

FREE-LIVING PROTOZOA

Ameba	Diseases
<i>Naegleria fowleri</i>	PAM
<i>Acanthamoeba</i> sp.	GAE; skin or lung lesions amebic keratitis;
<i>Balamuthia mandrillaris</i>	GAE; skin or lung lesions

Naegleria fowleri

- ubiquitous in nature, found in fresh water lakes and ponds
- three life cycle stages:
 - ameba with loblose pseudopodia and replicating by binary fission
 - motile bi-flagellated form
 - resistant cyst stage
- PAM first recognized by Fowler (1965)
- initially thought to be *Acanthamoeba*
- *N. fowleri* is only known *Naegleria* to be pathogenic in humans
- ~ 200 total cases described worldwide
 - 14 cases from same lake in Virginia
 - 16 cases from same stream feed pool in Czech republic

Primary Amebic Meningoencephalitis (PAM)

- 1-14 days incubation period
- symptoms usually within a few days after swimming in warm still waters
- infection believed to be introduced through nasal cavity and olfactory bulbs
- symptoms include headache, lethargy, disorientation, coma
- rapid clinical course, death in 4-5 days after onset of symptoms
- trophozoites can be detected in spinal fluid, but diagnosis is usually at autopsy
- 4 known survivors treated with Amphotericin B

Acanthamoeba

- ubiquitous ameba of the soil and water
- life cycle consists of amebic trophozoite and thick-walled cyst
- recognized on many occasions as contaminants of tissue cultures
- Culbertson (1958) produced an encephalitis by inoculating mice with a culture thought to contain virus
- GAE first reported in humans in the early 70's
- epidemiology as of 1991: 73 cases worldwide of GAE, 39 in U.S.
- majority of patients are chronically ill (eg., diabetes, alcoholism), immunocompromised, or debilitated with other diseases
- also produces an amebic keratitis

***Acanthamoeba* Encephalitis**

- portal of entry unknown, possibly respiratory tract, eyes, skin
- presumed hematogenous dissemination to the CNS
- infection associated with debilitation or immunosuppression
- chronic GAE (granulomatous amebic encephalitis)
- onset is insidious with headache, personality changes, slight fever
- progresses to coma and death in weeks to months
- amebas not yet detected in spinal fluid
- cysts and trophozoites detectable in histological specimens
- no human cures documented

Amebic Keratitis

- predisposing factors
 - ◆ ocular trauma
 - ◆ contact lens (contaminated cleaning solutions)
- symptoms
 - ◆ ocular pain
 - ◆ corneal lesions (refractory to usual treatments)
- diagnosis
 - ◆ demonstration of amebas in corneal scrapings
- treatment
 - ◆ difficult, limited success
 - ◆ corneal grafts often required

Balamuthia mandrillaris

- first report in mandrill baboon (1990)
- genus/species named 1993
- morphology similar to *Acanthamoeba*
- many GAE cases originally ascribed to *Acanthamoeba* have been retrospectively assigned to *Balamuthia*
 - as of 1997 63 cases of *Balamuthia* (30 in U.S.)
- thus far only identified post-mortem
- not yet identified from environment

Recavarren-Arce et al (Human Path. 30:269, 1999)

- 10 autopsies (1985-97) of *Balamuthia* cases in Peru
- all healthy and all died within days or weeks of neurological symptoms
- primary lesions: 8 nasal, 3 dermal
- questioned hematogenous dissemination in both *Acanthamoeba* and *Balamuthia*
 - no intravascular ameba (this study and literature)
 - perivascular infiltration frequently observed
 - propose perivascular route from primary mucosal lesion

RED TIDES

- large increases in the number of unicellular planktonic organisms (especially dinoflagellates)
- usually attributed to higher levels of nutrients in estuaries and coastal waters due to pollution and agricultural runoff
- shipping industry has also been blamed for increase worldwide distribution

Potential Impact of Red Tides

- deplete oxygen → dead zones
- produce toxins → fish kills
- accumulated dinoflagellate toxins pass up the food chain
 - 'Ciguatera'
 - 'shellfish' poisoning

Selected Toxic Dinoflagellates and Shellfish Poisoning (SP)

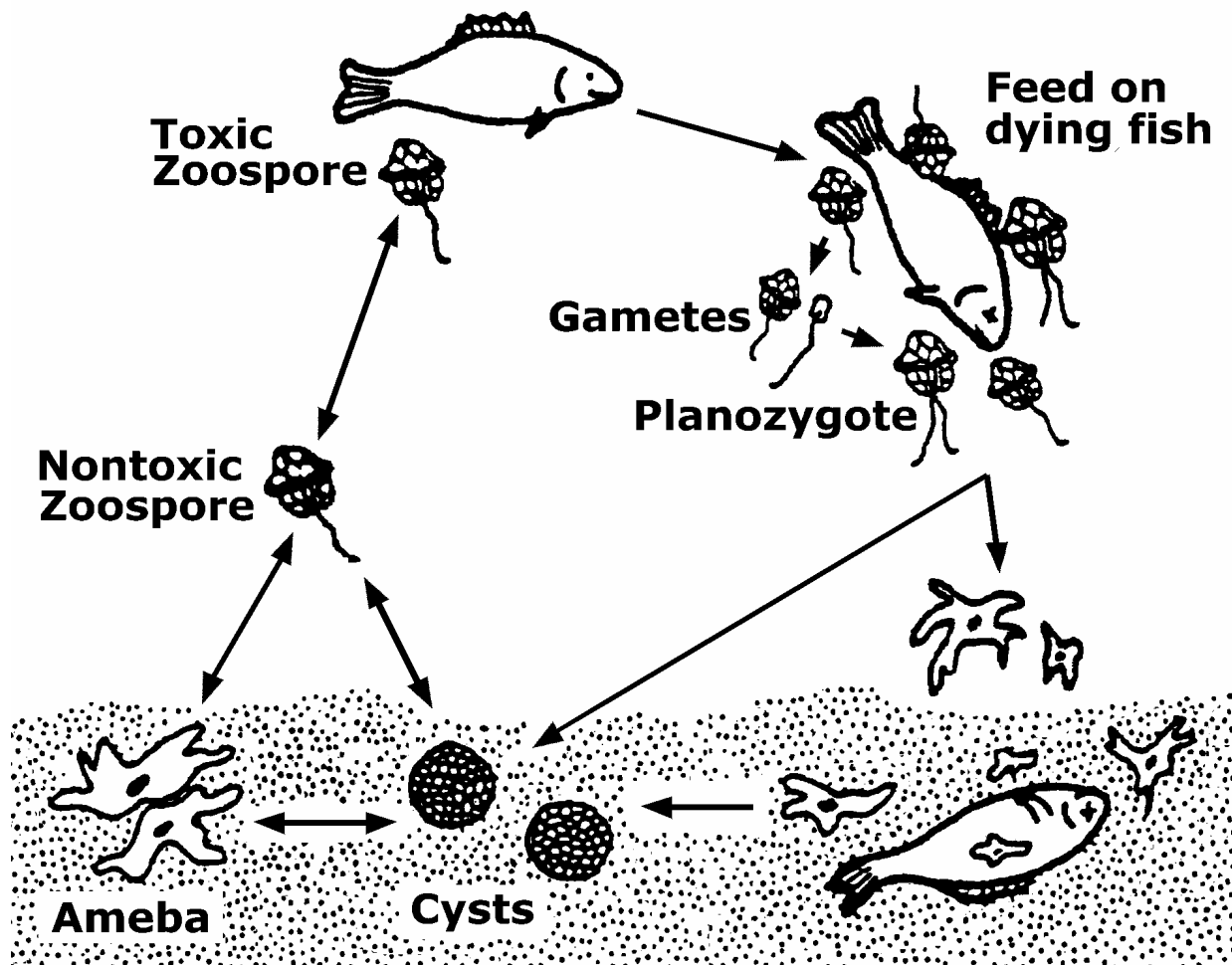
Dinoflagellate	Type of SP	Toxin	Comments
<i>Gymnodinium breve</i>	neurotoxic	brevetoxin	Known for fish kills in Gulf of Mexico. The toxin blocks Na-channels.
<i>Alexandrium tamerense</i>	paralytic	saxitoxins	Planktonic snails eat the dinoflagellate, fish eat the snails, etc. Toxin uncouples communication between muscle and nerve.
<i>Prorocentrum lima</i>	diarrheic	okadaic acid	Toxin is potent ser/thr phosphatase inhibitor.
<i>Pfiesteria piscicida</i>	neurotoxic + other	?	Newly described organism responsible for fish kills in mid-Atlantic estuaries. Complex ambush predator life cycle.

Pfiesteria piscicida

- effects observed in late 1980's (named 1996)
- fisherman and swimmers complaining of rashes, lesions, respiratory and neurological problems
 - massive fish kills in east coast estuaries
 - complex life cycle (at least 24 morphological forms)
- culture filtrates induce open ulcerative sores, hemorrhaging and death in fish
- at least two toxins
 - heat-stable, water-soluble toxin (fish become moribund within seconds and die within minutes)
 - lipophilic compound (causes the epidermis to slough off)

Human Exposure to Pfiesteria Aerosols

- narcosis/disorientation
- respiratory distress/asthma-like
- stomach cramping/nausea/vomiting
- eye irritation/blurred vision
- erratic heart beat (weeks)
- sudden rages/personality changes
- short term memory loss



Pfiesteria exhibits a complex life cycle with several morphologically distinct forms which undergo transformations depending on the types of food available and water conditions (eg., temperature, salinity, calmness). In the absence of fish, *Pfiesteria* can exist as a non-toxic zoospore (typical dinoflagellate morphology) which feeds on the plankton in the water column, or as an ameboid form which scavenges in the sediment (Figure). These trophic forms reproduce asexually and are capable of encysting.

Pfiesteria becomes toxic if fish linger in the area. One of the toxins causes the fish to become moribund and the other toxin damages the skin. The toxic zoospores feed on the fish tissues. Feeding on fish also induces a sexual cycle resulting in gametes and planozygotes which also feed on the fish. Planozygotes can convert back into zoospores, transform into ameba, or encyst. When the fish dies many of the zoospores will transform into ameba and continue feeding on the fish material. The toxic forms (both zoospores and ameba) will transform back into non-toxic forms or encyst when the fish disappears from the area.