Increased Patient Survival: Miltefosine for Treatment of Free-living Ameba Infections Caused by *Acanthamoeba* and *Balamuthia*

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BACKGROUND

Granulomatous amebic encephalitis (GAE)

- Subacute to chronic central nervous system infection
- Caused by the free-living amebae (FLA) *Balamuthia mandrillaris* and *Acanthamoeba* spp.
- Often fatal

Symptoms of GAE

- Personality and behavioral changes
- Depressed mental status
- Fever
- Photophobia
- Seizures
- Cranial nerve dysfunction
- Visual Loss

Brain imaging

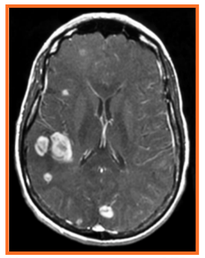
- Single or multiple ring-enhancing lesions

Other infections

- Disseminated
- *Acanthamoeba* keratitis (AK)

Treatment

- Ineffective
- Investigational drug miltefosine has *in vitro* activity against FLA
  - Given since 2009 under FDA compassionate use for FLA infections



Magnetic resonance imaging (MRI) of patient with *Balamuthia* GAE

For more information on *Acanthamoeba* and *Balamuthia* infections, visit:

http://www.cdc.gov/parasites/acanthamoeba/

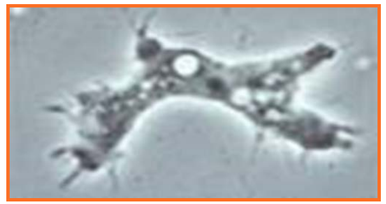
http://www.cdc.gov/parasites/balamuthia/

METHODS

- Reviewed the literature and case reports submitted to CDC
- Determined treatment regimens, including miltefosine use, and mortality for case patients with *B. mandrillaris* infection and non-keratitis *Acanthamoeba* spp. infection
- Analyzed proportions using Fisher's exact test

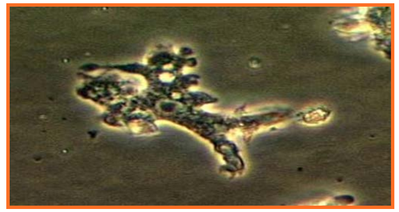
Acanthamoeba

- Photomicrograph of *Acanthamoeba* trophozoite



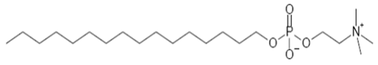
Balamuthia mandrillaris

- Photomicrograph of *Balamuthia mandrillaris* trophozoite



Miltefosine

- Alkylphosphocholine drug with antineoplastic and antiparasitic activity
- Used to treat leishmaniasis
- Mechanism of action unknown, but can inhibit the metabolism of phospholipids in cell membranes of parasites
- Not currently licensed in the U.S. for any indication
- Structure of miltefosine (below)



RESULTS

Comparing survival in patients who received miltefosine with patients who did not receive miltefosine

	N	Received Miltefosine Survived/Total (%)	Did Not Receive Miltefosine Survived/Total (%)	*P*-value
Non-keratitis *Acanthamoeba* infections (1955–2012)	63	5/7 (71)	9/56 (16)	0.005
Balamuthia infections (1974–2012)	60	6/14 (43)	6/46 (13)	0.05

Age and gender of patients who received miltefosine

	Median age in years (range)	Gender (% male)
Acanthamoeba miltefosine patients (n=7)	53 (2–64)	71.4
Balamuthia miltefosine patients (n=9)	24 (4–67)	66.7

Selected References:

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CONCLUSIONS

- Number of *B. mandrillaris* and *Acanthamoeba* spp. infections treated with a miltefosine-containing regimen is small.
- Miltefosine-containing treatment regimen does offer a survival advantage for these often fatal infections.
- CDC should provide drug to clinicians for FLA infections under an expanded access IND until it becomes commercially available in the United States.

CDC's Free-living Ameba Program

Activities include:

- Providing 24/7 diagnostic services and clinical guidance to health professionals
- Tracking, investigating, and reporting infections and disease outbreaks
- Leading CDC health promotion and communication activities
- Testing the efficacy of promising drugs against the ameba in the laboratory setting
- Developing new methods for detection of FLA in clinical and environmental samples

For 24/7 diagnostic assistance, specimen collection guidance, shipping instructions, and treatment recommendations, please contact the CDC Emergency Operations Center at 770-488-7100.

Acknowledgements and Contact Information

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