

## Opportunistic Pathogens/HIV

### HIV/AIDS

- HIV destroys CD4+ cells leading to suppression of cell-mediated immunity
- opportunistic pathogens
  - *Pneumocystis carinii*
  - Microsporidia
- increased disease severity and duration
  - intestinal coccidia (*Cryptosporidium*, *Cyclospora*, *Isospora*)
  - *Toxoplasma* (encephalitis)
- different manifestations
  - *Leishmania infantum* (dermotrophic strains producing visceral disease)
- little apparent affect (*Plasmodium*, *Trypanosoma*, *Entamoeba histolytica*)

### **AIDS AND MALARIA**

Whitworth et al (2000) Lancet 356:1046

	HIV+	HIV-
parasitemic	11.8%	6.3%
clinical malaria	2.0%	0.7%

- 484 participants made 7220 visits during 1990-1998 (rural Uganda)
- HIV-1 infection associated with ↑ frequency of parasitemia and clinical malaria
- lower CD4 counts associated with ↑ parasite densities

### Malaria may be deadly co-factor for AIDS

- AIDS progression in sub-Saharan Africa is ~5 years (½ normal)
- HIV-infected individuals deteriorate faster with every malaria episode
- infants born to dual infected mothers have 4X mortality as single infected mothers
- CD-4 cells stimulated in vitro with malaria antigens have 30-100 fold ↑ in viral load

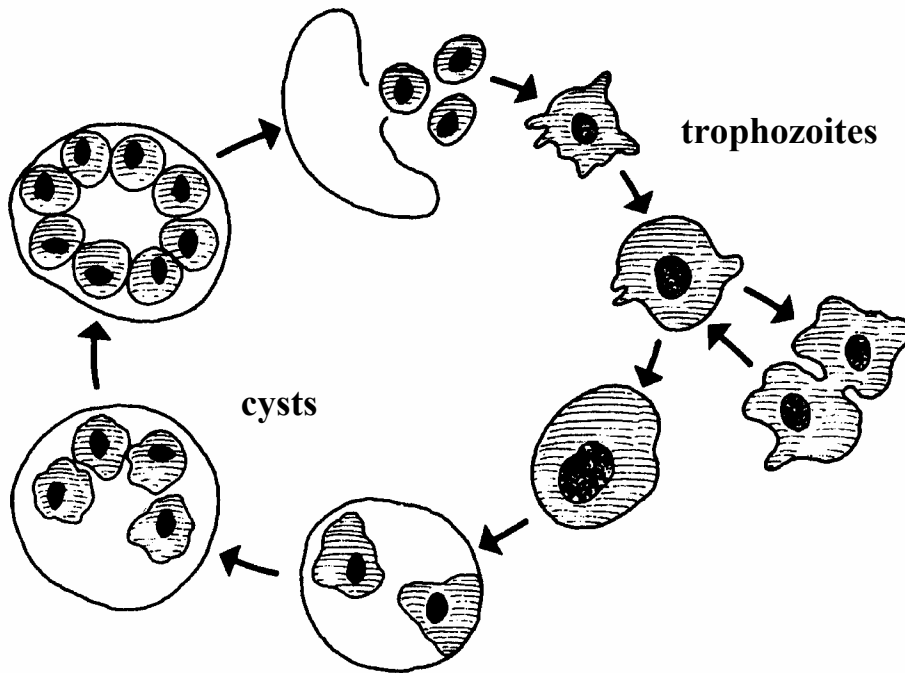
## ***Pneumocystis carinii* Pneumonia (PCP)**

### ***Pneumocystis carinii***

- first recognized in institutional epidemics (malnourished children and infants)
- serious opportunistic infection associated with immune suppression
- long-standing debate about fungus or protozoan resolved
  - cyst wall ( $\beta$ -1,3 glucans; staining with methenamine silver)
  - 16S rRNA branches between ascomycetes and basidiomycetes
  - separate DHFR and TS (bi-functional in protozoa)
  - elongation factor 3 (fungi specific)

### **Transmission**

- presumed to be due to inhalation of infective stage
- historically believed to be associated with activation of latent infection
- recent studies suggest active acquisition
  - clusters of PCP cases
  - duration of latency < 1 year
  - subsequent episodes due to different molecular genotypes
- life cycle unknown
  - person-to-person?
  - commonly encountered in the environment?



A proposed life cycle. Mature cysts rupture and release trophozoites which grow and replicate. Trophozoites mature into cysts which contain 8 intracystic bodies.

#### **Clinical Manifestations and Pathology**

- causes interstitial cell pneumonia
- shortness of breath
- nonproductive cough
- low grade fever
- X-ray: diffuse interstitial infiltration
- alveoli fill with foamy material
- death due to progressive asphyxia

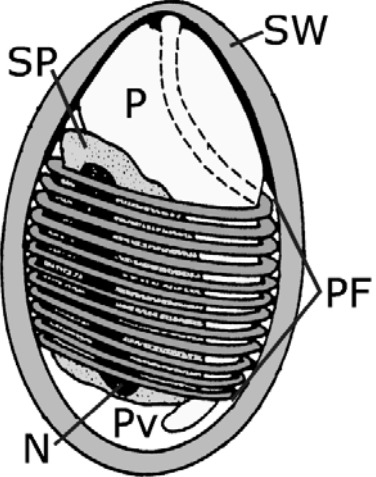
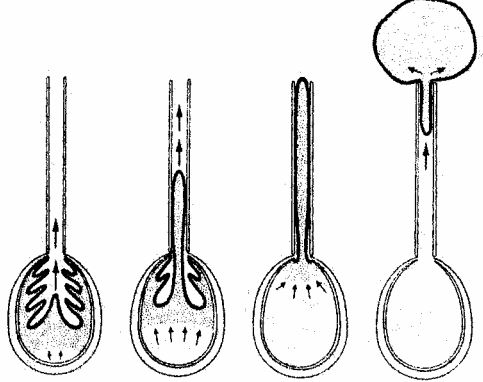
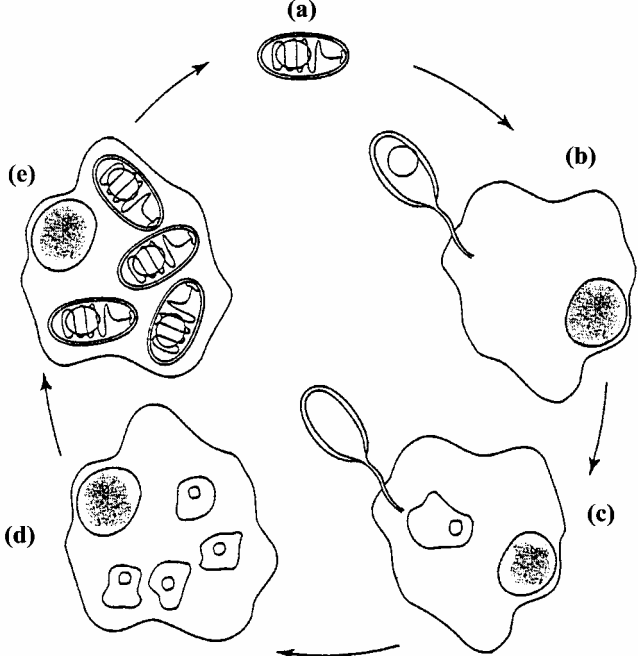
#### **Diagnosis (demonstrate organism)**

- sputum (poor yield)
- induced sputum (30-55%)
- bronchoalveolar lavage (50-95%)
- bronchial biopsy (>90%)

#### **Treatment and Prophylaxis**

- trimethoprim-sulfamethoxazole (Bactrim)
- pentamidine (parenteral, aerosol)
- oxygen for symptoms

## Microsporidia Handout

<p><u>Features of Microsporidia</u></p> <ul style="list-style-type: none"> <li>• obligate intracellular parasite</li> <li>• primarily found in fish and insects</li> <li>• small resistant spore stage (1-3 <math>\mu\text{m}</math>)</li> <li>• defined by 'polar filament' (extrusion apparatus)</li> <li>• highly derived fungi</li> </ul>	<p><u>Spore Germination</u></p> <ul style="list-style-type: none"> <li>• extrusion of polar filament <math>\rightarrow</math> polar tube             <ul style="list-style-type: none"> <li>• appears osmotic in nature</li> </ul> </li> <li>• penetrates host cell membrane in some species             <ul style="list-style-type: none"> <li>• sporoplasm inoculated into cytoplasm</li> </ul> </li> <li>• spores taken up by phagocytosis             <ul style="list-style-type: none"> <li>• escape from lysosome</li> </ul> </li> </ul>
	
<p><u>Generalized Life Cycle</u></p> <ol style="list-style-type: none"> <li>1) Infective Phase             <ul style="list-style-type: none"> <li>• spore germination</li> <li>• cell invasion</li> </ul> </li> <li>2) Proliferative Phase             <ul style="list-style-type: none"> <li>• intracellular <math>\pm</math> parasitophorous vacuole</li> <li>• many modes of replication</li> </ul> </li> <li>3) Sporogonic Phase             <ul style="list-style-type: none"> <li>• terminal differentiation</li> </ul> </li> </ol>	

## Human Microsporidia Infections

SPECIES	COMMENTS
<i>Enterocytozoon bieneusi</i>	Infects intestinal epithelial cells and causes chronic diarrhea in AIDS patients. It is the most common microsporidia in humans and is a major cause of AIDS related diarrhea (10-30%).
<i>Encephalitozoon intestinalis</i>	Originally described in 1993 as <i>Septata intestinalis</i> . Associated with chronic diarrhea (rarely disseminated disease) in AIDS patients.
<i>Encephalitozoon cuniculi</i>	Parasite of other mammals (rabbits, dogs, mice monkeys), but capable of causing disseminated disease (kidney, liver, lungs and eyes) in humans.
<i>Encephalitozoon hellem</i>	Similar to <i>E. cuniculi</i> , but thus far, disseminated disease only reported in HIV-infected individuals. Also causes ocular disease in both immunocompromised and immunocompetent.

Rare and sporadic reports: *Pleistophora*, *Trachipleistophora hominis*, *Nosema*, *Vittaforma corneae*.

### Intestinal microsporidiosis

- *Enterocytozoon bieneusi*,  
*Encephalitozoon intestinalis*
- enterocytes infected
- chronic diarrhea and wasting
  - organism is not life-threatening
  - debilitating diarrhea → cachexia

### Ocular microsporidiosis

- *Encephalitozoon hellem* +
- non-immunocompromised
  - keratitis or corneal ulcer
  - related to trauma?
- AIDS patient
  - kerato-conjunctivitis

### Systemic microsporidiosis

- *Encephalitozoon* species
  - rarely *E. intestinalis*
- concomitant infection of kerato-conjunctiva, urinary tract, & bronchia is typical

### Microsporidiosis Diagnosis

- demonstrate spores in stools or urine
  - chromotrope (modified trichrome) stain
  - Uvitex-2B or calcafluor staining (binds chitinous cyst wall and fluoresces)
- difficult, biopsy often required
  - small spores (~ 1  $\mu\text{m}$ )
  - irregular spore excretion

### Treatment Options

- no clearly effective treatment against *Enterocytozoon bieneusi*
- some effect of albendazole against *Encephalitozoon intestinalis*
- topical fumagillin against keratoconjunctivitis

### Prevention

- no specific preventive measures (sources of human infection not clear)
- general precautions for AIDS patients (personal hygiene, bottled or boil water, thorough cooking of meat)