



Free-Living Amebic Infections

Acanthamoeba spp., *Balamuthia mandrillaris*, *Naegleria fowleri*

DISEASE REPORTABLE WITHIN 24 HOURS OF DIAGNOSIS

Per N.J.A.C. 8:57, healthcare providers and administrators shall report by mail or by electronic reporting within 24 hours of diagnosis, confirmed cases of listeriosis to the health officer of the jurisdiction where the ill or infected person lives, or if unknown, wherein the diagnosis is made. A directory of local health departments in New Jersey is available at <http://localhealth.nj.gov/>.

If the health officer is unavailable, the healthcare provider or administrator shall make the report to the Department by telephone to (609) 826-5964, between 8:00 A.M. and 5:00 P.M. on non-holiday weekdays or to (609) 392-2020 during all other days and hours.

1 THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent and Background

Free-living amoebae belonging to the genera *Acanthamoeba*, *Balamuthia*, and *Naegleria* are rare causes of disease in humans and animals.

Acanthamoeba spp. are ubiquitous in the environment and have been found in a variety of sites, including soil; fresh, brackish, and sea water; field-grown vegetables; sewage; swimming pools; contact lens supplies; medicinal pools; dental treatment units; dialysis machines; heating, ventilating, and air conditioning systems; and tap water; mammalian cell cultures; and vegetables. *Balamuthia mandrillaris* has been isolated from soil and dust, and also from autopsy specimens of infected humans and animals.

Acanthamoeba spp. and *Balamuthia mandrillaris* are free-living amoebae capable of causing granulomatous amoebic encephalitis (GAE). *Acanthamoeba* may also cause cutaneous lesions, particularly in immunocompromised individuals. Because species level identification is not typically performed on *Acanthamoeba*, the full range of pathogenic species within the genus is not known. *B. mandrillaris* may also occur in association with skin lesions. *Naegleria fowleri* produces an acute, and usually lethal, central nervous system disease called primary amoebic meningoencephalitis (PAM).

B. Clinical Description

Acanthamoeba spp.: Disseminated infection typically shows up as inflammation of the lungs or sinuses, and/or skin infections but has the potential to spread to the brain. GAE has a chronic onset that progressively worsens over a span of weeks to months. Signs and symptoms are typical of meningoencephalitis and encephalitis and involve varying degrees of neurological impairment. There are very few known survivors of GAE. Cutaneous acanthamebiasis presents as single or disseminated chronic skin lesions, which are most commonly crusted or ulcerated, they may be indurated or have an eschar. Skin infections caused by *Acanthamoeba* can appear as reddish nodules, skin ulcers, or abscesses in the skin. The lesions may be mistaken for fungal or mycobacterial skin infection, cutaneous amoebiasis caused by *Entamoeba histolytica* or cutaneous leishmaniasis. These may occur with or without concurrent central nervous system disease.

Balamuthia mandrillaris: Infection with *B. mandrillaris* involves a similar course to *Acanthamoeba*-associated GAE. The disease might appear mild at first but can become more severe over weeks to several months. Often the disease is fatal with a case fatality rate of more than 89%. Plaque-like skin lesions, most often on the face, particularly in the cheek or nose area, but sometimes on the torso or limbs may precede the development of neurological symptoms by weeks or months.

Naegleria fowleri: PAM is characterized by severe CNS dysfunction with rapid degeneration caused by hemorrhagic-necrotizing meningoencephalitis. Unlike GAE, the onset of PAM symptoms occurs quickly following infection (1-9 days; median 5 days after swimming or other nasal exposure to *Naegleria*-containing water). Symptoms are similar to bacterial meningitis, for which it is often mistaken, with deteriorating neurological function and complications. The case fatality rate is extremely high.

C. Reservoirs

There is no major reservoir host as these amebic species are free-living in the environment and are only opportunistically parasitic. However, such infections have been documented in a variety of animal species.

D. Modes of Transmission

Acanthamoeba spp. are free-living amoebae widely distributed in soil; fresh, brackish, and sea water; swimming pools; tap water; contact lens solutions; heating and air conditioning systems; and other environmental sources. Transmission occurs when trophozoites or cysts enter the body through the eye, respiratory tract, or broken skin. Entry through the nasal passages or lower respiratory tract, or through ulcerated skin, may allow hematogenous dissemination to the central nervous system (CNS), causing granulomatous amebic encephalitis (GAE), primarily in immunocompromised persons. Both cysts and trophozoites may be found in infected tissues.

Balamuthia mandrillaris are soil- and dust-associated free-living amoebae transmitted through inhalation of contaminated dust into the lower respiratory tract or through direct inoculation via broken or ulcerated skin. Following entry, organisms may disseminate hematogenously to the CNS, leading to granulomatous amebic encephalitis (GAE), or cause disseminated disease and cutaneous lesions. Unlike *Acanthamoeba*, *Balamuthia* infection has also been documented through solid organ transplantation from infected donors. Both cysts and trophozoites are found in tissue, and infection can occur in immunocompromised as well as immunocompetent individuals.

Naegleria fowleri are thermophilic free-living amoebae found in warm fresh water, soil, geothermal sources, and inadequately chlorinated recreational or tap water. Transmission occurs when contaminated water enters the nasal passages, typically during swimming, diving, water sports, or sinus irrigation. Trophozoites penetrate the nasal mucosa and migrate along the olfactory nerves directly to the brain, where they cause primary amebic meningoencephalitis (PAM), a rapidly progressive and often fatal infection. *Naegleria* infection does not occur through ingestion of contaminated water, and cysts are not seen in brain tissue; trophozoites (and occasionally flagellated forms) are identified in cerebrospinal fluid and affected tissue.

E. Incubation Period

Infections from *Acanthamoeba* and *Balamuthia mandrillaris* often progress from weeks to months. *Naegleria fowleri* (causing PAM) has a rapid incubation of 1 to 14 days.

F. Period of Communicability or Infectious Period

Free-living amoebae are not known to spread from person to person.

G. Epidemiology

Between 1955 and 2015, there have been about 350 cases of free-living amebic infections reported in the United States caused by *Acanthamoeba* spp., *Balamuthia mandrillaris*, and *Naegleria fowleri* causing PAM. Recent developments include expansion of the geographic range of *N. fowleri* infection to northern and Midwestern states, the identification of nasal irrigation for either medical or religious purposes as a risk factor for infection, and the finding of *N. fowleri* in a treated public drinking water distribution system. Solid organ transplantation has also recently emerged as a risk factor for *Balamuthia mandrillaris* infection in organ recipients.

2 NJDOH CASE DEFINITION

A. Case Classification for *Acanthamoeba* spp.

1. Clinical Criteria

An infection presenting as meningoencephalitis or encephalitis, disseminated disease (affecting multiple organ systems), or cutaneous disease. *Acanthamoeba* spp. GAE presents similarly to *B. mandrillaris* GAE with early personality and behavioral changes, depressed mental status, fever, photophobia, seizures, nonspecific cranial nerve dysfunction, and visual loss. Skin lesions and sinus disease may also be seen.

2. Laboratory Criteria

Confirmatory laboratory evidence

Detection of *Acanthamoeba* spp. antigen or nucleic acid (e.g. immunohistochemistry or PCR) from a clinical specimen (e.g., tissue) or culture.

3. Epidemiologic Linkage

None specified for case classification

B. Case Classification for *Balamuthia mandrillaris*

1. Clinical Criteria

An infection presenting as meningoencephalitis or encephalitis, disseminated disease (affecting multiple organ systems), or cutaneous disease. Granulomatous amebic encephalitis (GAE) can include general symptoms and signs of encephalitis

such as early personality and behavioral changes, depressed mental status, fever, photophobia, seizures, nonspecific cranial nerve dysfunction, and visual loss.

2. Laboratory Criteria

Confirmatory laboratory evidence

Detection of *B. mandrillaris* antigen or nucleic acid or nucleic acid (e.g., immunohistochemistry or PCR) from a clinical specimen (e.g., tissue) or culture.

3. Epidemiologic Linkage

None specified for case classification

C. Case Classification for *Naegleria fowleri*

1. Clinical Criteria

An infection presenting as meningoencephalitis or encephalitis. The clinical presentation of PAM is like that of acute meningitis caused by other pathogens and symptoms include headache, nausea, vomiting, anorexia, fever, lethargy, and stiff neck. Disorientation, mental status changes, seizure activity, loss of consciousness, and ataxia may occur within hours of initial presentation.

2. Laboratory Criteria

Confirmatory laboratory evidence

Detection of *N. fowleri* antigen or nucleic acid from a clinical specimen (e.g., immunohistochemistry or PCR)

Supportive laboratory evidence

Visualization of motile amebae in a wet mount of CSF

OR

Isolation of *N. fowleri* in culture from a clinical specimen

3. Epidemiologic Linkage

None specified for case classification

D. Case Classification

1. Confirmed

- A case that meets clinical criteria AND confirmatory laboratory evidence.

2. Probable (*Naegleria fowleri* only)

- A case that meets clinical criteria AND supportive laboratory criteria linkage.

E. Comments

Acanthamoeba spp. and *B. mandrillaris* can cause clinically similar illnesses and might be difficult to differentiate using commonly available laboratory procedures. Definitive diagnosis by a reference laboratory might be required. Several species of *Acanthamoeba* are associated with infection (i.e., *A. castellanii*, *A. culbertsoni*, *A. hatchetti*, *A. healyi*, *A. polyphaga*, *A. rhysodes*, *A. astonyxis*, *A. lenticulate* and *A. divionensis*). A negative test on CSF does not rule out *Acanthamoeba* spp. infection because the organism is not commonly present in the CSF.

Although it is unknown if *Acanthamoeba* spp. can be transmitted via organ transplantation, patients presenting with the above clinical criteria who have received a solid organ transplant should be further investigated to determine if the infection was transmitted through the transplanted organ. An investigation of the donor should be initiated through notification of the organ procurement organization (OPO) and transplant center.

Naegleria fowleri might cause clinically similar illness to bacterial meningitis, particularly in its early stages. Definitive diagnosis by a reference laboratory is required. Unlike *Balamuthia mandrillaris* and *Acanthamoeba* spp., *N. fowleri* is commonly found in the CSF of patients with PAM. After the onset of symptoms, the disease progresses rapidly and usually results in death within 3 to 7 days. Patients presenting with the above clinical criteria and found to have a history of recreational freshwater exposure in the two weeks prior to presentation or are known to have performed nasal irrigation (e.g., use of a neti pot for treatment of sinus conditions or practice ritual ablution including nasal rinsing) in the absence of another explanation for their condition, should be investigated further. Urgent confirmatory testing and treatment should be initiated.

F. Criteria for Distinguishing a New Case from an Existing Case

None specified.

G. Differences from CDC Case Definition

There are no substantive differences between the NJDOH and CDC case definitions.

3 LABORATORY TESTING

Clinical and commercial laboratories are not required to submit clinical specimens to the NJDOH Public Health and Environmental Laboratories (PHEL). The Foodborne and Waterborne Disease Unit (FWD Unit) within the Communicable Disease Service (CDS) will approve and help coordinate clinical, product and environmental sample submission to PHEL for further testing at CDC if warranted.

4 PURPOSE OF SURVEILLANCE AND REPORTING REQUIREMENTS

- To identify transmission sources of public health concern and to stop transmission.
- To provide education about reducing the risk of infection.

5 CASE INVESTIGATION

A. Forms

It is the health officer's responsibility to investigate the case by interviewing the patient and others who may be able to provide pertinent information about the case patient's illness. Some of the required information can be obtained from the patient's healthcare provider or the medical record. Much of the information on exposure and history must be obtained from the parent or guardian as it is not likely to be found in the medical record. The "Free Living Ameba (FLA) Case Report Form" is the investigation tool for LHDs to use when conducting interviews. All information gathered using this tool should be entered into CDRSS.

B. Update CDRSS

Please refer to the disease prioritization guidance that provides LHDs with timeframes for public health response and enter critical details on all cases in CDRSS: demographics, signs/symptoms, clinical status, laboratory information, patient location, and sources of infections and risk factors. Free-Living Amebic Infections are a Priority Level 1 disease and critical details should be entered into CDRSS within 6 hours. If critical details cannot be obtained, local health departments (LHDs) should document the reason for the delay and the anticipated time when these details will be available.

C. Other Reporting/Investigation Issues

Once LHD completes its investigation and assigns a report status of "LHD CLOSED," the FWD Unit will review the case and approve the case by changing the report status to "DHSS APPROVED." At this time, the case will be submitted to CDC and locked for editing. If additional information is received after a case is "DHSS APPROVED," you will need to contact the FWD Unit at NJDOH to reopen the case. This should be done only if relevant exposure information becomes available or if the additional information changes the case status of the report.

6 CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements (NJAC 8:57)

None

B. Protection of Contacts of a Case

None

C. Managing Special Situations

Cases that have been linked to multistate clusters or outbreaks may require additional follow-up from LHDs. Specific investigation details will be provided by the FWD Unit on a case-by-case basis.

7 OUTBREAK SITUATIONS

If the number of reported cases in a facility or jurisdiction is higher than usual, or if an outbreak is suspected, LHDs should investigate to determine the source of infection and mode of transmission. NJDOH staff will help determine a course of action to prevent further cases and perform surveillance for cases across jurisdictions that may be difficult to identify at a local level. Suspected outbreaks should be immediately reported to the LHD where the facility is located. A directory of LHDs with after-hours contact information is available at www.localhealth.nj.gov. LHDs should immediately notify NJDOH by telephone at (609) 826-5964 during business hours and (609) 392-2020 after business hours and on weekends and holidays.

8 PREVENTIVE MEASURES

Unfortunately, at this point, steps that can be taken to prevent GAE and other types of non-keratitis *Acanthamoeba* infections are unclear. Some cases of GAE and severe sinus infections caused by *Acanthamoeba* have been linked to nasal or sinus rinsing. To prevent infection, it is recommended to always [use sterile water, distilled water, or boiled tap](#).

There are no known measures to prevent *Balamuthia* infections at this point.

Naegleria fowleri is present in all lakes, ponds, rivers, hot springs, and other fresh water. Primary amebic meningoencephalitis, or PAM are **not** caused by swimming in properly maintained and disinfected pools, surf parks, other recreational water venues or swallowing water containing *Naegleria fowleri*. There are also no known reports due to swimming in salt water. If an infection has been identified in the area, be sure to follow [prevention tips](#) to reduce risk:

- Avoid activities during warmer months when water temperatures rise and water levels go down.
- Hold nose shut or use a nose clip when jumping or diving into the water.

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- Keep head above water in hot springs and other naturally hot (geothermal) water.
- Avoid digging in or stirring up sediment in shallow fresh water.
- Environmental testing and signage are not recommended because:
 - The location and concentration can vary over time within the same body of water
 - There are no standardized testing methods to detect or determine concentration
 - Water in areas without signs may be considered to be safe

References

1. [NJ Administrative Code](#)
2. [NJDOH Disease Reporting](#)
3. [NJDOH Free Living Amebic Infection Webpage](#)
4. [CDC Free-Living Amebic Infections](#)
5. [CSTE Public Health Reporting and National Notification for Free-Living Amebic Infections](#)