Wisconsin Department of Health Services
Division of Public Health
P-02553 (Rev 07/2018)

Communicable Disease Case Reporting and Investigation Protocol

FREE-LIVING AMEBA INFECTIONS

(Other than *Naegleria fowleri*)

I. IDENTIFICATION AND DEFINITION OF CASES

A. **Background:** Free-living amebae (FLA) belonging to the genera *Acanthamoeba*, *Balamuthia*, *Naegleria* and *Sappinia* can cause disease in humans and animals. *Acanthamoeba* spp. and *Balamuthia mandrillaris* are opportunistic FLA capable of causing a chronic, insidious, mostly fatal disease called granulomatous amebic encephalitis (GAE), particularly in individuals with compromised immune systems. *Acanthamoeba* spp. can also invade the eye in otherwise healthy individuals and cause vision-threatening *Acanthamoeba* keratitis (corneal infection), especially in contact lens wearers. *Sappinia pedata* has been implicated in a case of non-granulomatous amebic encephalitis. *Naegleria fowleri* produces an acute, rapidly progressive, and usually lethal central nervous system disease called primary amebic meningoencephalitis (PAM), typically in young, healthy persons with a recent history of exposure to warm, untreated recreational water. PAM is a Category I notifiable condition in Wisconsin with distinct reporting and urgent treatment recommendations.

Acanthamoeba, *Balamuthia*, and *Sappinia* organisms are ubiquitous in nature and can be found in bodies of water, soil, and air. FLA have multiple stages in their life cycle, which can be completed in the environment without dependence on a host (hence, free-living). *N. fowleri* has three stages: amoeba (trophozoite), cyst, and flagellate, whereas *Acanthamoeba* spp., *B. mandrillaris*, and *Sappinia pedata* have two stages: amoeba and cyst. Cyst stages are hardy in the environment and tolerant to chlorine disinfection and most contact lens solutions. *Acanthamoeba* spp. have been found in swimming pools, therapy pools, contact lens equipment, dental treatment units, dialysis machines, heating, ventilating, and air conditioning systems and premise plumbing where biofilms protect them from disinfectants.

B. **Clinical Description:**

1. **Amebic Keratitis (*Acanthamoeba* spp.):** Amebic keratitis is a local infection of the cornea caused by direct invasion of the cornea by *Acanthamoeba* species. Symptoms, which appear days after infection, include foreign body sensation, photophobia, decreased visual acuity, tearing, intense pain, and redness of the eye. Bilateral involvement is seen in 11% of cases. It occurs most typically among healthy, contact lens users, or persons with pre-existing corneal trauma. Although treatable with topical medications, affected individuals are at risk for permanent visual impairment or blindness. Early recognition and treatment improves prognosis dramatically. For people who wear contact lenses, storing and handling lenses improperly or having lenses come into contact with contaminated water are major risk factors. The wearing of contact lenses while swimming or participating in other water sports may also be a risk factor.

2. **Free-Living Ameba Infections (Non-Keratitis):** Both *B. mandrillaris* and several species of the genus *Acanthamoeba* can cause infections that present as meningoencephalitis or encephalitis, disseminated disease (affecting multiple organ systems), or cutaneous disease. *Acanthamoeba* spp. and *B. mandrillaris* typically enter the body from a primary infection in the sinuses or skin. The amebae can then invade the central nervous system by hematogenous dissemination, causing disseminated disease or granulomatous amebic encephalitis (GAE). *Acanthamoeba* can cause GAE in persons who are immunosuppressed from a variety of causes (e.g., HIV/AIDS, cancer, diabetes), whereas *B. mandrillaris* can cause GAE in both immune-competent and immune-compromised individuals. *B. mandrillaris* can also be transmitted via solid organ transplantation.

   a. **Granulomatous amebic encephalitis (*Acanthamoeba* spp., *B. mandrillaris*):** GAE is a rare but serious infection of the brain and spinal cord. The incubation period is unknown but is believed to be weeks to months. It has a slow and insidious onset and develops into a subacute or chronic disease lasting several weeks to months. However, *B. mandrillaris* infections associated with organ transplantation have an especially rapid clinical course.

   B. mandrillaris GAE presents similarly to *Acanthamoeba* spp. GAE. Initial symptoms may include headache, photophobia, and stiff neck accompanied by positive Kernig's and Brudzinski's signs. Other

symptoms include nausea, vomiting, low-grade fever, muscle aches, weight loss, depressed mental state, personality changes, lethargy, dizziness, loss of balance, cranial nerve palsies, other visual disturbances, hemiparesis, seizures, and coma. Neuroimaging may show space-occupying or ring-enhancing lesions. Skin lesions and sinus disease may also be seen. Skin infections can appear as reddish nodules, skin ulcers, painless plaques, or abscesses in the skin. Skin lesions may precede the onset of neurologic symptoms by one month to approximately two years. Once the disease progresses to neurologic infection, it is generally fatal within weeks or months. However, a few patients have survived this infection.

b. **Disseminated Infection (*Acanthamoeba* spp., *B. mandrillaris*):** A widespread infection resulting from hematogenous dissemination of amoebae that can affect the skin, sinuses, lungs, and other organs independently or in combination. Disseminated infection typically presents as inflammation of the lungs or sinuses, and/or skin infections but has the potential to spread to the brain. It can occur both with and without GAE. Disseminated infection is more common in persons with compromised immune systems. While unusual, disseminated infection can also affect healthy children and adults.

c. **Amebic Encephalitis (*Sappinia pedata*):** *S. pedata* has been implicated in a single case of amebic encephalitis in an immunocompetent individual. Symptoms of headache, vomiting, photophobia, and loss of consciousness were preceded by a sinus infection. No granuloma was seen on imaging. The patient recovered following treatment.

C. Laboratory Criteria:

1. Free-living ameba infection, *Acanthamoeba* keratitis:

- **Confirmatory laboratory evidence:** Laboratory-confirmed *Acanthamoeba* spp. keratitis infections are defined as the detection of *Acanthamoeba* species:
  - Organisms in corneal scraping, or biopsy specimens, OR
  - Nucleic acid (e.g., polymerase chain reaction) in corneal scraping, or biopsy specimens, OR
  - Antigen (e.g., direct fluorescent antibody) in corneal scraping, or biopsy specimens.
- **Supportive laboratory evidence**: positive identification of *Acanthamoeba* trophozoites or cysts using confocal microscopy.

2. Free-living ameba infection, (*Acanthamoeba* spp. [Non-keratitis], *Balamuthia mandrillaris, Sappinia pedata*):

- **Confirmatory laboratory evidence:** Laboratory-confirmed free-living ameba infections (excluding keratitis) are defined as the detection of *Acanthamoeba spp., B. mandrillaris, or S. pedata*:
  - Nucleic acid (e.g., polymerase chain reaction) in cerebrospinal fluid (CSF), biopsy, tissue specimens, or culture, OR
  - Antigen (e.g., direct fluorescent antibody) in CSF, biopsy, tissue specimens, or culture.
- **Supportive laboratory evidence:** identification of *Acanthamoeba spp., B. mandrillaris, or S. pedata* organisms in CSF, biopsy, tissue specimens, or culture from a clinical specimen.

Notes: FLA species can cause clinically similar illnesses and may be difficult to differentiate using commonly available laboratory procedures; definitive diagnosis by a reference laboratory is required. A negative test on CSF does not rule out *B. mandrillaris* or *Acanthamoeba* infection because these organisms are not commonly present in CSF. Infections with *Naegleria fowleri*, which may be seen in a wet mount of CSF, should be reported as cases of Primary Amebic Meningoencephalitis (PAM)/*Naegleria fowleri* infection.

If suspected free-living amoeba trophozooites are visualized in a clinical specimen, telediagnosis can be arranged at the Centers for Disease Control and Prevention (CDC) by emailing photos through DPDx, CDC's Division of Parasitic Diseases and Malaria telediagnosis tool. Instructions for submitting photos through DPDx are available at https://www.cdc.gov/dpdx/contact.html.

Positive clinical specimens should be forwarded to CDC for laboratory confirmation and ameba identification via the Wisconsin State Laboratory of Hygiene (WSLH). Contact the Bureau of Communicable Diseases (BCD), Communicable Diseases Epidemiology Section, to obtain approval and instructions prior to submitting specimens to WSLH.

D. **Wisconsin Surveillance Case Definition:**

1. **Free-living ameba infection, *Acanthamoeba* keratitis:**
   - **Confirmed:** a clinically compatible illness that meets the confirmatory laboratory criteria for *Acanthamoeba* keratitis.
   - **Probable:** a clinically compatible illness that meets the supportive laboratory criteria for *Acanthamoeba* keratitis.

2. **Free-living ameba infection (*Acanthamoeba* spp. [Non-keratitis], *Balamuthia mandrillaris, Sappinia pedata*): Confirmed:** a clinically compatible illness that meets the confirmatory laboratory criteria.

II. REPORTING

A. **Wisconsin Disease Surveillance Category II— Methods for Reporting:** This disease shall be reported to the patient's local health officer or to the local health officer's designee within 72 hours of recognition of a case or suspected case, per Wis. Admin. Code § DHS 145.04 (3) (b). Report electronically through the Wisconsin Electronic Disease Surveillance System (WEDSS), or mail or fax a completed Acute and Communicable Disease Case Report (F-44151) to the address on the form.

Note: Suspected cases of *Naegleria fowleri* infection should be reported as Primary Amebic Meningoencephalitis (PAM)/*Naegleria fowleri* infection (Category I notifiable condition). See the Primary Amebic Meningoencephalitis Case Reporting and Investigation Protocol.

B. **Responsibility for Reporting**: According to Wis. Admin. Code § DHS 145.04(1), persons licensed under Wis. Stat. ch. 441 or 448, laboratories, health care facilities, teachers, principals, or nurses serving a school or day care center, and any person who knows or suspects that a person has a communicable disease identified in Appendix A (including eye care professionals).

C. **Clinical Criteria for Reporting**:

1. **Free-living ameba infection, Acanthamoeba keratitis:** An infection of the cornea characterized by eye pain, redness, excessive tearing, photophobia, foreign body sensation, and blurred vision, with confirmatory or supportive laboratory evidence of infection.

2. **Free-living ameba infection, (*Acanthamoeba* spp. [Non-keratitis], *Balamuthia mandrillaris, Sappinia pedata*):** An infection presenting as meningoencephalitis or encephalitis, disseminated disease (affecting multiple organ systems), or cutaneous disease, with confirmatory or supportive laboratory evidence of infection. The case report should specify the suspected or confirmed etiologic genus and species name.

Note: Infections presenting as acute meningoencephalitis or encephalitis with visualization of motile amebae in a wet mount of CSF should be reported immediately as suspect cases of Primary Amebic Meningoencephalitis/*Naegleria fowleri* infection until laboratory confirmation proves otherwise.

D. **Laboratory Criteria for Reporting:**

1. **Free-living ameba infection, *Acanthamoeba* keratitis:** Laboratory evidence of infection by:
   - Detection of *Acanthamoeba* spp. organisms in corneal scraping, or biopsy specimens, OR
   - Detection of *Acanthamoeba* spp. nucleic acid (e.g., polymerase chain reaction) in corneal scraping, or biopsy specimens, OR
   - Detection of *Acanthamoeba* spp. antigen (e.g., direct fluorescent antibody) in corneal scraping, or biopsy specimens, OR
   - Positive identification of *Acanthamoeba* trophozoites or cysts using confocal microscopy.

   When available, species designation and molecular characterization (e.g., genotype) should be reported.

2. **Free-Living Ameba Infection, (*Acanthamoeba* spp. [Non-keratitis], *Balamuthia mandrillaris, Sappinia pedata*):**
   Laboratory evidence of *Acanthamoeba* spp., *B. mandrillaris*, or *S. pedata* infection by:
   - Isolation of organisms in CSF, biopsy, tissue specimens, or culture from a clinical specimen, OR
   - Detection of nucleic acid in CSF, biopsy, tissue specimens, or culture of clinical specimen, OR
   - Detection of antigen in CSF, biopsy, tissue specimens, or culture of clinical specimen.

   When available, species designation and molecular characterization (e.g., genotype) should be reported.

Note: Laboratory visualization of motile amebae in a wet mount of CSF should be reported immediately as a suspected case of Primary Amebic Meningoencephalitis/*Naegleria fowleri* infection until laboratory confirmation proves otherwise.

III. CASE INVESTIGATION

A. **Responsibility for case investigation**: It is the responsibility of the local health department (LHD) to investigate or arrange for investigation of suspected or confirmed cases as soon as is reasonably possible. A case investigation may include information collected by phone, in person, in writing, or through review of medical records or communicable disease report forms, as necessary and appropriate. The investigation should begin as soon as possible after receiving report. Contact and work with Communicable Diseases Epidemiology Section (CDES) staff on the investigation. A source investigation is required. Investigation responsibilities are outlined below in section III C.

B. **Required Documentation:**
1. Complete the WEDSS disease incident investigation report, including all appropriate, disease-specific tabs. This can be facilitated by using the DPH *Acanthamoeba* Keratitis Interview Worksheet or Free-Living Ameba Infection (Non-Keratitis) Interview Worksheet (contact CDES).
2. Obtain copies of **all** laboratory test results and electronically attach or upload them to the disease incident filing cabinet.
3. Complete a CDC Free-Living Ameba Infection Case Report Form for all FLA infections **other than keratitis** (form will be uploaded to WEDSS disease incident filing cabinet by CDES). Request patient medical records, laboratory reports, and autopsy reports as needed to complete the case report form. Upload the completed CDC form to the disease incident filing cabinet and notify CDES.
4. Upon completion of investigation, set WEDSS disease incident process status to “Sent to State” and notify CDES.

C. **Additional Investigation Responsibilities:**
1. Enter all available initial case report information into WEDSS.
2. Review the case definition, background on the disease, and any laboratory testing results.
3. Contact the patient’s health care provider to confirm the diagnosis. Determine if patient exhibited clinically compatible illness, obtain current patient status, onset date of illness, and determine if patient is immunocompromised. Ask what information has been shared with the patient and family.
4. Assess patient risk factors by interviewing the patient or a proxy (parent/guardian, next of kin) if patient is deceased or too ill to be interviewed. Complete the interview using the appropriate sections of the *Acanthamoeba* Keratitis Interview Worksheet or Free-Living Ameba Infection (Non-Keratitis) Interview Worksheet (contact CDES) and enter the information into WEDSS. Exposure periods may vary according to type of disease present; consult the interview worksheet for instructions.
5. Provide education on pathogen-specific prevention and address case-patient family’s questions or concerns.
6. Follow up on special situations, including environmental assessments of agent-specific exposures elicited during interviews. Consult CDES.
7. In consultation with CDES, coordinate submission of positive patient specimens to CDC for confirmation and ameba identification. Contact CDES to obtain prior approval and submission instructions prior to submission. A completed CDC form 50-34 (specimen submission form) citing WSLH as the state public health laboratory/submitter must accompany the specimen to CDC. Definitive laboratory confirmation and diagnosis by the CDC is required.

8. Patients presenting with the above clinical criteria who have received a solid organ transplant must 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 and transplant center. Additional coordination with other local health jurisdictions and state or federal agencies may be required.

IV. PUBLIC HEALTH INTERVENTIONS AND PREVENTION MEASURES

A. In accordance with Wis. Admin. Code § DHS 145.05, local public health agencies should follow the methods of control recommended in the current editions of *Control of Communicable Diseases Manual*, edited by David L. Heymann, published by the American Public Health Association, and the American Academy of Pediatrics' *Red Book: Report of the Committee on Infectious Diseases*, unless otherwise specified by the state epidemiologist.

B. In the event of a locally acquired case (other than keratitis), it may be appropriate to conduct an assessment of the environment where the case was possibly exposed and collect environmental samples for testing. Consult CDES for guidance on how to conduct the assessment and collect samples. In some cases, remediation of contaminated environments may be indicated.

C. For keratitis cases, provide education on the prevention of *Acanthamoeba* keratitis infections and the importance of good contact lens hygiene:

Contact of soft contact lenses with water causes them to swell and stick to the eye, causing scratching of the cornea. This makes it easier for amebae in the water to enter the cornea and cause infection. Wearing contact lenses for long periods of time can scratch the cornea as well.

- Before handling contact lenses, wash your hands with soap and water. Dry them well with a clean cloth, every time, before touching your contact lenses.
- Don't sleep in your contact lenses unless prescribed by your eye doctor.
- Keep water away from your contact lenses. Avoid showering in contact lenses, and remove them before using a hot tub or swimming.
- Rub and rinse your contact lenses with contact lens disinfecting solution—never water or saliva—to clean them each time you remove them.
- Never store your contact lenses in water.
- Replace your contact lenses as often as recommended by your eye doctor.
- Rub and rinse your contact lens case with contact lens solution—never water—and then empty and dry with a clean tissue. Store upside down with the caps off after each use.
- Replace your contact lens case at least once every three months.
- Don't "top off" solution. Use only fresh contact lens disinfecting solution in your case—never mix fresh solution with old or used solution.
- Use only the contact lens solution recommended by your eye doctor.

Additional tips for hard, or rigid gas permeable, contact lens wearers:

- To clean hard contact lenses, rub and rinse them with contact lens cleaning or multipurpose solution—never water or saliva—each time you remove them. Rinse them well with the solution recommended by your eye doctor.
- Hard contact lenses can last much longer than soft contact lenses if cared for properly. Replace your hard contact lenses when recommended to do so by your eye doctor.

D. Provide education on how to prevent FLA infections during sinus rinsing. Very rarely, FLA infections have been reported when people use contaminated tap water for nasal rinsing during showering, irrigating, or cleansing their sinuses (nose and nasal passages) for health or religious reasons. FLA can grow in public and private water systems, tanks, and pipes, especially where little or no disinfectant (like chlorine or chloramine) is present.

When preparing a saline or other type of solution for irrigating, flushing, or rinsing your sinuses with a neti pot, sinus rinse bottle, or other irrigation device:

- Use water labeled distilled or sterile purchased from a store.
- If distilled or sterile water is not available, use water that has been previously boiled for 1 minute and left to cool. At elevations above 6,500 feet, boil for three minutes.

V. CONTACTS FOR CONSULTATION

A. Local health departments and tribal health agencies: https://www.dhs.wisconsin.gov/lh-depts/index.htm

B. Bureau of Communicable Diseases, Communicable Diseases Epidemiology Section: 608-267-9003

C. Wisconsin State Laboratory of Hygiene: 1-800-862-1013; after hours emergency number: 608-263-3280

VI. RELATED REFERENCES

A. Heymann DL, ed. Infections with Free-Living Ameba. In: *Control of Communicable Diseases Manual*. 20th ed. Washington, DC: American Public Health Association, 2015: 6-9.

B. Pickering LK, ed. Amebic Meningoencephalitis and Keratitis. In: *Red Book*: *2015 Report of the Committee on Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2015: 231-234.

C. CDC DPDx Telediagnosis:
https://www.cdc.gov/dpdx/contact.html

D. CDC - *Acanthamoeba*—Granulomatous Amebic Encephalitis; Keratitis:
https://www.cdc.gov/parasites/acanthamoeba/index.html

E. CDC - *Acanthamoeba* Keratitis Fact Sheet for Healthcare Professionals:
https://www.cdc.gov/parasites/acanthamoeba/health_professionals/acanthamoeba_keratitis_hcp.html

F. CDC - Healthy Contact Lens Wear and Care—Protect Your Eyes: https://www.cdc.gov/contactlenses/protect-your-eyes.html

G. CDC - *Balamuthia mandrillaris*—Granulomatous Amebic Encephalitis:
https://www.cdc.gov/parasites/balamuthia/index.html

H. CDC - *Sappinia*—Amebic Encephalitis:
https://www.cdc.gov/parasites/sappinia/index.html

I. CDC - Sinus Rinsing for Health or Religious Practice—best practices:
https://www.cdc.gov/parasites/naegleria/sinus-rinsing.html

J. DPH Free-Living Ameba Infections website