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accelerating drug development. exactly.

Encephalitozoon cuniculi
(ECUN, *E. cuniculi*)

Classification

Obligate intracellular eukaryotic parasite. Gram-positive. Currently considered a highly derived fungus in the class Microsporidia.

Family

Encephalitozoonidae

Affected species

All mammalian species are susceptible to infection with *E. cuniculi*. Rabbits, guinea pigs, and mice are considered the primary reservoirs of disease. In humans, it is generally described as an infection associated with severe immunodeficiency (HIV disease or transplant patients).

Frequency

Common in pet rabbits. Uncommon in laboratory rabbits and most rodents. Moderately prevalent in guinea pigs. Prevalence in wild rabbits and rodents varies by geographical area.

Transmission

Transmission is through ingestion of infective spores shed in urine. In rabbits, transmission may also be through inhalation. Vertical transmission has been documented in rabbits and is suspected to occur in guinea pigs.

Clinical Signs and Lesions

In most rodents, including guinea pigs, infection is subclinical. Infection may be fatal in immunocompromised animals. In rabbits, the clinical presentation is more varied, with some rabbits showing only renal changes at necropsy with no other clinical signs, and other rabbits presenting with neurologic or ocular signs. Renal changes at necropsy may be subtle and mischaracterized as incidental findings.

Typical histopathologic lesions seen with *E. cuniculi* infection are best described as granulomatous. At one month post-exposure, granulomatous lesions are seen in the lung, liver, and kidney. In the first month of infection, organisms are readily demonstrated in the kidney, generally in and around the tubules. Brain lesions do not appear until approximately a month after infection and are described as focal nonsuppurative granulomatous meningoencephalitis. Ocular lesions, including uveitis and cataract formation, have been described in dwarf rabbits.

Diagnosis

Screening for *E. cuniculi* infection is accomplished through serology (MFIA®, ELISA, IFA). PCR on kidney or urine may also be performed, but is not typically used as a screening method. Histologic lesions may also be diagnostic, especially if organisms are demonstrated in tissue.

Interference with Research

This organism targets organs of interest in toxicologic and many other types of studies. Although animals may appear normal, the growth of infected animals is likely compromised. Animals with *E. cuniculi* may have changes in their immune systems that make them of questionable utility, while immunodeficient or immunosuppressed animals may become severely ill. The granulomatous lesions associated with *E. cuniculi* can confound histologic evaluation of treatment-related effects, potentially resulting in failed studies. Severe infections may result in renal compromise or neurologic signs, either of which make animals unsuitable for use in research.

Prevention and Treatment

Spores of *E. cuniculi* are resistant to commonly encountered environmental conditions. Dry spores can survive at least four weeks at 22°C and several months under cool, wet conditions. Autoclaving or oxidizing disinfectants or sterilants will kill spores of *E. cuniculi*. Housing rabbits with rodents is generally not recommended, and animals should be regularly screened for *E. cuniculi* infection as part of a general health monitoring program.

There is no effective treatment for *E. cuniculi*. Since spore shedding is rare 3 months post-infection, choosing older animals for colony rederivation may be wise. Seroconversion generally precedes renal shedding, so a test and cull method for immunocompetent colonies may be effective. Since the organism may be transmitted via aerosol in rabbits, test and cull may not be effective unless rabbits can be isolated from aerosolized urine. The possibility of vertical transmission exists, so hysterectomy rederivation may not be suitable for eliminating this organism, but embryo transfer should be successful.

E. cuniculi does not induce tolerance, so if hysterectomy rederivation is attempted, serologic positives in the offspring indicate infection and those animals should be culled.

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