivers.

There are two types of amoebic encephalitis, namely

- Primary Amoebic Meningoencephalitis (PAM)
- Granulomatous Amoebic Encephalitis (GAE).

Primary amoebic meningoencephalitis (PAM) is a disease caused usually by infection with Naegleria fowleri, a microscopic amoeba commonly called a "brain-eating amoeba." This infection destroys brain tissue, causing severe brain swelling and death in most cases. PAM is rare and usually occurs in healthy children, teens and young adults. The initial symptoms of PAM are indistinguishable from bacterial meningitis, while the symptoms of GAE can mimic a brain abscess, encephalitis, or meningitis. These infections are almost uniformly fatal with only few reported survivors globally. Symptoms progress rapidly over around five days with characteristics of both meningitis and encephalitis, making it a type of meningoencephalitis. Death usually results within one to two weeks of symptom onset. The amoebae exhibit CNS tropism leading to meningoencephalitis.

Naegleria fowleri

Naegleria fowleri is the only human pathogenic species in the genus *Naegleria* that contains 47 species. *N. fowleri* is typically found in warm bodies of fresh water, such as ponds, lakes, rivers and hot springs. It is found in an amoeboid, temporary flagellate stage or microbial cyst in soil, poorly maintained municipal water supplies, water heaters, near warm-water discharges of industrial plants and in poorly chlorinated or unchlorinated swimming pools. There is no evidence of it living in salt water. As the disease is rare, it is often not considered during diagnosis. If water containing the ameba goes up the nose and to the brain, it can cause an infection called primary amebic meningoencephalitis (PAM). Typically, fewer than 10 people a year in the United States get PAM. Nearly everyone who gets PAM dies from it. Between 1962 and 2024, there were 167 reported cases of PAM in the United States. Only four have survived. Children younger than 2 years frequently carry the organism

asymptomatically in their nose and throat, especially in warmer months and climates without getting infected.

During a period of a few days to 2 weeks after inoculating a patient who had been swimming, diving, bathing, or playing in warm, usually stagnant, freshwater, the amoebae migrate through the cribriform plate, along the fila olfactoria and blood vessels, and into the anterior cerebral fossae, where they cause extensive inflammation, necrosis, and hemorrhage in the brain parenchyma and meninges.

Lifecycle of *N.fowleri*

Stages of the Life Cycle.

Naegleria fowleri exists in three forms during its life cycle:

A. Trophozoite

B. Amebo-flagellate Stage

C. Cyst Stage

A. Trophozoite (Active Feeding Stage)

This is the infective stage and the only form found in human tissues. The active replicating form is a trophozoite that can reproduce asexually. Trophozoite is the vegetative or feeding stage of the amoeba and is the infective form. In humans, this form is found in CSF or in tissue.

Infection: When contaminated water enters the nose, trophozoite migrate along the olfactory nerve to the brain, causing PAM.

B. Flagellate Stage (Motile Transitional Form)

The trophozoite can transform into a flagellate stage, in which state it can survive without nutrition. This is also the stage in which the amoeba is distributed through water bodies.

Trigger: Formed when trophozoites are exposed to a sudden change in ionic concentration, such as transfer to distilled water.

C. Cyst Stage (Dormant Form)

In harsher climates, the flagellated form can undergo encystation into a double-walled cyst and withstand unfavorable conditions. This enables the N. fowleri to survive cold temperatures, and nutritively hostile conditions.

Cysts are usually absent in clinical specimens, as the infection is so rapid and fatal that the patient typically dies before the trophozoites encyst.

Infection in Humans Occurs when trophozoites in warm freshwater enter through the nasal cavity → migrate along the olfactory nerve → reach the brain, causing PAM.

PATHOPHYSIOLOGY

When a healthy young individual exposed to the infected water such as in swimming pool, lake, river etc. The amoeba enters the individual through the olfactory mucosa and the cribriform plate. This may lead to the exaggerated inflammatory reaction. These inflammatory responses result to neuronal damage and subsequent irreversible brain damage.

CLINICAL FEATURES

EARLY SYMPTOMS

- Severe headache
- Pyrexia
- Meningism's
- Photophobia
- Nausea and vomiting

NEUROLOGICAL SYMPTOMS

- Seizures
- Hallucination
- Ataxia
- Confusion
- Disorientation

SOURCES OF CONTAMINATION

Amoebic meningoencephalitis is caused by N. fowleri, which lives in soil, warm fresh water, hot springs and pools. Infection occurs mostly when it is hot for a long period resulting in raised water temperature. Amoebic meningoencephalitis occurs when free-living pathogen enters and infect the Central Nervous System.

- Fresh water exposure

N. fowleri infection is mostly caused when people swim or submerge their head in warm fresh water like lakes, ponds, rivers etc.

- Tap water exposure

PAM is also caused when people uses contaminated tap water to rinse their sinuses. It is also caused from recreational water like splash pad and surf park.

- Geographic location

In the United States, most infections have been linked to swimming in warm, southern states. However, evidence suggests the range of N. fowleri is expanding northward as the climate warms.

- **HOW IT SPREADS?**

N. fowleri infect people by entering through the nose, while swimming. The amoeba enters the nose and reaches the brain and destroys the brain tissue, causing swelling.

- **HOW IT DOES NOT SPREAD**

N. fowleri does not spread by drinking water contaminated with the amoeba. It does not spread from one person to another.

TREATMENT OF N. FOWLERI INFECTION

N. fowleri can cause PAM which destroys the brain. Unfortunately, 97% of the people with PAM has died from the infection. As the early symptoms of PAM is like other illness, it is hard to identify the infection. PAM progresses quickly which causes difficulty in identifying the treatment for the infection. However, treatment with some antibiotics have proven to be effective against PAM. Antibiotics such as Amphotericin, Rifampin, Fluconazole, Azithromycin, Dexamethasone etc. and some antibiotic combinations have proved to be effective against PAM. As PAM progresses quickly and can become fatal within a week, early diagnosis and intense treatment is crucial. Since the disease progresses rapidly, empirical treatment should begin immediately upon suspicion, even before laboratory confirmation.

Specific (Anti-amoebic) Therapy

A. Amphotericin B (Mainstay of therapy)

Mechanism: Binds to ergosterol-like molecules in the amoebic cell membrane → increases permeability →causes leakage and cell death.

Form: Amphotericin B deoxycholate (conventional form).

Dosage and Route: Intravenous: 1.0–1.5 mg/kg/day.

Intrathecal or intraventricular: 0.1–1.5 mg/day (for direct brain/spinal fluid delivery).

Intranasal Duration: 10–14 days or until CSF cultures are negative.

Toxicity: Nephrotoxicity, fever, chills, electrolyte disturbances.

Monitoring: Serum creatinine, electrolytes, liver function.

Instillation: Sometimes used to clear nasal colonization early.

B. Miltefosine (Emerging and adjunct drug)

Mechanism: Disrupts cell membrane integrity, phospholipid metabolism, and apoptosis-like cell death in amoebae.

Dose: 50 mg orally 2–3 times daily (adjust per weight and tolerance).

Advantages: Active in vitro against Naegleria, Acanthamoeba, and Balamuthia.

Penetrates CNS effectively.

Clinical use: Successful in some survivors (e.g., 2013 Arkansas, USA case).

Side effects: Nausea, vomiting, diarrhea, elevated liver enzymes.

C. Azithromycin

Mechanism: Inhibits amoebic protein synthesis (50S ribosomal subunit).

Dose:500 mg once daily orally or IV.

Role: Acts synergistically with amphotericin B and miltefosine.

D. Rifampin

Mechanism: Inhibits RNA polymerase → suppresses nucleic acid synthesis.

Dose:10 mg/kg/day orally or IV.

Caution: Potent inducer of hepatic enzymes → affects metabolism of other drugs.

E. Fluconazole

Mechanism: Inhibits ergosterol synthesis → disrupts cell membrane.

Dose: 400–800 mg/day orally or IV.

F. Other possible adjuncts

Voriconazole, Miconazole, Chlorpromazine, Azoles (in combination) have been tested experimentally but are not standard.

➢ **Overview of Treatment Goals**

The treatment aims to

1. Eliminate the amoeba from the Central Nervous System.
2. Reduce brain inflammation and intracranial pressure.
3. Support vital functions (respiration, circulation, electrolyte balance).

➢ **Supportive management in PAM**

In PAM several supportive measures can be taken,

- Control of intracranial pressure by giving mannitol, hypertonic saline and ventriculostomy
- Body temperature can be controlled using induced hypothermia which helps to reduce brain damage.
- In case of coma, mechanical ventilation can be given.
- In case of seizures, antiepileptic drugs can be given.

PREVENTION OF AMOEBIC MENINGOENCEPHALITIS

1. Avoidance of contaminated water source.

- Do not swim or dive in freshwater ponds, lakes, rivers during hot seasons.
- Do not swim if the water is not clean as enough.

2. Proper nasal protection.

- Use distilled, filtered or distilled water for nasal irrigation.
- Avoid the use of untreated tap water for nasal cleaning.
- Hold your nose before jump into the water.
- Use plugs.

3. Public health awareness.

- Public awareness campaigns about the danger of Naegleria fowleri.

KERALA CURRENT SCENERIO

In Kerala, India, the first reported case of PAM in 2024 was on May 21, involving a five-year-old girl. The second case, reported on June 25, involved a 13-year-old girl. As of mid-September 2025, Kerala had reported around 70 cases and 19 deaths from the "brain-eating amoeba". The cases over the last 2 months have been reported in children aged 5,13,12, 13 and 15 years respectively with a male-to-female ratio of 3:2 [n=5].

CONCLUSION

Amoebic meningoencephalitis remains a rare but devastating central nervous system infection caused primarily by Naegleria fowleri, Acanthamoeba species, and Balamuthia mandrillaris. Despite advances in diagnostic imaging and microbiological techniques, early recognition continues to be a major challenge due to its nonspecific clinical presentation and rapid progression. The mortality rate remains exceedingly high, underscoring the urgent need for heightened clinical awareness and prompt initiation of empiric therapy.

Recent studies have highlighted the importance of molecular diagnostic tools such as PCR and next-generation sequencing in improving early detection. However, effective treatment protocols are still limited, and current therapeutic regimens often involving amphotericin B in combination with miltefosine and other agents show variable success. Preventive strategies focused on public education, improved water sanitation, and awareness of environmental exposure risks play a critical role in reducing incidence.

In conclusion, amoebic meningoencephalitis demands a multidisciplinary approach that integrates rapid diagnosis, aggressive treatment, and preventive public health measures. Continued research into novel therapeutic agents, pathogen biology, and host parasite interactions will be essential to improve outcomes and reduce the fatality associated with this neglected but highly lethal disease.

ACKNOWLEDGEMENT

We sincerely thank our guide, Associate Prof. Arun G Krishnan for his constant encouragement, valuable feedback and guidance throughout this study. We would like to express our sincere gratitude to Dr. Joseph Mar Thoma Institute Of Pharmaceutical Sciences And Research Kattanam, Alappuzha. We express our heartfelt gratitude to our respected Principal Dr. Ansa Mathew and Vice Principal Dr. Subash Philip and our Associate Prof. Dr. Jini Jith.

We would like to express our special thank for our beloved parents for their moral support and blessing throughout the work.

REFERENCES

1. https://www.cdc.gov/meningitis/about/amebic-meningitis.html
2. https://en.wikipedia.org/wiki/Primary_amoebic_meningoencephalitis
3. https://www.ncbi.nlm.nih.gov/books/NBK430754/
4. https://kerala.gov.in/assets/ckupload/219%20Health_1721651318.pdf
5. https://my.clevelandclinic.org/health/diseases/24485-brain-eating-amoeba
6. https://www.sciencedirect.com/science/article/pii/S2214250924001045
7. Schuster FL, Visvesvara GS. Free-living amoebae as opportunistic and non-opportunistic pathogens of humans and animals. Int J Parasitol, 2004 Aug; 34(9): 1001-27.
8. Visvesvara GS. Infections with free-living amebae. Handb Clin Neurol, 2013; 114: 153-68.
9. Clinical Care of Naegleria fowleri Infection, CDC USA.
10. Capewell LG, et al. Diagnosis, clinical course, and treatment of primary amoebic encephalitis in the United States, 1937-2013. J Ped Infec Dis Soc., 2014; 1-8.
11. Epidemiology and Clinical Characteristics of Primary Amebic Meningoencephalitis Caused by Naegleria fowleri: A Global Review Radhika Gharpure, John Bliton, Alexandra Goodman, Ibne Karim M. Ali, Jonathan Yoder, and Jennifer R. Cope: Clinical Infectious Diseases · May 2020.
12. Regu K, Rajendran R, Bhaskaran K S, Rajendran A, Tamizharasu W. Primary Amoebic Meningoencephalitis in Kerala – An Emerging Public Health Concern. J Commun Dis., 2024; 56(1): 25-35.