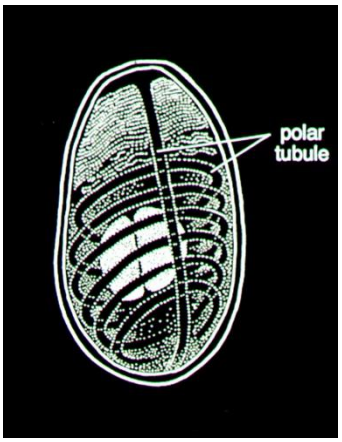
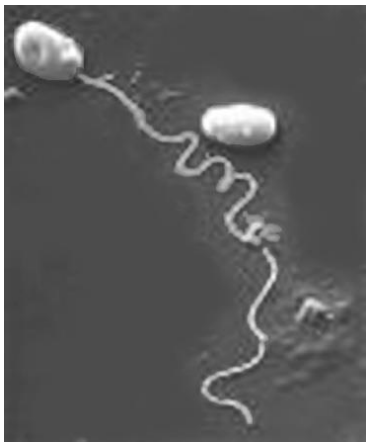
Microsporidia (Other Genera and Species

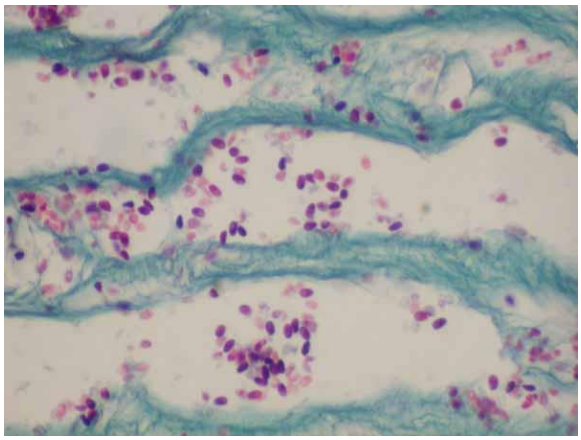
Organism:

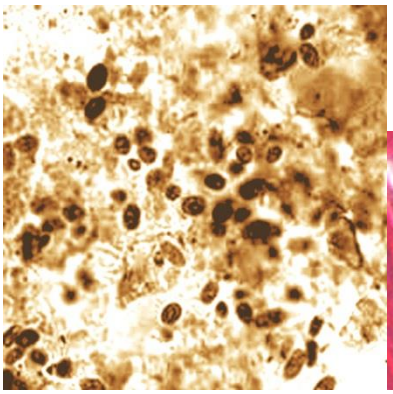
The microsporidia are obligate intracellular parasites that have been recognized in a variety of animals, particularly invertebrates; they have been reclassified with the Fungi in the Phylum Microsporidia. Typical sizes range from 1.5 to 5 µm wide and 2 to 7 µm long; unfortunately, the organisms found in humans tend to be quite small, ranging from 1.5 to 2 µm. Until recently, awareness and understanding of human infections have been marginal; only with increased understanding of AIDS within the immunosuppressed population has attention been focused on these organisms.



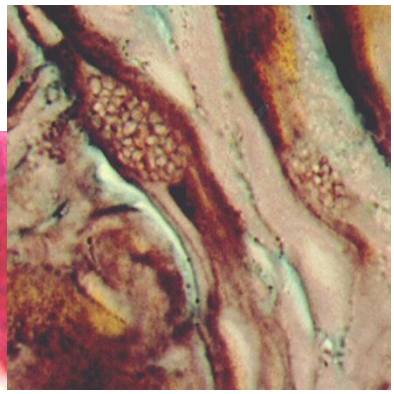
Spore with Polar Tubule


Extruded Polar Tubule


Spores in corneal tissue button


Silver stain


PAS stain, eye tissue


Silver stain, eye tissue

Life Cycle:

Infection occurs with the introduction of infective sporoplasm through the polar tubule into the host cell. The microsporidia multiply extensively within the host cell cytoplasm; the life cycle includes repeated divisions by binary fission (merogony) or multiple fission (schizogony) and spore production (sporogony). Both merogony and sporogony can occur in the same cell at the same time. During sporogony, a thick spore wall is formed, thus providing environmental protection for this infectious stage of the parasite. An example of infection potential is illustrated by *Enterocytozoon bieneusi*, an intestinal pathogen. The spores are released into the intestinal lumen and are passed in the stool. These spores are environmentally resistant and can then be ingested by other hosts. There is also evidence for inhalation or spores and evidence in animals that suggests that human microsporidiosis may also be transmitted via the rectal route.

Currently, there are a number of genera that have been recognized as human pathogens: the more common, *Encephalitozoon* and *Enterocytozoon*, and the less common, *Nosema, Anncaliia* (*Brachiola)*, *Pleistophora*, *Trachipleistophora*, *Vittaforma*, and "*Microsporidium*," a catch-all genus for organisms that have not yet been classified (or may never be classified due to a lack of specimen). Classification criteria include spore size, configuration of the nuclei within the spores and developing forms, the number of polar tubule coils within the spore, and the relationship between the organism and host cell.

Acquired:

Fecal-oral transmission via infective spores; contaminated food and water

Epidemiology:

Worldwide, primarily human-to-human transmission

Clinical Features (Other Microsporidia):
Organisms have been recovered from the eye, CNS, urine, sinuses, conjunctivae, nasal epithelium, respiratory tract, myocardium, diaphragm, arterial walls, kidney tubules, adrenal cortex, liver, lungs, and muscle fibers.

Clinical Specimen:
Intestinal: Stool, examination of mucosal surface (biopsy); dissemination to kidneys, lower airways and biliary tract appears to occur via infected macrophages.
Extraintestinal: Fluids, biopsy specimens

Laboratory Diagnosis: Note: ID to the species level is not possible from special stains.
Intestinal: Ova and Parasite examination (concentration ONLY); from concentrate sediment, (500 x *g* for 10 min) modified trichrome stains are performed. Some fecal immunoassays are available in Europe, but are not FDA approved for use within the United States. Multiple fecal examinations may be required to recover the organisms, particularly if the stools are formed; there is a direct relationship between the stool consistency and the number of spores present (diarrhea = more spores).
Stool preparations must be very thin, the staining time is 90 min, and the slide must be examined at x 1,000 (or higher) magnification. Unfortunately, there are many objects within stool material that are oval, stain pinkish with trichrome, and measure approximately 1.5 to 3 µm. If this stain is used for the identification of microsporidia in stool, positive control material should be available for comparison. Additional modifications of this method include the use of heat and a shorter staining time. There is also some evidence to indicate that pretreatment of fecal specimens (1:1) with 10% KOH may provide a better quality smear to examine when using the modified trichrome stains.
Another approach involves the use of chemofluorescent agents (optical brightening agents) such as Calcofluor, Fungi-Fluor, or Uvitex 2B. These reagents are sensitive, but nonspecific; objects other than microsporidial spores will also fluoresce. This is a particular problem when examining stool specimens; both false positive and false negative results have been seen.

Extraintestinal: Modified trichrome stains

Tissue: Tissue stains such as PAS, Silver, tissue Gram stains and others are specifically recommended for the microsporidial spores. Microsporidial infections can be misdiagnosed in tissues and can be confused with *Cryptococcus neoformans* infections. Mucus granules in goblet cells can take up stain and can be very confusing. Good preservation and thin tissue sections (1 µm) that have been resin-embedded enhance the resolution of cellular detail. Demonstration of the coiled polar tube within spores is diagnostic for microsporidial infection. *Encephalitozoon intestinalis* is not confined to epithelial cells, but is seen in macrophages in the lamina propria. Although the primary site appears to be the small bowel, these organisms can disseminate to other sites, including duodenum, jejunum, ileum, colon, kidney, liver, and gallbladder. Although electron microscopy is very specific, the sensitivity is not that high.

Organism Description:
Spore: Oval spores, containing a coiled polar tubule. However, the polar tubule is not visible in every spore; when seen, it appears as a horizontal or diagonal line across the spore. Without seeing the polar tubule, it is not possible to definitively ID the structures as polar tubules/microsporidial spores (Microsporidial spores present.)
Tissue: Developing spores (groups) can be seen within the tissue cells.

Laboratory Report:
Microsporidial spores present; if in stool, the two most likely species are *Enterocytozoon bieneusi* and *Encephalitozoon intestinalis*. If from tissues, other genera and species are also possibilities.

Treatment:
Garcia, L.S. 2007. Diagnostic Medical Parasitology, 5th ed., ASM Press, Washington, D.C.
Although a number of drugs have been tested, few are totally effective. This species responds well to albendazole, whereas *Enterocytozoon bieneusi* does not. Although apparently static rather than cidal effects are seen with *E. bieneusi* infections, treatment with albendazole results in reduction of symptoms in as many as 50% of patients infected with this organism. Albendazole as a systemic agent is recommended when the organisms have been confirmed in urine or nasal smears.
Fumagillin (soluble salt Fumidil B) has activity against microsporidia, and solutions applied topically have been used in corneal infections. The effects of this drug are static rather than cidal, and relapses of infection occur when the treatment has been discontinued. In one study, the efficacy of fumagillin was measured by clearance of *E. bieneusi* from stools and intestinal biopsy specimens; four patients who received fumagillin remained free of *E. bieneusi* after a mean follow-up of 10 months.

Itraconazole can also be recommended to treat ocular, nasal, and paranasal sinus infection caused by *E. cuniculi* parasites when albendazole fails.

Control:

Improved hygiene, adequate disposal of fecal waste, adequate washing of contaminated fruits and vegetables. The presence of infective spores in human clinical specimens suggests that precautions when handling body fluids and personal hygiene measures such as hand washing may be important in preventing primary infections in the health care setting. However, comprehensive guidelines for disease prevention will require more definitive information regarding sources of infection and modes of transmission.