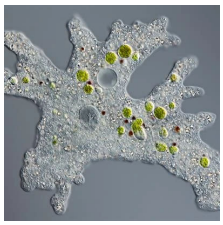

Free-living amoebae

Martin Montes MD
Instituto de Medicina Tropical A. von Humboldt
Universidad Peruana Cayetano Heredia
October 9, 2025

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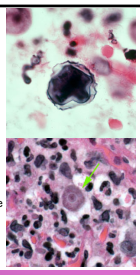
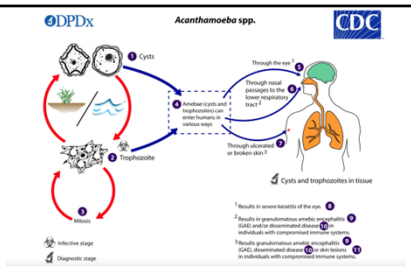
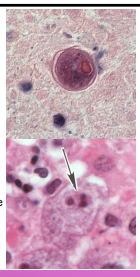
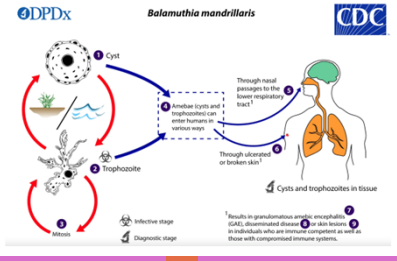




Acantamoeba spp

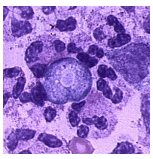
2

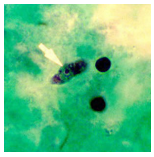




Balamuthia mandrillaris

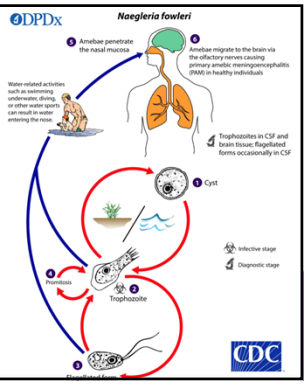
3





trophozoites

Naegleria fowleri



4

Amoeba Species	Primary Disease	Main Clinical Features	Typical Entry Route	Prognosis
Acanthamoeba spp.	Granulomatous Amebic Encephalitis (GAE); Keratitis	Subacute meningoencephalitis (headache, confusion, focal deficits); keratitis (eye pain, photophobia, corneal ulcer)	Inhalation or through broken skin; corneal contact with contaminated water	Poor (often fatal for GAE)
Balamuthia mandrillaris	Granulomatous Amebic Encephalitis (GAE); Skin lesions	Chronic skin plaques or ulcers; neurologic symptoms (headache, seizures, confusion)	Through skin wounds or inhalation of cysts	High mortality
Naegleria fowleri	Primary Amebic Meningoencephalitis (PAM)	Rapid-onset headache, fever, nausea, altered smell/taste, meningitis signs, rapid progression to coma	Nasal inhalation of contaminated warm freshwater	Almost always fatal
Sappinia pedata (rare)	Amebic Encephalitis	Single brain abscess; seizures, headache, confusion	Unknown (likely environmental exposure)	rare cases

Clinical Presentations of Free-Living Amoebas in Humans

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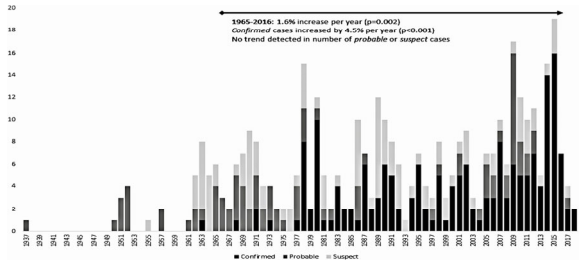
Primary amoebic encephalitis (PAM)

CID, Volume 73, Issue 1, 1 July 2021, Pages e19–e27, https://doi.org/10.1093/cid/ciaa520

6

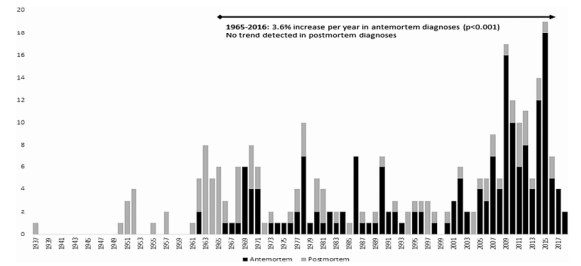
Figure 2. Reported cases of primary amebic meningoencephalitis (n = 381) by case year and classification. Negative ...



Clin Infect Dis, Volume 73, Issue 1, 1 July 2021, Pages e19–e27, https://doi.org/10.1093/cid/ciaa520

7

Figure 3. Reported cases of primary amebic meningoencephalitis (n = 283) by case year and timing of diagnosis ...



Clin Infect Dis, Volume 73, Issue 1, 1 July 2021, Pages e19–e27, https://doi.org/10.1093/cid/ciaa520

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Clinical signs and symptoms

Table 3.
Clinical Signs on Initial Presentation to a Healthcare Facility for Reported Cases of Primary Amebic Meningoencephalitis (N = 256) by Classification

Group and Symptoms	Total (N = 256) n (%)	Confirmed (n = 131) n (%)	Probable (n = 75) n (%)	Suspect (n = 50) n (%)
Early (flu-like prodrome only)	41 (16)	27 (21)	8 (11)	6 (12)
Fever	226 (88)	113 (86)	68 (91)	45 (90)
Headache	209 (82)	111 (85)	64 (85)	34 (68)
Nausea/vomiting	147 (57)	80 (61)	41 (55)	26 (52)
Fatigue/lethargy	65 (25)	44 (34)	17 (23)	4 (8)
Respiratory	19 (7)	7 (5)	7 (9)	5 (10)
Late (central nervous system involvement)	215 (84)	104 (79)	67 (89)	44 (88)
Altered mental status	128 (50)	70 (53)	34 (45)	24 (48)
Nuchal rigidity	90 (35)	38 (29)	34 (45)	18 (36)

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CSF findings

Table 4.
Initial Cerebrospinal Fluid Laboratory Findings on Admission for Reported Cases of Primary Amebic Meningoencephalitis (N = 237) by Classification

	Total (N = 237)		Confirmed (n = 118)			Probable (n = 80)			Suspect (n = 39)		
Test (Reference Value)	n	Median (Range)	n	Median (Range)	*P* Value	n	Median (Range)	*P* Value[a]	n	Median (Range)	*P* Value[b]
Opening pressure (100–200 mm H_2O)	31	290 (36–570)	11	380 (36–530)	Ref	14	255 (138–570)	.261	6	215 (55–500)	.312
Red blood cell count (0 cells/μL, CSF)	124	212 (0–30 750)	87	212 (0–30 750)	Ref	29	350 (0–24 606)	.392	8	756 (0–2600)	.545
White blood cell count (0–5 cells/μL)	232	1238 (0–30 000)	117	1830 (10–29 000)	Ref	78	1510 (7–30 000)	.296	37	415 (0–22 800)	**<.001**
% Neutrophils (2% ± 5%)	181	82 (0–100)	97	80 (12–100)	Ref	64	90 (15–100)	**.002**	20	73 (0–100)	.104
% lymphocytes (62% ± 34%)	128	20 (2–100)	72	20 (2–90)	Ref	38	15 (2–85)	.691	18	65 (5–100)	**<.001**
Protein (15–60 mg/dL)	215	326 (20–1374)	109	326 (24–1342)	Ref	70	361 (20–1374)	.978	36	135 (20–731)	**<.001**
Glucose (40–80 mg/dL)	208	29 (0–223)	106	29 (0–180)	Ref	69	22 (0–223)	.401	33	42 (0–185)	**.035**

P values <.05 are represented in bold text.
[a]Probable vs confirmed cases by Wilcoxon-Mann-Whitney test.
[b]Suspect vs confirmed cases by Wilcoxon-Mann-Whitney test.

10

Treatment of Confirmed Survivors of Primary Amebic Meningoencephalitis (n = 7)

Table 5.
Treatment of Confirmed Survivors of Primary Amebic Meningoencephalitis (n = 7)

Ref.	Country of Exposure	Year	Age (y)	Sex	Amphotericin B Route, Duration, days	Azole Route, Duration, days[a]	Azithromycin Route, Duration, days	Miltefosine Route, Duration, days	Rifampin Route, Duration, days	Dexametha- sone Route, Duration, days	Symptom Onset to Start of Treatment, days
[19]	Australia	1971	14	M	IV (Unk.)[b] IT (Unk.)[b]	…	…	…	…	…	Unk.
[20]	United States	1978	9	F	IV (9) IT (10)	IV (9) IT (9)	…	…	PO (9)	IV (Unk.)[b]	3
[21]	Mexico	2003	10	M	IV (14)	IV/PO (30)[c]	…	…	PO (30)	IV (Unk.)[b]	0
[22]	United States	2013	12	F	IV (26) IT (10)	IV (26)	IV (26)	PO (26)	IV (26)	IV (4)	2
[23]	United States	2013	8	M	IV (19) IT (5)	IV (19)	PO (19)	PO (19)	PO (19)	IV (29)	5
[24]	Pakistan	2015	25	M	IV (Unk.)[b] IT (Unk.)[b]	Unk.[d] (Unk.)[b]	Unk.[d] (Unk.)[b]	PO (Unk.)[b]	IV (Unk.)[b]	…	3
N/A[e]	United States	2016	16	M	IV (14) IT (10)	IV (28)	IV (28)	PO (28)	IV/PO (28)[c]	IV (4)	2

2024: Two additional cases reported in India and Pakistan: milgtefosine, amphotericin B, rifampin and azirthromycin

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Acanthamoeba spp kheratitis

12

global annual incidence

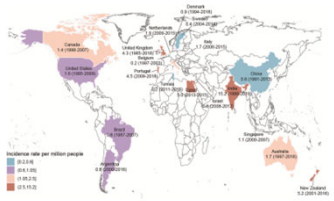

Fig. 1. The estimated annual incidence of *Acanthamoeba* keratitis by regions (as defined by the UN). The figure used with permission from co-author Xu.

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worldwide genotype distribution

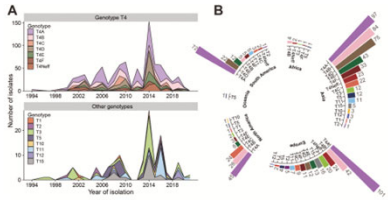

Fig. 3. Genotype distributions of 940 *Acanthamoeba* isolates in this study. (A) Temporal distribution of the *Acanthamoeba* genotypes included in the study. The top and bottom panels display the temporal distribution of the T4 genotype and the remaining genotypes, respectively. (B) Prevalence of *Acanthamoeba* genotypes in different continents.

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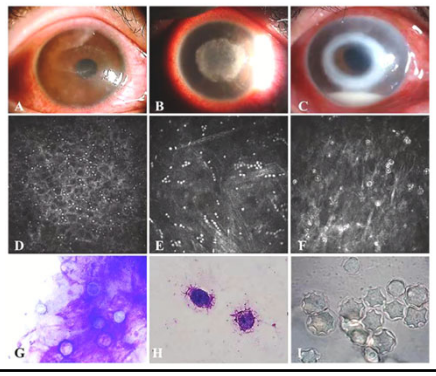

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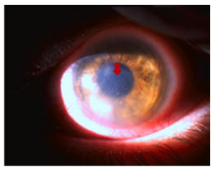
Treatment: Cationic Antiseptics and Diamidines

Table 1. Guidelines for treatment of *Acanthamoeba* keratitis.

Initial Therapy	Concentration	Frequency
Chlorhexadine combined with Brolene	0.02% (200 ug/ml) 0.1% (1000 ug/ml)	q1 hour x 2-3 days around the clock, then q1 hour while awake x 3 days, then tapered to qid.
Second Line Therapies	**Concentration**	**Frequency**
PHMB	0.02%-0.06%	q1 hour x 2-3 days around the clock, then q1 hour while awake x 3 days, then tapered to qid.
Hexamidine	0.1%	
Pentamadine	0.1%	
Third Line Therapies	**Concentration**	**Frequency**
Imidazoles	1% (10,000 mg/l) and po	Anti-fungals are used as frequently as q1 hour initially.
Neomycin	10 mg/ml	Neomycin must be titrated based on toxicity and response.
Adjunctive Therapies	**Concentration**	**Frequency**
NSAIDs	Topical and po	bid-qid
Prednisolone	1%	Avoid if possible



PHMB: Polyhexamethylene biguanide
Chlorhexidine in conjunction with
- Propamidine isethionate (Brolene-Rhone Poulanc)
- Dibromopropamidine, hexamidine 0.1%
- Desomedine and neomycin

Two weeks may be required before a response is observed and the total duration of therapy is a minimum of 3–4 weeks

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UNIVERSIDAD PERUANA CAYETANO HEREDIA | Instituto de MEDICINA TROPICAL ALEXANDER VON HUMBOLDT

Granulomatous amoebic encephalitis:

Clinical and Epidemiological Characteristics of Balamuthia mandrillaris Infection in Peru: a Retrospective Case Series

17

Results

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Table 1. Patient characteristics

Total number of confirmed patients	51 (100%)
Sex	
Male	37 (72.5%)
Female	14 (27.5%)
Median age of presentation	13.5 (IQR 9-29)
Immunosuppression	11 (21.6%)
HIV	0 (0%)
Chronic glucocorticoid use	0 (0%)
Malnutrition	10 (19.6%)
DM2	1 (2.0%)
Freshwater body exposure	
Yes	14 (27.5%)
No	37 (72.5%)
Season skin lesion appears	
Summer	10 (19.6%)
Fall	13 (25.5%)
Winter	13 (25.5%)
Spring	8 (15.7%)
No cutaneous manifestations	2 (3.9%)
Data unavailable	5 (9.8%)

Table 2. Clinical characteristics

Cutaneous manifestations	
Yes	49 (96.1%)
No	2 (3.9%)
Number of skin lesions (n=49)	
1	37 (75.5%)
2	5 (10.3%)
3 or more	4 (8.2%)
Location of skin lesions	
Perineal	38 (77.6%)
Limbs/Body	10 (20.4%)
Type of skin lesion	
Plaque	42 (84.6%)
Papule	1 (2.6%)
Nodule	1 (2.6%)
Macule	1 (2.6%)
Ulcer	1 (2.6%)
Neurological manifestations at time of diagnosis	
Yes	36 (70.6%)
No	10 (19.6%)
Unknown	5 (9.8%)
Neurologic syndrome (n=36)	
Headache	32 (88.9%)
Intracranial hypertension	21 (58.3%)
Seizures	16 (44.4%)
Encephalopathy	16 (47.2%)
Pyramidal syndrome	19 (52.8%)
Cerebellar syndrome	6 (16.7%)
Meningism	4 (11.1%)

Gotuzzo E, Cornejo-Esparza B, Bravo F, et al. Clinical and Epidemiological Characteristics of Balamuthia mandrillaris infection in Peru: a Retrospective Case Series (unpublished)

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Results

- 68 cases of suspected B. mandrillaris infection were identified.
  - 51 cases have positive immunofluorescence testing or direct trophozoite identification on biopsy
  - 17 have a compatible clinical picture and biopsy findings, but no direct trophozoite visualization
- The most common type of lesion was a **centrofacial, indurated, painless, erythematous plaque**
- Median time from **cutaneous lesion appearance until onset of neurologic symptoms** was **175.5 days** (IQR 75-389)
- Median time from **neurologic symptom onset until death** was **38 days** (IQR 19.0-69.5).

Gotuzzo E, Cornejo-Esparza B, Bravo F, et al. Clinical and Epidemiological Characteristics of Balamuthia mandrillaris infection in Peru: a Retrospective Case Series (unpublished)

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Results

- 33 (64.7%) of the patients died, 9 (23.5%) were lost to follow-up, 9 (17.6%) patients survived.
  - **94.4% Mortality** if the patient developed **neurologic symptoms**
- 23.5% were immunosuppressed
  - 11 had malnutrition
  - 1 DM2
  - **No patients had HIV infection**

Gotuzzo E, Cornejo-Esparza B, Bravo F, et al. Clinical and Epidemiological Characteristics of Balamuthia mandrillaris infection in Peru: a Retrospective Case Series (unpublished)

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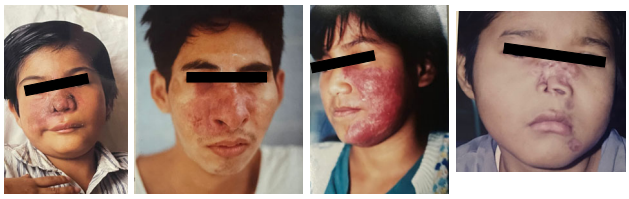
Results

Figure 1. Classic skin lesion



Gotuzzo E, Cornejo-Esparza B, Bravo F, et al. Clinical and Epidemiological Characteristics of Balamuthia mandrillaris infection in Peru: a Retrospective Case Series (unpublished)

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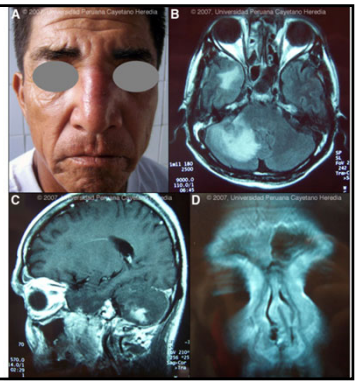
57 y.o male, 4 mo history of nassal lesion, progressed with epistaxis, nasal obstruction and anosmia. Two weeks prior to admission developed frontal headaches, no seizures.

Cerebrospinal fluid with 364 white cells, 62% polymorphonuclear cells, 38 mononuclears; glucose 45 mg/dl (normal), proteins 95 mg/dl (high); gram stain negative, India ink negative and bacterial culture negative. HIV negative.

MRI shows multiple enhancing lesions located in the cerebral parenchyma, cerebellum and brainstem



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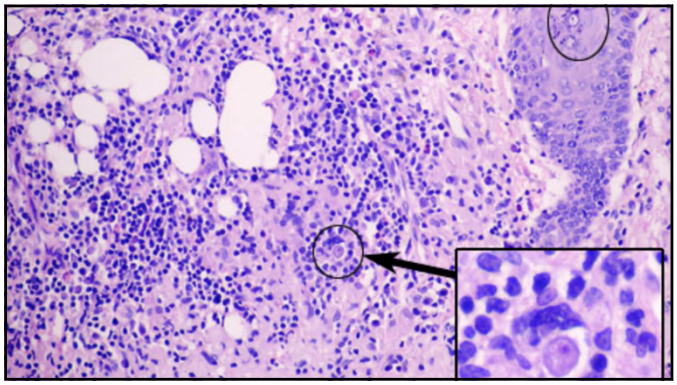

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Figure 2. Contrast brain CT scan of *B. mandrillaris* patient

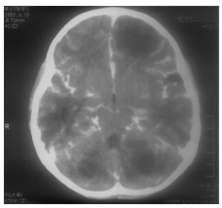
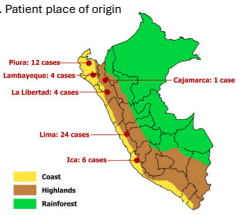


Figure 3. Patient place of origin



Gotuzzo E, Cornejo-Esparza B, Bravo F, et al. Clinical and Epidemiological Characteristics of Balamuthia mandrillaris infection in Peru: a Retrospective Case Series (unpublished)

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Conclusion

- Most patients with B. mandrillaris encephalitis die
- Almost all cases came from the coast of Peru
- Most cases presented in winter or fall
- No patients had HIV
- Isolated cutaneous balamuthiasis has a lower mortality rate
- Early detection before the development of neurologic symptoms may improve survival

Gotuzzo E, Cornejo-Esparza B, Bravo F, et al. Clinical and Epidemiological Characteristics of Balamuthia mandrillaris infection in Peru: a Retrospective Case Series (unpublished)

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In-Vitro Activity of Miltefosine and Voriconazole on Clinical Isolates of Free-Living Amebas: *Balamuthia mandrillaris, Acanthamoeba* spp., and *Naegleria fowleri*

FREDERICK L. SCHUSTER,[a] B. JOSEPH GUGLIELMO,[b] and GOVINDA S. VISVESVARA[c]

F. Shuster et al
J. Eukaryot Microbiol 2006;53(2):121-126

IN VITRO ACTIVITY AGAINST *B. mandrillaris*

➢Concentration ≥40µM of Miltefosine is amebacidal for *B. mandrillaris* and for *Acanthamoeba*

➢ Voriconazole had no inhibitory effect on Balamuthia but had a strong inhibitory effect upon *Acanthamoeba* spp. and *Naegleria fowleri*

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Successful Treatment of *Balamuthia mandrillaris* Amoebic Infection with Extensive Neurological and Cutaneous Involvement

Dalila Y. Martínez,[1] Carlos Seas,[1,2] Francisco Bravo,[1,2] Pedro Legua,[1,2] Cesar Ramos,[2] Alfonso M. Cabello,[1] and Eduardo Gotuzzo[1,2]

CID 2010:51 (15July) BRIEF REPORT

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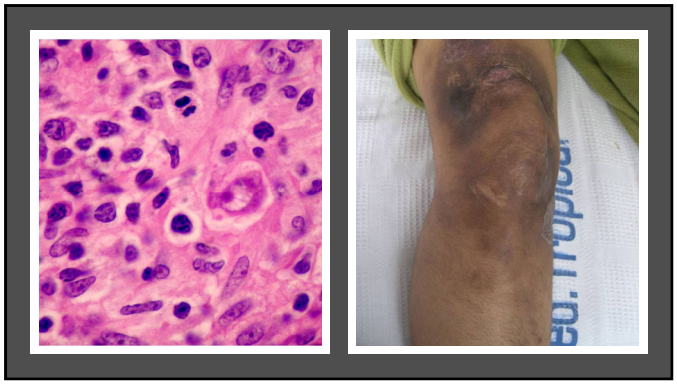

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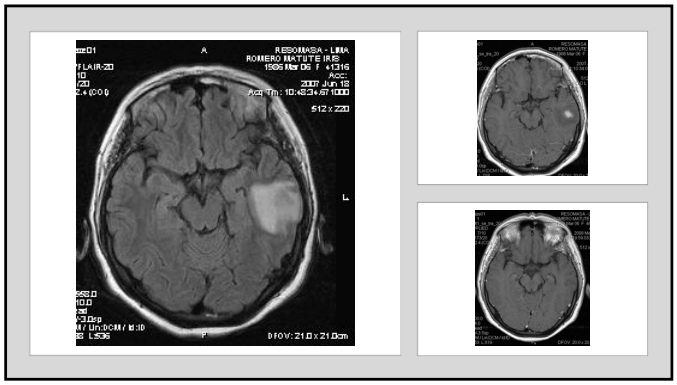

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Drug	Dose	Notes
Pentamidine (IV)	4 mg/kg given once per day	Although pentamidine has been used successfully in combination with the drugs listed below, pentamidine is very toxic and doesn't cross the normal, intact blood-brain barrier well. Its use must be a clinical decision.
Sulfadiazine (oral)	1.5 g every 6 hours in adults; 200 mg/kg/day in 4–6 doses in pediatric patients (maximum 6 g/day)	
Flucytosine (oral)	37.5 mg/kg every 6 hours (maximum 150 mg/kg/day)	
A mold-active azole (e.g., voriconazole, posaconazole, or isavuconazole)	Dosing will vary based on drug and patient. Consult a clinical pharmacist with dosing questions.	Fluconazole and itraconazole are NOT recommended due to poor *in vitro* efficacy.
Azithromycin (oral or IV)	20 mg/kg/day in 1 dose (max 500 mg/day) in pediatric patients; 500 mg/day in 1 dose for adults	

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Miltefosine (oral)[3]	**Up to 45 kg body weight**: 100 mg daily (i.e., one 50 mg cap po with breakfast and dinner) For pediatric cases, 2.5 mg/kg/day up to 100 mg daily **45 kg body weight and higher**: 150 mg daily (i.e., one 50 mg cap po with breakfast, lunch, and dinner)	Miltefosine is now commercially available. Visit impavido.com for more information.	
Nitroxoline	Contact CDC for dosing	Nitroxoline is an investigational drug that may be effective for *Balamuthia* infections. It is not FDA-approved in the United States, but available for treatment of free-living ameba infections through CDC's expanded access Investigational New Drug program. Contact the CDC Emergency Operations Center at 770-488-7100 for more information.	

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Thanks

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