JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

REVIEW ON THE BRAIN EATING AMOEBA

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Abstract: This project explores Naegleria fowleri, a thermophilic free-living amoeba that causes Primary Amoeba Meningoencephalitis (PAM), a rare but devastating brain infection with a mortality rate exceeding 97%. The amoeba thrives in warm freshwater environments such as lakes, rivers, hot springs, and poorly chlorinated swimming pools. Infection occurs when contaminated water enters the nasal passages, allowing the organism to migrate along the olfactory nerve to the brain, causing severe inflammation and tissue destruction. Symptoms, including severe headache, fever, nausea, seizures, and confusion, typically manifest within 2-7 days and progress rapidly to death within one week. The project discusses the organism's classification, epidemiology across global regions, pathophysiology, diagnostic approaches using CSF analysis and PCR testing, and treatment options involving combination antimicrobial therapy with Amphotericin B, Miltefosine, and other agents. Emphasis is placed on prevention through public awareness and proper water safety measures.

KEYWORDS: CSF, PCR, PAM (primary amoeba meningoencephalitis), Amoeba

INTRODUCTION

The Brain-Eating Amoeba, scientifically known as Naegleria fowleri, is a thermophilic, free-living amoeba commonly found in warm freshwater bodies such as lakes, rivers, hot springs, and poorly chlorinated swimming pools. It was first identified in 1965 in Australia, and since then, it has been recognized as the causative agent of a rare but devastating infection known as Primary Amebic Meningoencephalitis (PAM) — an acute, fulminant, and often fatal disease of the central nervous system. Unlike many other pathogenic organisms, Naegleria fowleri does not need a host to survive. It thrives independently in warm, stagnant freshwater and moist soil. The amoeba exists in three stages of its life cycle — the cyst, trophozoite, and flagellate stages — with the trophozoite stage being the infectious form. Infection occurs when contaminated water enters the nasal cavity, allowing the amoeba to travel along the olfactory nerve to the brain, where it causes severe inflammation and destruction of brain tissue. Although cases of PAM are extremely rare, the infection is almost always fatal, with a mortality rate exceeding 97%. Symptoms typically begin within 2–7 days of exposure and include headache, fever, nausea, vomiting, stiff neck, confusion, loss of balance, seizures, and hallucinations. Death usually occurs within a week after symptom onset. Because early symptoms resemble bacterial meningitis, diagnosis is often delayed, making treatment difficult. The significance of studying Naegleria fowleri lies not only in understanding the biology of this deadly organism but also in developing strategies for early detection, effective treatment, and public awareness.

ETIOLOGY

N fowleri is the causative agent of PAM, which is a rare but rapidly progressive and usually fatal infection of the CNS. Although Acanthamoeba A and B mandrillaris are opportunistic pathogens that cause granulomatous amebic encephalitis in immunocompetent and immunocompromised individuals, N fowleri primarily affects healthy, immunocompetent children and young adults who have been exposed to contaminated freshwater. Widely distributed worldwide, N fowleri thrives in warm freshwater environments as a thermophilic ameboflagellate, growing at temperatures up to 45 °C. This amoeba is commonly found in soil, lakes, and rivers and can also persist in inadequately chlorinated water sources, such as swimming pools, tap water, and industrial wastewater. Infection occurs when contaminated water enters the nasal passages, usually through freshwater exposure or nasal rinsing with nonsterile water. Once inside, N fowleri migrates to the CNS via the olfactory nerves and cribriform plate, leading to severe and nearly always fatal infection.Notably, ingestion of N fowleri does not cause infection. The disease caused by the Brain Eating Amoeba is known as Primary Amebic Meningoencephalitis (PAM). The etiological agent responsible for this infection is Naegleria fowleri, a free-living, thermophilic (heatloving) amoeba belonging to the phylum Percolozoa, class Heterolobosea, and order Schizopyrenida. It is an amoeboflagellate organism, meaning it can exist in both amoeboid and flagellated forms depending on environmental conditions. The disease known as Primary Amoebic Meningoencephalitis (PAM) is caused by the freeliving amoeba Naegleria fowleri. This organism is a thermophilic, pathogenic protozoan that naturally inhabits warm freshwater and soil. It is the only species of the genus Naegleria known to infect humans. Naegleria fowleri belongs to the phylum Percolozoa, class Heterolobosea, and order Schizopyrenida. It is commonly referred to as the “brain-eating amoeba” because of its ability to invade and destroy brain tissue. The amoeba exists in three forms—the cyst, trophozoite, and flagellate stages. The trophozoite is the infective stage responsible for human disease. Infection occurs when contaminated water enters the nasal passages, allowing the amoeba to migrate along the olfactory nerve to the brain, where it causes severe inflammation and tissue

damage. CLASSIFICATION= Kingdom= Protista Phylum= Percolozoa Class= Heterolobosea Order= Schizopyrenida Genus= Nargleria Species= naegleria Fowleri.

EPIDEMIOLOGY

The first case of free-living amoebae, in particular Naegleriafowleri, causing human disease was documented in 1965. The Central Nervous System (CNS) is a tropism for N. fowleri, a pathogenic organism. It comes in three different shapes: the spherical cyst, the pear-shaped motile flagellate form, and the invasive, reproducing trophozoite (ameboid form). Temperatures between 27°C and 37°C are sufficient to maintain the motile form, while temperatures between 35°C and 46°C are ideal for the trophozoite form. The trophozoite form can return in the presence of favourable conditions, while the cyst form can endure lower temperatures. Trophozoites consume bacteria in their free-living stage, but when they are inside of tissues, they phagocytose red and white blood cells, causing tissue damage. While unfavourable circumstances result in cyst formation, changes in ionic concentration can cause the trophozoites to change into a biflagellate form [6,7]. More than 30 different Naegleria species have been found, but only N. fowleri is known to infect humans. Other species, such N. italica and N. australiensis, have not been identified to infect humans but are capable of infecting experimental animals. Due to the prevalence of these amoebae in warm, stagnant bodies of water and even chlorine swimming pools, contact with people is unavoidable [8,9]. According to the disease's epidemiology, the majority of primary amoebic meningoencephalitis (PAM) cases were found in nations like Australia, the United States, Great Britain, the Czechoslovak Republic, Thailand, and Mexico. These occurrences often took place in warm, muggy climates throughout the summer. Cases have been documented in both the USA and Mexico in North America, with the majority of illnesses there happening following a swim in naturally warm or geothermal waters. Cases were documented in
Venezuela and Brazil in South America, with swimming in untreated or natural water being a common risk factor. Other nations like Cuba, Guadeloupe, Australia, New Zealand, India, China, Japan, Nigeria, Namibia, Madagascar, and Egypt have also reported isolated cases.

PATHOPHYSIOLOGY

N fowleri is a thermophilic amoeba that thrives in temperatures up to 45 °C and is widely distributed in warm freshwater environments. This amoeba is commonly found in soil, lakes, and rivers but can also persist in inadequately chlorinated water sources, such as swimming pools and tap water. N fowleri infection occurs when contaminated freshwater enters the nasal passages, typically during swimming in freshwater bodies, using poorly chlorinated pools, or performing nasal rinses with nonsterile water. After entering through the nose, N fowleri migrates via the olfactory nerves, crosses the cribriform plate, and invades the CNS, thereby causing PAM. This infection is characterized by cerebral edema, hemorrhagic necrosis, herniation, and, in most cases, death.The most severely affected regions of the brain include the olfactory bulbs, the basilar portion of the frontal cerebrum, and the cerebellum. N fowleri triggers a strong innate immune response, and its virulence is influenced by multiple factors, including the protein Nfa1, nitric oxide production, and poreforming proteins. The Nfa1 protein facilitates amebic attachment to target cells, while specialized feeding structures enable the amoeba to ingest bacteria and fungi in the environment and directly phagocytose brain cells. The organism further contributes to tissue destruction by secreting cytolytic molecules, including cysteine proteases, phospholipases, and phospholipolytic enzymes, which mediate extensive necrosis. This intense immune response and aggressive virulence of N fowleri result in significant destruction of brain parenchymal tissue, leading to the rapid progression of PAM. The amphizoic amoeba Naegleria fowleri can live in the human Central Nervous System (CNS), soil, or water in a free-living condition.7 Naegleria fowleri infections have been reported in healthy people, especially in kids and adults who participate in water sports including swimming, diving, and water skiing. The amoeba is thought to enter the human body through the nose when water is forced or splashed into the nasal canal. Naegleria fowleri attaches to the nasal mucosa to start the infection, then moves through the porous cribriform plate and along the olfactory nerve until it reaches the CNS's olfactory bulbs.

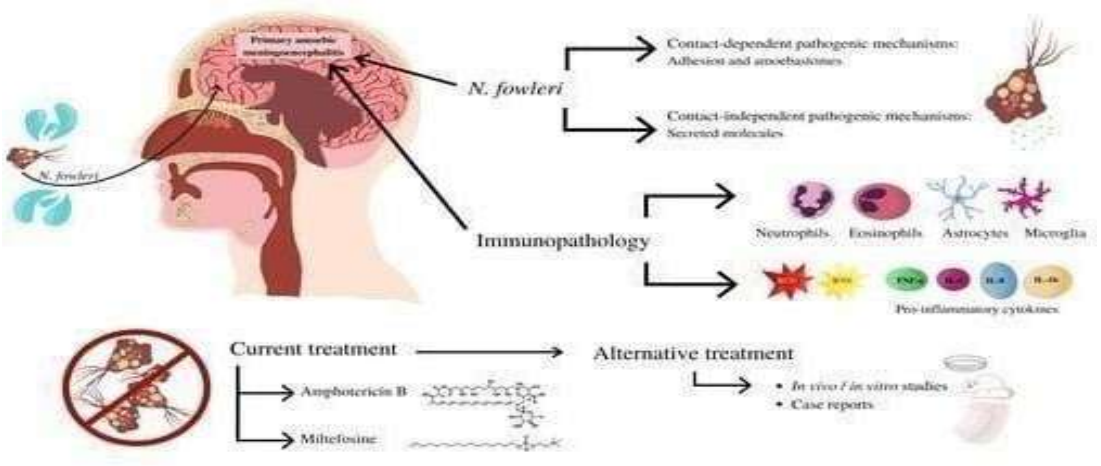

Figure.1: PATHOPHYSIOLOGY

When Naegleria fowleri enters the olfactory bulbs,the innate immune system,which is activated by macrophages and neutrophils , results in a strong immunological response(Figure1).The amoeba enters the body in its trophozoite form, where it can devour bacteria, fungus ,and human tissue thanks to food cups on its surface 9,10.Further more,Naegleria fowleri pathogeni city is dependent on the release of a variety of cytolytic molecules, including as acid hydrolases , phospholipases, neuraminidases, and phospholipolytic enzymes, which help destroy host cells and neurons.7 Due to the pathogenicity of Naegleria fowleri and the strong immunological reaction it elicits, the CNS suffers substantial nerve injury and subsequent tissue damage that frequently leads in death. The infection advances quickly, producing swelling, necrosis of brain tissue, and the symptoms typical with Primary Amebic Meningoencephalitis (PAM), including a strong headache, a fever of more than 100 degrees, a stiff neck, and altered mental status. Haemorrhage, brain enlargement, and coma may happen in extreme circumstances.The severity and lethality of PAM are attributed to Naegleria fowleri's capacity to enter the CNS through the nasal passages and its aggressive destruction of brain tissue.

HISTORY AND PHYSICAL

A detailed patient history and thorough physical examination are crucial for diagnosing PAM. The disease is challenging to identify clinically, as its early symptoms are often nonspecific and can resemble flu-like illnesses, bacterial meningitis, or viral meningoencephalitis. Clinicians must maintain a high index of suspicion and be aware of epidemiological risk factors and potential exposures, as failure to recognize PAM can result in delayed diagnosis and rapid fatality.

IDENTIFYING DATA

•Name: [Patient Name]
• Age/Sex: [Age]/[Sex]
• Date of Admission: [Date]
Chief Complaint: "Severe headache and fever for 2 days"

HISTORY OF PRESENT ILLNESS

The patient is a [age]-year-old [sex] with no significant past medical history who presents with acute onset of severe frontal headache, fever, nausea, and vomiting for [X] days. Symptoms began [X] days after swimming/diving in warm freshwater (lake, river, or poorly chlorinated pool).

Over the past 24–48 hours, the patient developed:

• Neck stiffness • Photophobia
• Altered mental status / confusion
• Seizures (in some cases)
• Loss of taste or smell (early symptom due to olfactory nerve involvement)

PAST MEDICAL HISTORY

• Chronic illnesses: None / [list]
• Past surgeries: [list]
• Allergies: [list]
• Medications: [list]

FAMILY HISTORY

Non-contributory.

SOCIAL HISTORY

• Exposure: Recent freshwater swimming/diving, typically in warm lakes, rivers, or hot springs.
• No alcohol, tobacco, or drug use.

REVIEW OF SYSTEMS

• Constitutional: Fever, chills, malaise
• Neurologic: Severe headache, neck stiffness, photophobia, confusion, possible seizures

PHYSICAL EXAMINATION

General: Ill-appearing ,febrile ,possibly obtunded.

Vital Signs:
• T: 39.5°C
• HR: 110 bpm
• BP: 100/60 mmHg

• RR: 24/min

HINT:

• Possible nasal discharge, photophobia, meningismus.

Neck:

• Positive nuchal rigidity, Kernig and Brudzinski signs.

Neurologic:
• Altered level of consciousness
• Cranial nerve abnormalities (esp. CN I – loss of smell)
• Possible focal deficits, seizures, coma in advanced cases.
Skin/Other systems: Usually unremarkable.

LABORATORY AND DIAGNOSTIC STUDIES
CSF Findings (Lumbar puncture):
• Appearance: Purulent or cloudy
• WBC: 100–1000/mm³, predominantly neutrophils
• Glucose: Low
• Protein: Elevated
• Wet mount or Giemsa stain: Motile trophozoites of Naegleria fowleri PCR or antigen detection confirms diagnosis.
Neuroimaging (CT/MRI):
• May show cerebral edema, especially in frontal lobes and temporal regions.

ASSESSMENT

Primary Amebic Meningoencephalitis (PAM) due to Naegleria fowleri infection, acquired from recent freshwater exposure.
• Bacterial meningitis (esp. Neisseria meningitidis, Streptococcus pneumoniae) Viral encephalitis (HSV)
• Acanthamoeba or Balamuthia infection

EVALUATION

Diagnosing PAM is challenging, as patients do not always present with the classic symptoms of meningitis. Early symptoms are often vague and nonspecific, resembling mild viral or bacterial infections. Patients may initially experience fever and headache, which can progress to meningismus and confusion, depending on the stage of the disease at the time of presentation. Given its rapid progression and high fatality rate, PAM should be suspected in any patient with meningoencephalitis or meningitis who has a recent history of freshwater exposure.

Laboratory findings in PAM can be nonspecific. CSF analysis often mimics bacterial meningitis, showing low to normal glucose levels, elevated protein, and leukocytosis with a polymorphonuclear predominance. CSF pressures are typically elevated, with recorded values reaching up to 600 mm H2O in some cases.However, standard laboratory tests may not be sufficient for diagnosis.

Rapid diagnosis is critical due to the aggressive nature of PAM. Few laboratories in the United States and worldwide can test for N fowleri. Even when specimens are sent to reference laboratories, the disease often progresses too quickly for the results to be clinically useful. If CSF is obtained, several diagnostic tests can help identify N fowleri. A quick method involves visualizing trophozoites directly using a wet mount. Staining techniques, including Giemsa, Wright, hematoxylin and eosin (H&E), and periodic acid– Schiff (PAS), can also be utilized.

Polymerase chain reaction (PCR) testing can detect N fowleri DNA directly from CSF and is now considered the gold standard for PAM diagnosis. However, PCR limitations include limited availability and the necessity of clinical suspicion. Gram staining and standard bacterial cultures are unreliable, as the fixation process destroys the amoebae. Antigen detection via immune histochemical staining can also be performed on CSF samples.

EVALUATION – Naegleria fowleri (Primary Amebic Meningoencephalitis) INITIAL CLINICAL IMPRESSION Based on the history of:

• Recent freshwater exposure (especially warm lakes or rivers), and
• Acute onset of meningoencephalitic symptoms (severe headache, fever, neck stiffness, altered mental status, vomiting, photophobia, seizures)

LABORATORY EVALUATION

1. Cerebrospinal Fluid (CSF) Analysis
2. • Appearance: Turbid or purulent
3. • Opening pressure: Elevated
4. • WBC count: 100–1000 cells/mm³ (predominantly neutrophils)

5. • Glucose: Low (hypoglycorrhachia)
6. • Protein: Elevated
7. • Gram stain: No bacteria seen
8. • Wet mount or Giemsa stain: Motile trophozoites of Naegleria fowleri (diagnostic finding)
9. • PCR testing: Highly sensitive and specific for Naegleria fowleri DNA (confirmatory test).

Culture: On non-nutrient agar with E. coli overlay may demonstrate trophozoite growth

BLOOD AND OTHER LABS

• CBC: Leukocytosis with neutrophil predominance
• Electrolytes: May show hyponatremia secondary to SIADH or cerebral edema
• Blood cultures: Negative

IMAGING STUDIES CT or MRI of the Brain: May show cerebral edema, particularly involving frontal and temporal lobes. Lesions may appear hypodense (CT) or hyperintense (MRI T2), often without contrast enhancement early in the course.

CONFIRMATORY TESTS

• Direct visualization of trophozoites in CSF (wet mount)
• PCR or antigen detection (definitive diagnosis)
• Brain biopsy (rarely performed; shows necrosis and trophozoites in tissue) SYMPTOMS AND CAUSES

The signs and symptoms of primary amoebic meningoencephalitis (PAM) come on suddenly and are severe at the start, Including:

• High fever.
• Very painful headache
• Nausea and vomiting.
• Trembling.
• Symptoms like those of meningitis, including and stiff neck and extreme sensitivity to light (Photophobia).
• Mental confusion.
• Coma.

The fatality rate is higher than 97% even with treatment.

Symptoms usually begin 1–9 days after exposure (average: 5 days). The illness progresses very rapidly and is almost always fatal if not treated immediately.

STAGE 1

• Resemble acute bacterial meningitis
• Severe frontal headache
• Fever and chills
• Nausea and vomiting
• Loss of smell (anosmia) or loss of taste
• Nasal congestion or runny nose

LATER SYMPTOMS (STAGE 2)
Indicate spread to the brain:
• Neck stiffness
• Photophobia (sensitivity to light)
• Confusion, disorientation, or hallucination
• Seizures
• Altered mental status → coma
• Ataxia (unsteady movements)
• Increased intracranial pressure
• Eventually, coma and death usually occur within 5–7 days after symptom onset.

• Natural Habitat
• Found in warm freshwater environments, including:
• Lakes, rivers, and hot springs o Geothermal water sources
• Warm-water discharge from industrial plants Poorly maintained or pools o Tap water or neti pots (when not properly sterilized
• Mode of Transmission
• Entry point: Through the nose — not by drinking contaminated water. under-chlorinated swimming
• Occurs when contaminated water is forcefully inhaled into the nasal passages (e.g., while swimming, diving, or using contaminated nasal irrigation).
• The amoeba travels up the olfactory nerve, through the cribriform plate, and into the brain.

DIAGNOSIS

Cerebro Spinal Fluid (CSF) examination can yield important diagnostic data in

N. fowleri infections. Due to an increase in red blood cells, abnormalities in CSF colour are seen, ranging from grey in the early stages of the disease to red in the late stages. Up to 26,000 mm3 of polymorphonuclear cells can frequently be seen in abundance. Additionally, trichrome or Giemsa stain can be used to confirm the presence of trophozoites in the CSF.

Isolation of trophozoites from either the CSF or brain tissue is required for the diagnosis of an N. fowleriinfection. The diagnosis can be aided by CSF analysis, which includes measurements of glucose and protein concentration. Microscopic analysis of a CSF wet mount may reveal trophozoites that are actively moving and have distinctive features such visible nuclei, cytoplasmic vacuoles, and pseudopodia. Non-nutritional agar can be used as a culture medium to isolate trophozoites.

N. fowleri can be found in environmental and clinical samples thanks to recent developments in molecular methods like PCR and real-time PCR. These methods can identify certain genotypes and find N. fowleri DNA in cerebrospinal fluid and brain tissue samples. Some techniques enable prompt identification in a matter of hours. These developments have also aided in the distinguishing of distinct Naegleria species and the detection of N. fowleri in diverse types of brain tissue. PAM imaging characteristics are frequently nonspecific and have not frequently been discussed before. Despite initially seeming normal, CT and MR imaging can eventually reveal signs of brain edoema and basilar meningeal enhancement. Imaging has occasionally shown signs of brain edoema, hydrocephalus, cistern obliteration with increased basilar exudates, and infarction of brain tissue. Although noted, there is little imaging evidence of cerebral infarctions in PAM. Amphotericin B, rifampicin, and miconazole are a few of the medications used as the primary treatment for PAM. Immunofluorescence, immunohistochemistry, or DNA probes are frequently necessary for amoeba detection. However, neither these methods were available nor used on the study's participants, which is one of the drawbacks. The N. fowleri CNS disease progresses quickly, and quick diagnosis methods make it possible to administer fast therapy, which is crucial for a positive patient result. Patients with PAM do not always exhibit the classic symptoms of meningitis, making diagnosis challenging. Early symptoms are often vague and nonspecific, resembling mild viral or bacterial infections. Patients may initially present with fever, headache, and general malaise, which can progress to meningismus and confusion depending on the disease's stage at presentation.

TREATMENT/ MANAGEMENT

Treatment options for PAM remain limited due to the lack of controlled trials or clinical studies. Current therapeutic approaches are based on in-vitro studies and case reports. The recommended treatment regimen typically involves a combination of 5 or 6 antimicrobial or antifungal agents that either demonstrate in-vitro activity against N fowleri or have been associated with survival in patients. Miltefosine is the most recent addition to this regimen, which commonly includes
amphotericin B, azithromycin, fluconazole, rifampin, and dexamethasone. However, the efficacy of these drugs remains inconsistent, and their use is often linked to significant toxicity.
Amphotericin B – IV and intrathecal/intraventricular.
Miltefosine – Oral.
Azithromycin – IV or oral.
Fluconazole – IV or oral.

PREVENTION

It's critical to take specific precautions in warm climates to lower the danger of N. fowleri infection. If at all possible, stay away from freshwater areas like lakes, rivers, and ponds. Choose saltwater or chlorinated settings instead because they are safer. Avoid dipping the head or splashing water if engaging in freshwater activities since these actions can prevent N. fowlerifrom entering the nasal passages. Infection risk can be reduced by using nasal clips while engaging in water-related activities. Some people advise cleaning the nose with clean water after swimming in freshwater, however it's unclear whether this is actually useful. Use of commercially available distilled or purified bottled water is advised for sinus rinsing. The risk of N. fowleri infection can be further decreased by boiling or filtering water with pores of 1 m or smaller. In order to avoid contracting N. fowleri, it is crucial to be aware of and abide by local water safety regulations as well as to inform oneself and others about the dangers of this organism.

CONCLUSION

In conclusion, Naegleria fowleri, widely known as the brain-eating amoeba, represents one of the most dangerous yet rare infections affecting humans. It causes Primary Amebic Meningoencephalitis (PAM), a severe and rapidly progressing brain infection that almost always leads to death if not treated immediately. The amoeba is typically found in warm freshwater environments such as lakes, hot springs, and poorly chlorinated swimming pools, and it infects humans when contaminated water enters the nose.

Despite its deadly nature, awareness and understanding of Naegleria fowleri remain limited.

The treatment mainly involves a combination of drugs—Amphotericin B, Miltefosine, Azithromycin, Fluconazole, and Rifampin—which have shown some effectiveness when administered early and aggressively. However, prevention remains the most powerful weapon. Practicing simple safety measures, such as avoiding water activities in warm freshwater, using nose clips, and using sterilized or boiled water for nasal cleansing, can significantly reduce the risk of infection.

Ultimately, this project highlights the importance of public education, early diagnosis, and ongoing scientific research to develop better diagnostic tools and more effective treatments. Understanding the biology, transmission, and prevention of Naegleria fowleri can save lives and help control future cases of this tragic but preventable disease.

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