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A REVIEW ON NAEGLERIA FOWLERI

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Abstract:

Primary amoebic meningoencephalitis (PAM), a dangerous and debilitating waterborne disease that affects both humans and animals, is caused by the thermophilic flagellate amoeba naegleria fowleri, also known as a "brain eating" amoeba. Naegleria amoebae are common in the environment and may be found in soil and freshwater bodies, where they feed on bacteria. Although primary amoebic meningoencephalitis appears to be rather uncommon compared to other infections, N. fowleri infection is destructive and almost usually deadly. There haven't been any clinical trials that compare the effectiveness of various treatment plans due to the rarity of N. fowleri infections in people. Infections with N. fowleri in humans: Epidemiology, Life Cycle, Mode of Transmission, Aetiology, Pathogenesis, Diagnosis, Pharmacotherapy, and Prevention.

Keywords:

Naegleria fowleri, primary amoebic meningoencephalitis (PAM), “braineating” amoeba, olfactoryneuroepithelium, trophozoites, amphotericin B.

INTRODUCTION:

"Primary Amoebic Encephalopathy" is a potentially fatal illness caused by the amoeba Naegleria fowleri in the central nervous system (CNS) Meningoencephalitis" (PAM), which has a fatality incidence of 95% and 97%, which causes death.[1]

According to the environmental circumstances, the life cycle of Naegleria fowleri has three distinct morphological phases.

a) Trophozoite stage: This stage, which ranges in size from 10 to 25 millimeters, is active, infectious, feeding, and reproductive. It has a single nucleus and replicates through mitosis under ideal climatic circumstances.

b) The flagellate stage, which ranges in size from 10 to 16 millimeters, is pear-shaped, removable, and non-feeding.

c) Cyst stage: Non-feeding, non-reproductive phases that range in size from 8 to 20 millimetres.[2]

When there is a nutritional deficiencies in the presence of water and the temperature is between 27 °C and 37 °C, Trophozoites can change to the flagellate. Their ideal temperature range is 35 to 46 °C.[3]

By using chemotaxis and chemokines, Naegleria fowleri draws in Gram positive and negative bacteria, feasts on them by creating feeding containers, and can also consume yeast and algae.[4]

The capacity of a number of pathogens, including various bacteria, viruses, fungi, and parasites, to infect the human central nervous system (CNS), has been demonstrated.[5]

They have a number of molecular pathways that enable them to cross the blood-brain barrier (BBB) or the blood-cerebrospinal fluid barrier (BCSFB), and their major sites of infection are the brain and spinal cord.[6]

A category of opportunistic protozoa known as free-living amoebas (FLA) generate serious health issues among parasites that can infect the nervous system. FLA are eukaryotic, mitochondrial microorganisms that may live out their whole cycle as free-living amoebas or parasites that live in their native surroundings. Due of this, FLA are referred to as amphizoic creatures.[7,8]

These amoebas are common and have been discovered in the soil, water, and atmosphere. They have also been found in commonplace items including flower pots, humidifiers, sewers, swimming pools, water pipelines, water parks, and even hospital settings.[7]

One of the few FLA that may infect people fatally is Naegleria fowleri. Primary amoebic meningoencephalitis (PAM), which is caused by this parasite, is an acute and fulminating illness that can be fatal 7 to 10 days after the amoeba enters the body. PAM is frequently seen in immunocompetent kids and teens, especially after coming into contact with water infected with amoebas. Despite the condition being incredibly uncommon, it has a 98% fatality rate[9].

Early diagnosis, according to studies, is essential for a patient to survive PAM. However, because of its low morbidity, little is known about the aetiology of the illness. It is challenging to create viable treatments and efficient diagnostics tools because of this final difficulty.[7]

Naegleria fowleri :

a FLA genus is a member of the Vahlkampfiidae family, Schizopyrenida order, and Heterolobosea class.[10]

There are 47 species in the genus, and changes in their genomes, notably in their internal transcribed spacers (ITS) and 5.8S rDNA, can be used to distinguish them. Only N. australiensis, N. italica, and N. fowleri have been identified as pathogenic Naegleria species. All laboratory animals are solely affected by N. australiensis and N. italica. However, the deadly human illness primary amoebic meningoencephalitis (PAM) is only known to be caused by N. fowleri. .Although N. lovaniensis is thought to be non-pathogenic, N. fowleri is most closely linked to it[11,12]

An abundant and thermophilic amoeba called N. fowleri may be found in the soil, air, and warm seas.[13]

Its natural habitats include freshwater lakes, rivers, ponds, and hot springs. Additionally, it has been found in drinking water distribution systems, untreated swimming pools, fountains, hospitals, thermal waters, untreated drinking water, and water parks.[14]

Since N. fowleri has been found on all continents except Antarctica, it is a widely dispersed parasite.[13]

There are three main forms of N. fowleri. The amoeba changes into a metabolically inactive cyst when the environment becomes too hostile. This cyst is described as a spherical structure with a diameter of 7 to 12 m, a thick endocyst, a thin ectocyst, and several mucoid-plugged holes.[15,16]

diameter, a thick endocyst, a thin ectocyst, and some holes with mucoid blocked Because of the cyst's extreme resistance and ability to tolerate a wide range of physical and chemical circumstances, including temperatures as low as 4 C, this amoeba may remain dormant throughout the chilly winter months and proliferate during the summer.[13]

The amoeba changes into a transient flagellate when it encounters non-nutritive circumstances but is still in the presence of water. This type has two flagella that are around the same length and is pear-shaped, measuring between 10 and 16 m. They have mitochondria, a rough endoplasmic reticulum, vacuoles, cytoplasmic inclusions, and a nucleus.[15]

Since N. fowleri flagellate flourish between 27 and 37 °C, they are typically found in warm waters or in the summer.[14,17]

When conditions are right, the amoeba appears as a long, thin structure that is around 22 mm long and 7 mm broad and is known as a reproductively active trophozoite. These trophozoites have several mitochondria, food vacuoles, a single contractile vacuole, an endoplasmic reticulum, ribosomes, and membrane-bound cytoplasmic organelles in addition to a big nucleus with a nucleolus.[13,15]

Additionally, they show foodcup structures (amoebastomes) that have been linked to their eating[18]

The only N. fowleri form that can procreate, feed, encyst, and infect other species is in the form of trophozoites. Although algae and yeast can also be consumed by trophozoites, gram-positive and gram-negative bacteria are their main food supply. They split by binary fission and grow best between 35 and 46 C since they are thermophilic.[14]

EPIDEMIOLOGY:

Naegleria fowleri is a global endemic that is primarily found in freshwater lakes, hot springs, chlorinated pools, and thermally contaminated water bodies.[19]

Seawater has not been discovered to contain it. Since this organism was discovered, invasive human infections have been recorded in Australia, New Zealand, Europe, Africa, Asia, and Latin America. It has primarily been seen in the southern states of the United States.

The amoeba can be found in :

- Geothermal (naturally heated) water, like that found in hot springs
- Industrial facilities' warm water outflow
- Drinking water sources with geothermal heat
- Water warmers Swimming pools that are not properly kept, are only lightly chlorinated, or are unchlorinated. Up to 115°F (46°C), Naegleria fowleri grows best, though it can endure greater temps for brief times.
- Soil

Primary amoebic meningoencephalitis was first identified in Florida, USA, in 1962, then South Australia, where it was identified by Malcom Fowler and Carter in 1965. For this reason, the illness was given the name Naegleria fowleri. (Fowlerand Carter, 1965).

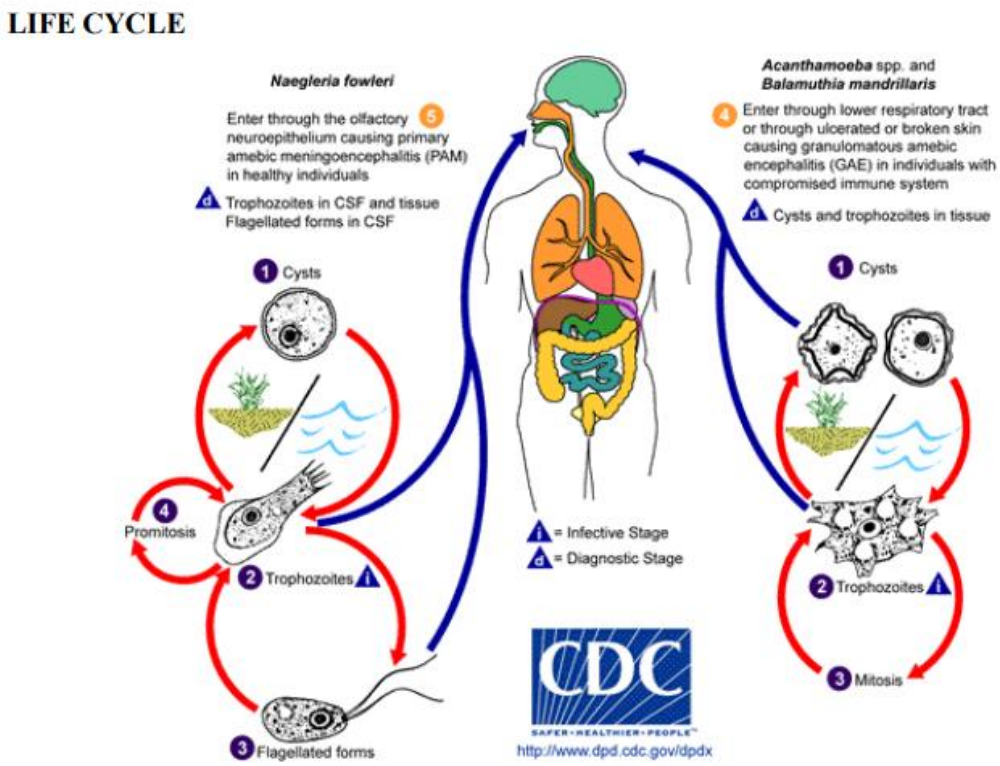
Primary Amoebic Meningoencephalitis (PAM) was the term Butt gave the illness in 1966. Fowler and Carter later changed it to Entamoeba histolytica of brain infection. (1965)[15]

WHAT IS A BRAIN-EATING AMOEBA?

Amoebas are creatures with a solitary cell. In 1965, a type of amoeba known as the "brain-eating amoeba" was identified. Naegleria fowleri is its scientific name. This organism is thought to have developed in the United States even though it was initially discovered in Australia. Naegleria comes in a variety of species, but only the fowleri species can infect people. Numerous varieties of Fowleri exist. All are thought to be equally hazardous. The size of N. fowleri ranges from 8 micrometres to 15 micrometers, based on its life cycle and surroundings. A strand, by contrast, is 40–50 micrometres broad. Naegleria reproduces through cell division, like other amoebas. The amoebas develop into inactive cysts when circumstances are unfavourable. The amoeba's eating form, trophozoites, develops from the cysts when circumstances are right.[20]

2} ETIOLOGY :

When tepid fresh water is pushed up the nostrils while swimming, diving, water skiing, using hose-fed water toys, or participating in another leisure activity, N. fowleri exposure happens. Both well water and tap water may be unsafe to consume. Symptomatic illness brought on by N. fowleri is not frequently documented, despite the fact that contact with infected water is prevalent in the United States. The nerve system is primarily impacted by naegleria illness.

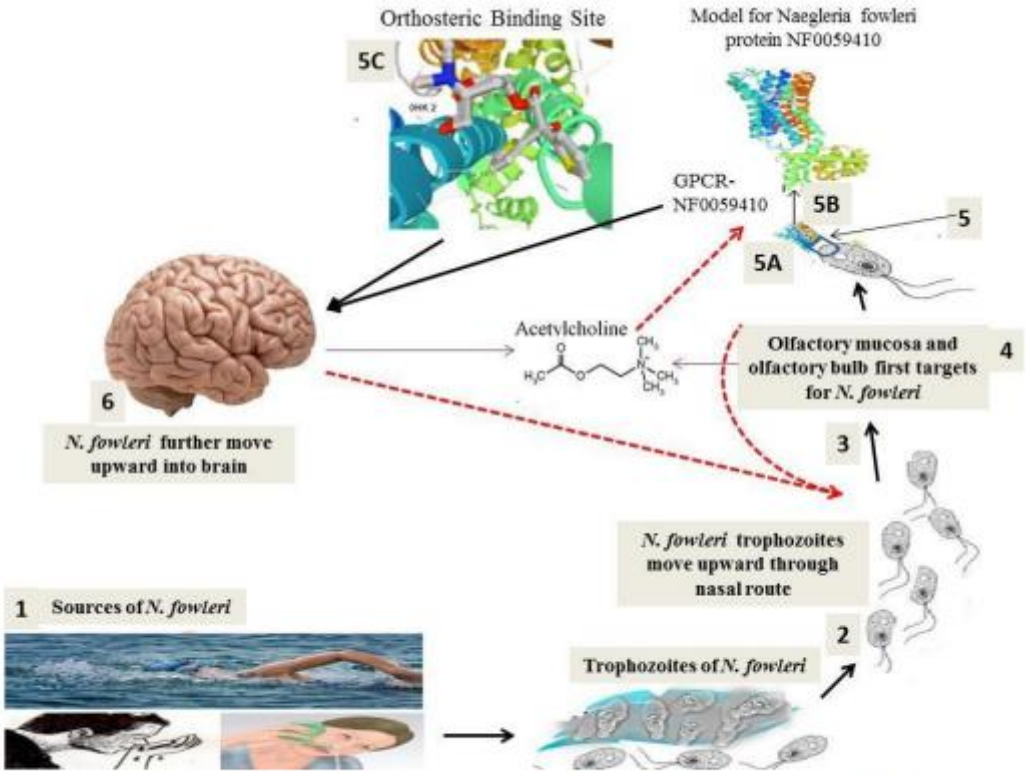


3} PATHOGENESIS :

It has been hypothesised that N. fowleri enters the human body through the nose when water is placed or splashed into the nasal cavity. To reach the olfactory bulbs inside the CNS, infection first attaches to the nasal mucosa and then travels via the olfactory nerve and through the cribriform plate (which is more porous in children and young adults).[21]

Once N. fowleri enters the olfactory bulbs, it stimulates the innate immune system, which includes neutrophils and macrophages, to produce a strong immunological response. As trophozoites, N. fowleri penetrates the human body. Food cups, which are features on the surface of trophozoites, allow the organism to consume human tissue, bacteria, and fungus.[22,23]

The production of cytolytic molecules, such as acid hydrolases, phospholipases, neuraminidases, and phospholipolytic enzymes, is necessary for N. fowleri's pathogenicity in addition to tissue destruction caused by the feeding cup. These molecules contribute to host cell and neuron death.[24]



Diagrammatic representation of N. fowleri pathophysiology.

Due to N. fowleri's pathogenicity and the ensuing strong immune response, there is substantial nerve injury and subsequent CNS tissue destruction that frequently culminates in death.

(1) N. fowleri got into the nose by contaminated water. (3) & (4) The olfactory mucosa and olfactory bulb are the primary targets for N. fowleri. (2) N. fowleri trophozoites travel upward to reach the brain. The acetylcholine binding receptor GPCR NF0059410, which is structurally similar to the human muscarinic M1 receptor, is expressed on N. fowleri Trophozoites as indicated by its bluish shade in (5A). In (5B) a model for the GPCR NF0059410, and in (5C) the amino acid sequence of the acetylcholine binding receptor N. fowleri protein NF0059410. (6) Acetylcholine binding to the GPCR NF0059410 rather than the human receptor causes neurotropic chemotaxis in the trophozoites, which cross and damage the cribriform plate as they travel upward. This movement is further facilitated by the production of acetylcholine (red lines).

3.1] Contact-dependent mechanism :

The damage caused to host cells by N. fowleri is mostly caused by adhesion. Disease development is significantly influenced by N. fowlerito's capacity to adhere to nasal mucosa, move about, and react chemotactically to components of nerve cells.[25,26,27]

Adhesins present on the surface of N. fowleri act as a binding mediator. N. fowleri has been shown to contain two integrin-like proteins that co-localize to the structures that resemble focal adhesions. Anti-integrin antibodies decreased N. fowleri's ability to attach to extracellular matrix (ECM), supporting this.[28]

The cytotoxicity of host cells caused by N. fowleri is mediated by a 60 kDa fibronectin binding protein, which is characterised. N. fowleri extracts exhibit protein kinase C activity, which impacts the cytotoxicity and binding to host cells.[27]

It has been demonstrated that N. fowleri damages host cells by producing reactive oxygen species (ROS) in them (Song et al., 2011).

After binding, phagocytosis and amoebastomes contribute to N. fowleri-induced host cell destruction by the piecemeal consumption of target cells, which is mediated by a sucker mechanism extending from N. fowleri's surface.[29,30]

3.2] . Contact-independent mechanisms:

N. fowleri produces NPFP, a 66 kDa membrane-bound cytolytic pore-forming protein. Depolarization of the membrane potential concerns the integrity of the membrane.

Naegleriapores A and B, pore-forming polypeptides from N. fowleri, have been discovered. Both polypeptides share structural similarities with cytotoxic natural killer and T cells, amoebapores from E. histolytica, and antibacterial and cytolytic polypeptides.[31]

Sphingomyeline is broken down by amoebae with the release of choline, sphingosine, and fatty acids. The production of phospholipases including lysophospholipase and sphingomyelinase, as well as other substances that harm cells' lipid-rich cytoplasmic membranes and demyelinate nerve tissue, by N. fowleri has also been proven.[32,33]

Protease activity may be suppressed mostly by cysteine protease inhibitors, while serine protease activity is also shown at pH 7.0 and 35 °C, where the best protease activity is seen.[34]

Alpha-glucosidase, acid proteinase, N-acetylglucosaminidase, acid phosphatase, 5 -nucleotidase, aspartate aminotransferase, and aminopeptidase activities have also been shown. Among them, cytoplasmic granules simulating lysosomes are related to acid proteinase, N-acetylglucosaminidase, and acid phosphatase; Alpha-d-glucosidase and an aminopeptidase are connected to surface membrane as well as lysosomes, whereas 5 -nucleotidase and aspartate aminotransferase are linked to mitochondria.[35]

Nitric oxide may have a role in the pathophysiology of N. fowleri since it is synthesised by N. fowleri in vitro and the amoebal and human nitric oxide synthases share epitopes.[36]

A heat shock protein 70 (HSP70) has just been discovered. The cytoplasm, pseudopodia, and phagocytic food-cups all contain Nf-cHSP70. N. fowleri proliferation is inhibited by the reduction of Nf-cHSP70 production, and host cell cytotoxicity is also decreased. These findings imply that the proliferation and control of the host immune system may be significantly influenced by Nf-cHSP7[37,38]

Other putative pathogenicity factors include (i) cyclophilin, which is overexpressed in dangerous N. fowleri, and (ii) apoptosis-linked gene-2-interacting protein X1 (AIP1), which controls the sorting of cellular material between organelles in endosomes.[37]

By preventing the incorrect sorting of peptides to lysosomes for destruction, the golgi-localized transmembrane protein HID-1 participates in vesicular exocytosis.[39,40]

Both AIP1 and HID-1 are believed to be helpful in the pathogenicity of N. fowleri, possibly]functioning to control vesicular trafficking in the amoeba. Other factors include (iii) the Ras-related protein Rab-1, which may play a role in vesicular trafficking and, consequently, in the phagocytosis of target cells; (iv) the myosin II heavy chain and myosin Ie (likely involved in phagocytic processes); and (v) the villin-1 protein, which is probably involved in actin-dependent pathogenic processes and may also be significant for N. fowler[37]

DIAGNOSIS :

People who have been exposed to freshwater and exhibit the aforementioned symptoms of meningitis or meningoencephalitis should be immediately suspected of having Naegleria fowleri. Since the symptoms of the presentation may initially be vague, doctors may assume more widespread illnesses like bacterial or viral meningitis. A normal brain scan might be accompanied by a high blood white cell count from routine examinations. If you can avoid it, avoid delaying a spinal tap while expecting a brain scan. Early spinal taps may not reveal a significant infection, and several patients who were discharged from the ER later returned with a declining condition. The spinal tap should be repeated in 8 to 12 hours if suspicion is strong.

Increased amounts of white and red blood cells in spinal fluid are a sign of inflammation. The amoeba cannot be detected on a normal Wright-Giemsa stain, but it can be seen on a routine Gramme stain, which is used to count the number of cells. It is necessary to do a wet mount of fresh spinal fluid immediately in order to check for moving amebae under a microscope.

If the fluid is not warmed, the amoeba do not migrate. If distilled water is introduced to the spinal fluid on the slide, they will also move. If there are numerous white blood cells as a result of severe inflammation, this test may not be successful since most technicians who are not trained to check for Naegleria find amoeba and white blood cells to be quite similar.

In just a few labs across the nation, including the CDC, are conclusive testing for N. fowleri infection performed. They employ one of the three approaches listed below:

1. PCR-based N. fowleri nucleic acid assays in biopsy tissue or CSF

2. N. fowleri antigen tests using immunohistochemistry (IHC) in CSF or biopsy tissue

3. You may also cultivate N. fowleri on a petri dish that has a layer of bacteria on top of it. After that, the culture is examined for twisting trails left by amoebae eating the bacteria. This is not a common prac

The CDC PCR test for Naegleria fowleri is extremely sensitive and specific, which means it detects even minute quantities of amoebae and is seldom negative if the amoeba is indeed present.[22]

Clinical symptoms and indications of N. fowleri infection typically appear 2 to 8 days after infection, while rare cases have been documented in as little as 24 hours.[41,42]

The most typical symptoms of N. fowleri infection are a strong headache, fever, chills, a positive Brudzinski sign, a positive Kernig sign, photophobia, disorientation, seizures, and potential coma, despite the lack of particular signs and symptoms. In few cases, myocardial necrosis and aberrant heart rhythms have also been noted.[43]

The clear correlation between elevated cerebral spinal fluid (CSF) and intracranial pressure and mortality is, arguably, the most significant finding. Patients with N. fowleri infection have shown CSF pressures of 600 mm H2O.[41]

CSF research has revealed a variety of colour anomalies, from grey in the early stages of infection to crimson in the late stages of sickness due to a large increase in red blood cells.[44,45]

Additional increases are observed in the number of polymorphonuclear cells (up to 26,000 mm3) and the presence of trophozoites in the CSF (when stained with trichrome or Giemsa). The midbrain and subarachnoid spaces are among the areas of the brain that magnetic resonance imaging (MRI) of the brain frequently reveals abnormalities in.[41,43]

TREATMENT OPTIONS:

There haven't been any clinical trials that compare the effectiveness of various treatment plans due to the rarity of N. fowleri infections in people. Case reports or in vitro studies are the main sources of information used to determine the effectiveness of medications. Amphotericin B, which has been used in multiple case reports and has been examined in vitro, is possibly the most widely accepted drug for the treatment of N. fowleri infection. In case reports, anti-infectives such fluconazole, miconazole, miltefosine, azithromycin, and rifampin have also been utilised. Other substances including hygromycin, rokitamycin, clarithromycin, erythromycin, roxithromycin, and zeocin have also been investigated in vitro and/or in vivo.[46]

AMPHOTERICIN B:

The minimum amoebicidal concentration of amphotericin B against N. fowleri is 0.01 g/ml. However, in vitro research has indicated that amphotericin B concentrations as low as 0.1 g/ml were required to at least partially inhibit growth, while as high as 0.39 g/ml were required to entirely stop amoeba proliferation. In the in vitro investigations, the associated MIC of amphotericin B to completely eradicate all of the organisms was 0.78 g/ml[47,48]

Although amphotericin B has become the preferred medication for treating primary amoebic meningoencephalitis (PAM), its usage is linked to a number of adverse effects, including kidney toxicity, which limits how much may be used.[49]

Amphotericin B has a number of issues that can be attributed to its inability to dissolve in water, which has an impact on dissolution, compartmental concentration, and clearance. For the treatment of PAM, corifungin, which is referred to as a novel medicinal entity, recently received orphan drug classification. Initial studies on the in vivo effectiveness of corifungin in a mouse model of PAM indicated that it was more active at an equivalent dose than amphotericin B. Corifungin is an outstanding aqueous solubility compound that is chemically the sodium salt of amphotericin B (100 mg/ml). The stated increase in activity is probably explained by the enhanced solubility of corifungin. Unfortunately, there have been no reports of human investigations that would show if the greater solubility would translate into therapeutic advantages such improved blood-brain barrier penetration and/or less kidney toxicity.[50]

MILTEFOSINE :

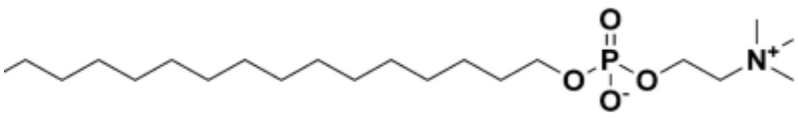


FIG 1 Miltefosine chemical structure.

Miltefosine was used to treat two N. fowleri-infected individuals in 2013, and they both recovered (see more information below). Despite these limitations, these findings indicate potential for miltefosine usage in cases of early diagnosis. Miltefosine is an alkylphosphocholine, which is a phospholipid with a connected choline (Fig. 1). The whole molecule is amphiphilic and has an aliphatic tail and polar phosphocholine head region. It also comes in the zwitterionic form, which is produced by the anionic phosphate and the permanently charged quaternary ammonium ion. Miltefosine's claimed mode of action is an inhibitory effect on protein kinase B (PKB or Akt). This mechanism is conceivable given that phosphatidylinositol 3-kinase (PI3K) and PKB are involved in cell survival and the reason miltefosine was investigated and approved as an anticancer drug (19). Studies are still being conducted on miltefosine to identify its precise bioavailability in people. In rats, it has shown favourable oral bioavailability (80%).[51]

Evidence to date suggests that miltefosine absorption after oral treatment involves both a passive and an active transport mechanism.[52]

In mouse models, miltefosine has a high degree of plasma protein binding (95%) and a broad tissue distribution, with the organ tissues of the lung, adrenal glands, spleen, and liver containing the greatest levels of the drug. Without an active transport mechanism, it is challenging to explain miltefosine's CNS penetration as a continuously charged species. Although specific investigations on miltefosine concentrations in the brain have not been reported, the drug's successful treatment of N. fowleri infection suggests some amount of penetration. It is unclear if the patients' blood-brain barriers have been weakened in any manner as a result of the illness. There haven't been any metabolism studies on human participants. Miltefosine has, however, been examined for its capacity to stimulate CYP3A isoforms as well as its oxidative metabolism against a panel of cytochrome P-450 (CYP450) isoforms. None of those analyses indicated a substantial level of metabolism or the possibility of induction, indicating a minimal risk of drug-drug interactions.[53]

Miltefosine has been made accessible by the CDC under an investigational new drug (IND) process on a need-basis for the treatment of infections brought on by free-living amoebas, such as Acanthamoeba species, Balamuthia mandrillaris, and N. fowleri. Miltefosine is advised by the CDC to be taken orally two to three times day at dosages of 50 mg with a maximum dose of 1.5 mg/kg/day for a total of 28 days.

ADJUNCTIVE THERAPIES :

Fluconazole

Some N. fowleri infections have been treated with the azole antifungal fluconazole in combination with amphotericin B.[54]

It has been demonstrated that the addition of fluconazole to amphotericin B treatment offers some additional advantages.[55,56,57]

The enhanced penetration of fluconazole into the CNS may be the cause of its effectiveness. Through the activation of neutrophils, fluconazole and amphotericin B work together to eradicate N. fowleri infection. [58]

In individuals with probable N. fowleri infections, fluconazole can be used as an additional treatment to amphotericin B, according to these data. The CDC advises administering fluconazole intravenously once day at a dosage of 10 mg/kg/day (600 mg/day at the maximum) for a total of 28 days.[59]

It has been demonstrated in vitro that voriconazole, a broader-spectrum azole antifungal drug, successfully kills N. fowleri at dosages of 1 g/ml.[60]

Azithromycin :

At dosages of 10 and 100 g/ml, the macrolide antibiotic azithromycin has been tested in vitro against N. fowleri and has been proven to suppress more than 90% of organism development.[61]

It has been demonstrated that azithromycin has a 10 g/ml MIC against N. fowleri. Mice infected with N. fowleri had to receive azithromycin at a rate of 75 mg/kg/day in order to survive, according to in vivo investigations. The CDC suggests administering azithromycin intravenously once day at dosages of 10 mg/kg/day (with a daily dose cap of 500 mg) for 28 days.[62]

It should be noted that other medications, including chlorpromazine (an antipsychotic), rifampin (an antibiotic that inhibits RNA polymerase), hygromycin (an aminoglycoside antibiotic not available in the United States), clarithromycin (a macrolide antibiotic), erythromycin (a macrolide antibiotic), and roxithromycin (a macrolide antibiotic) have been tested in vitro against N. fowleri, with either no effect or ineffectiveness.[48,63]

Rifampin:

Rifampin has been utilised in every PAM survivor case in the US and Mexico (all three instances in the US and one survivor in Mexico), but its effectiveness is still in doubt.[64]

The main question is whether rifampin penetrates the CNS sufficiently at the recommended therapeutic dose. According to medication concentrations in the CSF, several publications have shown that rifampin has favourable concentrations in the CNS.[65,66]

But in one study, Mindermann et al. looked at compartmental rifampin concentrations in the CNS and discovered considerable differences.[67]

The concentrations were 0.32 0.11 g/ml and 0.29 0.15 g/ml in normal brain tissue, respectively, in the cerebral extracellular space. These concentrations would be above the necessary MIC for the majority of sensitive bacteria, but they might not be enough to completely eradicate N. fowleri. Rifamycin, a natural substance, was shown to slow the development of N. fowleri by 30 to 35% at doses of 10 g/ml over a 3-day incubation period, according to a preliminary study by Thong et al. in 1977. By the sixth day of incubation, however, rifamycin had lost its capacity to stop N. fowleri growth.[68]

Only when greater quantities of rifampin, a semisynthetic counterpart of rifamycin (100 g/ml), were employed for the 6-day period did growth inhibition (>80%) remain maintained. In a subsequent publication, Ondarza failed to establish a MIC for rifampin against N. fowleri and instead reported an inhibitory concentration (IC50) of >32 g/ml, the highest value assessed in the investigation. The use of rifampin at recommended dosages for the treatment of PAM is not supported by these results.

These findings show that there is no evidence in favour of using rifampin for the treatment of PAM at recommended levels.[69,70]

PREVENTION:

Avoiding exposure to freshwater bodies of water like lakes, rivers, and ponds is one precaution that those who engage in water-related sports in warmer areas can take, particularly in the summer when the water temperature is greater. Due to the fact that N. fowleri cannot thrive in chlorinated or salt water, both dramatically reduce the risk of infection. In order to prevent N. fowleri from entering the nasal passages, people are advised to refrain from leaping into bodies of freshwater, splashing, or dipping their heads under the water. People should wear nasal clips to lessen the possibility that contaminated water may enter the nose if such activities cannot be avoided.

Some recommend cleaning the nose and nasal passages with clean water after swimming in freshwater bodies of water, however the efficacy of this treatment is speculative at this time. The CDC advises using commercially available distilled or purified bottle water if water is going to be used for sinus rinsing.

The CDC advises boiling or filtering water with pores that are 1 m or smaller in order to prepare water for sinus rinsing in the absence of the aforementioned choices.[69]

Conclusion :

Primary amoebic meningoencephalitis (PAM) is caused by the thermophilic flagellated amoeba Naegleria fowleri, sometimes referred to as the "brain-eating" amoeba and with a fatality rate of over 95% in both humans and animals. PAM is a disease that is more common in wealthy nations, yet reports have lately come from emerging nations with warmer climates as well. Warmer water that has been polluted is the most favourable setting for N. fowleri to induce this illness. If not identified and treated right once, infectious trophozoites develop to enter the body through the nose, cross the cribriform plate to the human brain, cause significant CNS damage, result in brain haemorrhage, and ultimately cause death within 3–7 days. The current PAM treatment regimen employs AmB in combination with other medications, however it is seldom effective and has negative side effects. Different in vitro and in vivo research have been conducted in an effort to discover a safer and more efficient medication to treat PAM, some of which have demonstrated strong amoebicidal action. In fact, anti-inflammatory chemicals could aid in lowering the immunopathological response that has been connected to severe tissue damage. Furthermore, it has been proven that these medications' coupling with nanoparticles improves their absorption, amoebicidal efficacy, and cell toxicity in PAM infections. To confirm the full potential of these medications, however, more research is required. The greatest strategy to prevent PAM until a more efficient therapy is created is through preventative measures.

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