

Amoebic meningoencephalitis: granulomatous amoebic encephalitis (GAE), *Balamuthia* amoebic encephalitis (BAE) and primary amoebic encephalitis (PAM)

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What are amoebas?

Amoebas are organisms usually found in water, wet soil, rotting vegetation, animals and humans. Although most types are harmless, a few of them such as *Acanthamoeba*, *Balamuthia mandrillaris*, *Naegleria fowleri* and *Sappinia pedata* can produce life-threatening diseases in humans such as GAE and PAM. These diseases are difficult to diagnose and probably under reported. Most of the time, the diagnosis is made post-mortem (after death).

Amoebas enter the human body through nasal (nose) or cutaneous (skin) route. Recently, organ transplantation has become a new mode of entry. A recent study claims that the brain damage in these types of encephalitis is caused by the immune system (the natural defence mechanism of the body), which overreacts rather than the amoeba itself.

Granulomatous amoebic encephalitis (GAE)

Granulomatous is a serious infection type that develops gradually over an extended period of time. It is caused by *Acanthamoeba*, *Balamuthia mandrillaris* and *Sappinia pedate*.

Acanthamoeba is the most common amoeba found in a wide range of locations: soil, water, air, dust, ventilation and air conditioning systems. In addition, it has been found in hospitals, medicinal pools, dental treatment units, dialysis machines and contact lenses.

Despite the many opportunities for contact with amoeba, the *Acanthamoeba* infections are rare in humans, except for the *Acanthamoeba* keratitis (AK), it mostly occurs in immunocompromised individuals (those having an immune system weakened by the illness or treatment). *Acanthamoeba* enters the body through lesions in the skin contaminated by the soil or through upper respiratory tract (mouth or nose). Most people have a history of skin lesion or lung infection occurring a few months earlier.

Once in the body, amoeba can spread to the central nervous system (CNS) and various organs. The types of infections produced include GAE, nasopharyngeal, cutaneous and disseminated infections and AK when *Acanthamoeba* directly attacks the corneal surface (eyes). Symptoms can include fever, headache, behavioural manifestations, and hemiparesis, which can progress to seizures, coma and death. [*Acanthamoeba* is not usually found in cerebrospinal fluid (CSF), but it can be isolated through brain biopsy. It is usually misdiagnosed; hence the mortality rate is high.]

The treatment consists in various antimicrobial drugs (drugs to treat the infection) sometimes used at the same time. Drugs that result in a cure in one patient may have no success in other patients. The outcome is influenced by the following factors: early treatment, the infective dose of amoeba, the type and characteristics of amoeba, and the immune system of the individual. Most survivors had skin lesions that helped in the early detection of GAE. Their treatment consisted in both surgical resection of the affected lesion and multiple antimicrobials.

***Balamuthia* amoebic encephalitis (BAE)**

Balamuthia Mandrillaris, a newest discovered type of amoeba, can cause Balamuthia Amoebic Encephalitis (BAE), which leads to death in most of the cases. *Balamuthia* is present in soil and possibly water although there was no obvious history of swimming or other water activities for individuals who have developed BAE. The contamination happens through respiratory route or skin lesions (breaks in the skin).

Patients present with headache, fever, characteristics skin lesions, stiff neck, nausea, vomiting, acutely confused state, aphasia (impairment of language) and seizures. Though the course of the illness is gradual, the disease progresses within weeks to months. The diagnosis is made most of the time after death through autopsy. The treatment is problematic, as there is no antimicrobial treatment protocol determined yet.

Over 200 cases of BAE have been reported worldwide, with only 12 confirmed survivors, most of the cases presenting within the US. In each instance the key was to initiate antimicrobial treatment early, with Miltofosine being suggested for its therapeutic effects in the role of anti-microbial treatment of BAE. However further studies have to be done to test its efficacy. The patients who survived ranged from 2 years old to 80 years old, suggesting age may not play a factor in prognosis.

Primary amoebic meningoencephalitis (PAM)

Naegleria fowleri produces primary amoebic meningoencephalitis (PAM). This is a very rare, but serious disease with a mortality rate of more than 95%. From 1962 up to present, there were 440 cases reported in the USA, Australia and Europe, and up to few cases in China.

Naegleria fowleri is more sensitive to the environment than *acanthamoeba* and it cannot survive in seawater. Contamination can happen through swimming in contaminated fresh water or through nasal irrigation for cleansing (religious practice, medical indication or recreational play). Warm fresh waters (lakes, rivers, and hot springs) together with a bacterial food supply are ideal habitats for *Naegleria fowleri*. Usually, it affects healthy children and young people, more males than females, who have a history of swimming or bathing in fresh water. Most people have become infected during periods of very warm temperatures.

After entering the nostrils, *Naegleria fowleri* circulates towards the brain along the olfactory nerve's tract. It develops within a few days of contamination, with fever, headache, behavioural disturbances, nausea, and vomiting. Death occurs 1-2 weeks after hospitalisation. The dramatic outcome could be a result of the rapid onset and delay in diagnosis.

Treatment consists of a mixture of drugs ranging from antimicrobial drugs to experimental anti-cancer drugs. *Naegleria* are highly sensitive to the antifungal drug amphotericin B (AmB), and it has been used in all cases as the core antimicrobial where recovery occurred.

The level of *Naegleria fowleri* in swimming water should be controlled. In 2000, Australia adopted a legal standard for *Naegleria fowleri* in surface water: a guideline level of five thermophilic *Naegleria fowleri* per litre, and an action level of two thermophilic *Naegleria fowleri* per litre.

Greater awareness of these amoebas and the diseases they cause could improve the timescale to reach a diagnosis before death occurs. This together with an effective antimicrobial treatment may improve the chances of survival for people with GAE or PAM.

Further information:

- Centers for Disease Control and Prevention www.cdc.gov/parasites/naegleria/general.html
- 'A Single Swim' by Kristina Circelli. This book is a combination of stories as told by family members and scientific facts by medical specialists. www.kristinacircelli.com/books/a-single-swim/

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