Review Article

Journal of Advanced Veterinary Research
(2026) Volume 16, Issue 4, 648-653

Encephalitozoon cuniculi infection in rabbits: An updated comprehensive review

Wafaa A. Abd El-Ghany*

Poultry Diseases Department, Faculty of Veterinary Medicine, Cairo University, Giza, 12211, Egypt

ARTICLE INFO

Recieved: 04 April 2026

Accepted: 02 June 2026

*Correspondence:

Corresponding author: Wafaa A. Abd El-Ghany
E-mail address: wafaa.soliman@cu.edu.eg

Keywords:

Clinical disease, Control, Diagnosis, *Encephalitozoon cuniculi*, Rabbits

ABSTRACT

Encephalitozoon cuniculi (*E. cuniculi*) is a pervasive, obligate intracellular microsporidian parasite that represents a significant clinical challenge in domestic rabbit (*Oryctolagus cuniculus*) medicine. This review synthesizes current knowledge regarding encephalitozoonosis, beginning with the pathogen's unique spore-forming biology and the high susceptibility of leporids. Transmission primarily occurs via the ingestion or inhalation of spores shed in the urine, though vertical transmission is also documented. The pathogenesis is characterized by the parasite's predilection for the central nervous system, kidneys, and ocular lenses, where it triggers chronic granulomatous inflammation. While host immunity, specifically cell-mediated responses, often keeps infections subclinical, triggers such as stress or immunosuppression can lead to overt disease. Three primary clinical manifestations: neurological syndromes (notably torticollis and ataxia), renal failure, and phacoclastic uveitis are characteristics for *E. cuniculi* infection in rabbits. Diagnostic challenges are a focal point of this review, as high seroprevalence in asymptomatic populations complicates the interpretation of results. The efficacy of combining quantitative serology, molecular techniques, and protein electrophoresis to achieve a definitive diagnosis are discussed. Finally, the review addresses management strategies, centering on the administration of benzimidazole anthelmintics and anti-inflammatory therapy, alongside rigorous husbandry practices. By integrating these facets, this review provides a comprehensive framework for clinicians and researchers to better understand, diagnose, and mitigate the impact of this resilient zoonotic pathogen in rabbit populations.

Introduction

The genus Encephalitozoon has two species, *Encephalitozoon cuniculi* (*E. cuniculi*) and *E. intestinalis*, while *E. hellem* primarily infects birds (Hinney *et al*., 2016). The species, *E. cuniculi*, is a unicellular eukaryote and spore-forming obligatory intracellular organism in the phylum Microsporidia. They are characterized as protozoon parasites, however they have been shown to be closely related to fungi. Microsporidians are ubiquitous microorganism that cause economic losses in livestock and fish (Han *et al*., 2019). Moreover, certain species can infect humans, particularly immunocompromised persons that have AIDS or organ transplant patients. Encephalitozoonosis is a disease caused by Encephalitozoon spp. and causes high morbidity in rabbit's farms, besides its zoonotic importance. Therefore, the disease can directly impact the rabbits' industry particularly in countries where rabbits have become an important source of meat (Santaniello *et al*., 2009; Espinosa *et al*., 2020; Morsy *et al*., 2020).

Encephalitozoonosis in rabbits may induces several forms of infection including acute infection with neurological, renal, and ocular picture, or chronic or subclinical infection which is usually asymptomatic (Ozkan *et al*., 2018). The clinical diagnosis is confirmed by the microscopic examination of the brain, kidney, eyes, and liver of infected rabbits (Morsy *et al*., 2020). The different molecular techniques are crucial for the detection of *E. cuniculi* DNA (Javadzade *et al*., 2021). Moreover, serological tests are used for the detection of circulating antibodies or maternal antibodies for *E. cuniculi* in young rabbits (Cray *et al*., 2020). Moreover, some blood parameters could be used for the detection of acute renal dysfunction related to encephalitozoonosis (Ozkan *et al*., 2019a). The management of the disease in rabbits is based on the treatment with benzimidazole anthelmintics and anti-inflammatory therapy, besides rigorous husbandry practices (Fisher and Graham, 2023).

This article aims to review the current available data regarding encephalitozoonosis in rabbits, from the pathogen, susceptibility, mode of transmission, pathogenesis, host immunity, clinical signs, and diagnostic methods to methods of treatment and prevention of the disease.

Susceptibility, mode of transmission, and pathogenesis (Fig. 1)

The main host of *E. cuniculi* is domestic farmed rabbits (*Oryctolagus cuniculus*) as well as pet and wild species of rabbits, however, the parasite has been identified in many other hosts including monkeys, foxes, dogs, cats, mice, birds, and humans. Genotyping of *E. cuniculi* revealed presence of 4 host specific types; genotype I (rabbit's strain), genotype II (murine strain), genotype III (canine strain), and genotype IV (human strain) (Hinney *et al*., 2016). Some breeds of rabbits show resistant to encephalitozoonosis such as Lop-eared and Rex rabbits (Fukui *et al*., 2013).

The frequency of *E. cuniculi* occurrence is more common in younger rabbits (1-day to 4-months old) which may be due to the underdevelopment of immune systems and the inability to fight the parasite (Espinosa *et al*., 2020). Moreover, it has been suggested that females (does) are more susceptible to *E. cuniculi* than males. Generally, encephalitozoonosis in rabbit farms is most likely due to poor management and husbandry practices with inadequate prophylactic health measures.

Horizontal and vertical (trans-placental or intrauterine) are the main routs of *E. cuniculi* transmission in rabbits (La'Toya *et al*., 2014). Horizontal infection occurs via oral ingestion of contaminated food or water, or rarely via inhalation of the parasite spores. Following ingestion of *E. cuniculi,* the parasite replicates in intestinal epithelium and then the infected macrophages circulate and reach the central nervous system, kidneys, liver, lungs, and heart. Finally, the *E. cuniculi* infected cells rupture with releasing of infective spores causing inflammatory and granulomatous lesions in tissues (Meredith and Richardson, 2015). Spores of *E. cuniculi* have been identified in the urine for up to 35 days till 3 months or more post-infection (Jeklova *et al*., 2020).

Vertical or transplacental route from the infected doe to the offspring has also been confirmed to be another route of *E. cuniculi* transmission in rabbits. Spores were detected in the eye lens of the offspring causing cataracts and uveitis. This can be explained by presence of the parasite in the lens placode and anterior capsule in the first trimester of doe ges-

ISSN: 2090-6277/2090-6269/

tation during embryonic development (Ozkan *et al*., 2019a). Rupture of the lens capsule causes release of proteins of the parasite which initiates immune response against normal lens proteins and development of unilateral phacoclastic uveitis (Jeklova *et al*., 2019). Other experimental transmission routes through traumatic transmucosal, intravenous, intrathecal, and rectal infection were also reported (La'Toya *et al*., 2014).

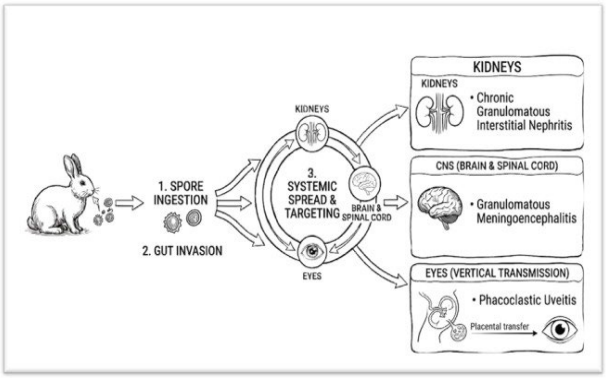

Figure 1. The pathogenesis of E. cuniculi infection in rabbits

Clinical disease

Signs

The clinical signs associated with *E. cuniculi* infections in rabbits depend mainly on the host's immunity as immunosuppressed animals show severe clinical picture, while Immuno-competent individuals show mild sub-clinical infection (Baldotto *et al*., 2015). The infection with *E. cuniculi* was identified in rabbits as a main cause of neurological disorders in the world (Wright and Craighead, 1922; Harcourt-Brown and Holloway, 2003; Valencakova *et al*., 2008; Baldotto *et al*., 2015; Wang *et al*., 2022; Škrbec *et al*., 2023). Acute, chronic, or even mild sub-clinical infections are the forms of encephalitozoonosis in rabbits. The most affected organs affected with clinical *E. cuniculi* infections in rabbits are central nervous system (Brain and spinal cord), kidneys, or eyes (Harcourt-Brown and Holloway, 2003). Acute cases with encephalitozoonosis in rabbits exhibited neurological signs due to affection of the central nervous system and the manifestations are called Vestibular disease (Harcourt-Brown and Holloway, 2003). Granulomatous inflammation of rabbits' brain is caused by *E. cuniculi* and consequently vestibular disease is commonly observed as a possible secondary effect (Gruber *et al*., 2009; Jeklova *et al*., 2010). However, the mechanism by which *E. cuniculi* can induce the development of clinical signs in rabbits is not definitive, and encephalitis is mostly common, while labyrinthitis (inflammation of the middle ear) or vestibular neuritis is not (Csokai *et al*., 2009; Dobos *et al*., 2022). Longitudinal rolling, circling, head tilt, seizures, tremors, ataxia, hemiparesis or paresis, falling to one side, paralysis of the hind limb, rapid involuntary movements of the eyes (nystagmus), and urinary incontinence are the most prominent signs of acute vestibular disease in rabbits (Künzel *et al*., 2008; Valencakova *et al*., 2008; Csokai *et al*., 2009; Škrbec *et al*., 2023). However, chronic form of the disease is associated with weight loss, renal failure, polyuria, polydipsia, pollakisuria, azotemia, and cystitis of the infected animals (Harcourt-Brown and Holloway, 2003; Valencakova *et al*., 2008; Baldotto *et al*., 2015). The parasite may invade the rabbits' eye lens causing inflammation, damage and rupture of the anterior eye lens capsule, and release of lens material into the anterior chamber of the eye globe with phacoclastic uveitis (Harcourt-Brown and Holloway, 2003). Glaucoma and cataracts may also occur secondary to uveitis (Baldotto *et al*., 2015). It is important to mention that the previous clinical pictures are less specific and confused with other infections or disorders in rabbits (La'Toya *et al*., 2014). The disease course varies from days to weeks (Künzel *et al*., 2008). In addition, concomitant infections of *E. cuniculi* encephalomyelitis with bacterial causes of otitis media and interna have been reported in rabbits showed head tilt (Valencakova *et al*., 2008; Gruber *et al*., 2009; Jeklova *et al*., 2010; Liatis *et al*., 2024). Moreover, parasitic (*Toxoplasma gondii* and *Neospora caninum*) (Zanet *et al*., 2013; Neumayerová *et al*., 2014; Mäkitaipale *et al*., 2022) as well as virus (herpes simplex) infections have been detected as comorbidities infections with *E. cuniculi* in farmed, pet, and wild rabbits. Bacterial encephalitis, hydrocephalus, malignant lymphoma, and bacterial encephalitis may also occur as concurrent conditions with encephalitozoonosis (Csokai *et al*., 2009; Gruber *et al*., 2009). Asymptomatic carriers or shedder animals should be taken in consideration during diagnosis and prevention of *E. cuniculi* transmission (La'Toya *et al*., 2014).

The incidences of *E. cuniculi* were 58.5% (Gruber *et al*., 2009) and 77.1% (Künzel *et al*., 2008) among rabbits have mean age of 2.8 years and showed nervous manifestations. Out of 184 rabbits, 54.2% of the animals showing neurological manifestations were recovered within a few days (Künzel *et al*., 2008).

Post-mortem lesions

The post-mortem lesions of encephalitozoonosis in rabbits have been reported (La'Toya *et al*., 2014; Morsy *et al*., 2020). Dead animals revealed severe congestion of the cerebral and meningeal blood vessels with acute severe multifocal necrosis of cerebrum. Enlarged, pale, and fibrosed kidneys with adherence of capsule to the parenchyma. The globes of eye usually show unilateral focal uveitis of the anterior chamber, lens opacity, and increased corneal thickening (Ozkan *et al*., 2018).

Microscopic lesions

The histopathological alterations of encephalitozoonosis in the brain and spinal cord are characteristics. Sections of the infected organs with *E. cuniculi* could be stained with Hematoxylin and Eosin (H & E), Gram's, Masson's trichrome, and calcofluor white stains are used to identify the parasite or spores microscopically (Wasson and Peper, 2000; Rodríguez-Tovar *et al*., 2017; Addie *et al*., 2020).

After *E. cuniculi* infection, the infected cells rupture and release spores extracellularly and resulted in chronic diffuse cellular infiltration and granuloma formation in target tissues such as the central nervous system (Didier *et al*., 2000). Stained sections of brain stem or cerebrum in with HE or Giemsa stains presented non-suppurative or granulomatous meningoencephalitis for at least one month (Csokai *et al*., 2009; La'Toya *et al*., 2014). The brain tissue with *E. cuniculi* showed meningitis, perivascular cuffing in all cerebral lobes, and granulomatous lesions of plasma cells, lymphocytes, and macrophages aggregations (Maestrini *et al*., 2017). Glial nodules composed of multifocal gliosis, microglia, astrogliosis, neuronophagia, and neuronal degeneration have also been detected (Cox and Gallichio, 1978; Morsy *et al*., 2020). The spores of *E. cuniculi* may remain in parasitophorous vacuoles in macrophages, microglia, and endothelial cells or rupture and reside in the neuropils of cerebral cortex and hippocampus (Sadeghi-Dehkordi *et al*., 2019; Morsy *et al*., 2020). Severe lesions showed fibrosis and interstitial deposition of collagen with inflammatory infiltration of lymphocytes, macrophages, and plasma cells.

The affected kidneys tissues with *E. cuniculi* revealed atrophy and thickening of the basement membrane with glomerular lesions (Sadeghi-Dehkordi *et al*., 2019). Spores of the parasite could be detected in the tubular epithelial cells' cytoplasm or in the renal tubules (Sadeghi-Dehkordi *et al*., 2019; Morsy *et al*., 2020).

The eye lens of rabbits hs encephalitozoonosis showed thinning and rupture of the anterior capsule with a destruction of the lens fibers, followed by cellular necrosis and degeneration (Ozkan *et al*., 2018; Morsy *et al*., 2020). Oedema of cornea, ulceration of epithelium, necrosis of endothelium, and infiltration of mononuclear cells with fibrin in the corneo-scleral trabecular meshwork were also noted (Morsy *et al*., 2020). The other observed eye lesions were loss of epithelial integrity of Bowman's capsule and descemet's membrane, edema of the iris with degeneration

of the posterior epithelium, and atrophy and detachment of the retina.

Liver also displayed mild hepatocytes degeneration in the centri-lobular area and peri-portal mononuclear cell infiltration. Similar lesions were observed in lungs where the cell degeneration and mononuclear cells infiltration are less abundant, but hyperemic capillaries were abundant (Jeklova *et al*., 2020). Hyperemic red pulp and lymphocyte infiltration in spleen were seen in spleen of can be observed in *E. cuniculi* infected rabbits (Jeklova *et al*., 2020).

Diagnosis

Careful exanimation of diseased rabbits may enable the veterinarian to differentiate between peripheral vestibular disease and other central vestibular disorders that could be probable in rabbits have encephalitis caused by *E. cuniculi* (Künzel *et al*., 2008). However, the definitive diagnosis of *E. cuniculi* infection in rabbits has been difficult over the last several decades. The diagnosis is based mainly on clinical picture, histopathology, serology, and molecular techniques (La'Toya *et al*., 2014). Other parameters such as blood parameters (renal function tests, protein, etc.) and ultrasound for assessing kidney functionsl function (La'Toya *et al*., 2014). Moreover, radiology, computerized tomography scan, and magnetic resonance imaging could be used for the detection of fluid filling tympanic bulla (King *et al*., 2012; Coeuriot *et al*., 2022) or the middle ear diseases of rabbits showing nervous signs (Richardson *et al*., 2019). Iodinated contrast is also used to enhance the imaging for evaluation of the central nervous system of rabbits (Isaac *et al*., 2022) or may be used to identify the extent of cerebral lesions or differentiate them from ear lesions (Mancinelli, 2015).

Molecular diagnosis

Samples for the molecular detection of suspected infected cases with *E. cuniculi* could be taken from cerebrospinal fluid, urine, feces, or tissues from brains, kidneys, eye lenses, livers, lungs, hearts, and spleen (Csokai *et al*., 2009; Kimura *et al*., 2013). It has been found that destruction of the thick cell wall of microsporidian using different methods is very important in order to release of DNA easily (Csokai *et al*., 2009; Kimura *et al*., 2013). Besides, some difficulties were found during the molecular detection of *E. cuniculi* from urine, feces, or cerebrospinal fluid samples due to the short and intermittent excretion of spores from these samples (Kimura *et al*., 2013). Thus, timing of sample collection (spores load) during the stages of infection (acute, chronic, or latent) is very important to obtain accurate molecular testing results (La'Toya *et al*., 2014).

Conventional polymerase chain reaction (PCR), nested PCR, and RT-PCR have are the molecular techniques that have been recently carried out for the molecular detection of *E. cuniculi* in rabbits (Csokai *et al*., 2009). Successful results were obtained using conventional PCR when eye lens samples were taken (Csokai *et al*., 2009). Nested PCR also showed high sensitivity for the detection of *E. cuniculi* when brain tissues were used (Csokai *et al*., 2009; Javadzade *et al*., 2021). In addition, *E. cuniculi* had been identified in urine samples of infected pet rabbits with neurological signs using RT-PCR (Adaszek *et al*., 2014).

Serology

Serological monitoring of *E. cuniculi* infection in rabbits testing is an important tool for the diagnosis (Montiani-Ferreira *et al*., 2024). It is important to note that clinical manifestations of encephalitozoonosis are not necessarily associated with increasing antibody titers, but only a negative result can rule out the disease (La'Toya *et al*., 2014). Serological tests including enzyme-linked immunosorbent assay, indirect immunofluorescence test, Western blot analysis, mass spectrometry, carbon immunoassay, and C-reactive protein measurement are commonly applied for the detection of the circulating anti-*E. cuniculi* immunoglobulins (Ig)G and IgM antibodies in rabbits (Boot *et al*., 2000; Harcourt-Brown and Holloway, 2003; Tee *et al*., 2011; Desoubeaux *et al*., 2017a,b; Sadeghi-Dehkordi *et al*., 2019; Cray *et al*., 2020).

Maternal derived antibodies play an important role in the protection of young rabbits up to 4 weeks of age. During this time, animals will be serologically positive, followed by the absence of antibodies from 4 to 8 weeks of age (Dipineto *et al*., 2008). Therefore, the lower sero-prevalence of encephalitozoonosis in rabbits aged less than 4 months compared to those over than 4 months indicated that rabbits aged 4 and 8 weeks are possible to show false sero-negative reactions (Dipineto *et al*., 2008; Santaniello *et al*., 2009).

The presence of specific anti-*E. cuniculi* IgM and IgG may indicate previous exposure of rabbits to *E. cuniculi*. Detecting IgG and IgM in encephalitozoonosis cases is an indicator of a humoral response, but not a clear indication of exposure to the parasite or even ascertain whether *E. cuniculi* is the causative agent of the disease (Harcourt-Brown and Holloway, 2003; Csokai *et al*., 2009; La'Toya *et al*., 2014; Jeklova *et al*., 2020). Also, previously treated *E. cuniculi* infected rabbits or even sub-clinically infected animals showed positive IgM titers (Jeklova *et al*., 2010; Cray *et al*., 2015). Jeklova *et al*. (2010) demonstrated that a high titer of IgM point to an early or acute *E. cuniculi* infection, high titers of IgG indicate a latent or chronic infection, and high titers of both IgM and IgG reveal presence of infection-either acute, a reactivated infection, or reinfection. In the study of Keeble and Shaw (2006), the results indicated a decrease in IgM titers, but an increase in IgG titers in serum of *E. cuniculi* infected domestic rabbits. Besides, oral and ocular infections of rabbits with *E. cuniculi* resulted in high IgG and IgM serum levels up to 18 weeks post-infection, while the IgM and IgG titers reach the peak within the first and third week, respectively. After 18 weeks post *E. cuniculi* infection, the serum titers of IgM decline and will no longer be indication of animals' acute infection (La'Toya *et al*., 2014). Jeklova *et al*. (2010) demonstrated IgM within 1 week after *E. cuniculi* and continued for at least 4 months, while IgG could be detected from 2 weeks post-infection.

On the other side, negative titers for *E. cuniculi* are not indication of absence of exposure of rabbits to *E. cuniculi* infection. Infected rabbits may present negative antibodies titers for up to 2 weeks post-infection. So, we can depend on the second negative IgG titer results in the apparently healthy rabbits 3 weeks later to assure absence of infection. A single positive IgG titer to *E. cuniculi* in apparently healthy animals may point to an early infection, a chronic infection, and/or previous exposure infection and recovery from the disease. Rabbits showed nervous manifestations could be considered positive to *E. cuniculi* if they have 2 negative IgG titers 3 weeks a part (La'Toya *et al*., 2014).

Blood parameters

Despite hematology shows a little significance in diagnosis of encephalitozoonosis infections in rabbits (Meredith and Richardson, 2015), measuring of some blood parameters could be important in rabbits showing acute renal dysfunction. Infected animals showed increased count of absolute heterophil with low hematocrit values (less than 33%). Ozkan *et al*. (2019b) observed significant elevated levels of blood urea nitrogen, creatinine, alkaline phosphatase, cholesterol, phosphorus, and glucose in *E. cuniculi* seropositive rabbits compared to seronegative animals. Similarly, encephalitozoonosis seropositive rabbits which have renal affections displayed increased level alkaline phosphatase and concentration of urea (Ozkan *et al*., 2019a), while decreased levels of phosphorus and potassium (Meredith and Richardson, 2015). Also, infected animals with *E. cuniculi* showed reduced albumin: globulin ratio, β-globulin fraction, but increased γ-globulin fraction when compared to control non-infected rabbits (Meredith and Richardson, 2015). Similarly, Cray *et al*. (2009) demonstrated significant increase in γ- and β-globulin fractions, but low albumin: globulin ratio in encephalitozoonosis affected rabbits.

Differential diagnosis

Based on the similarity of the clinical picture of encephalitozoonosis with other disease conditions in rabbits, the disease signs and lesions are not specific, and the diagnosis tools are difficult and expensive, searching other similar conditions is crucial for the accurate diagnosis.

The nervous signs induced by *E. cuniculi* in different species should be differentiated with other infectious (bacterial, viral, or parasitic), non-infectious (metabolic, inflammatory, congenital, neoplastic, or degenerative disorders) as well as lead toxicity (Fisher, 2021). Bacterial infection causing otitis media or interna and consequent nervous signs should be also differentiated from *E. cuniculi* infection (Künzel and Fisher, 2018; Liatis *et al*., 2024). *Pasteurella multocida*, *Listeria monocytogenes*, *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* are the most frequently encountered bacterial infections causing nervous manifestations of rabbits. In addition, nervous signs associated with Rabies (Eidson *et al*., 2005), *Baylisascaris procyonis* (Kazacos *et al*., 1983), *Toxoplasma gondii* (Mäkitaipale *et al*., 2022), and human herpes-1 virus (Müller *et al*., 2009) are similar to those of encephalitozoonosis (Künzel *et al*., 2008). Despite tumor diseases (lymphosarcoma or metastatic neoplasia) are rarely induced central nervous signs, cases have been reported in rabbits showing glioblastoma with neurological disorders (Bertram *et al*., 2021). Facial nerve deficit is a clear indication of otitis media or interna, are helpful in the differentiation from *E. cuniculi* infection (Eatwell *et al*., 2013). In addition, focal spinal disease in the cerebral-brainstem-spinal cord axis is the cause of paresis, plegia, and ataxia (La'Toya *et al*., 2014). The peripheral vestibular syndrome should be also differentiated from bacterial otitis externa/interna, rupture of the tympanic bulla, ototoxicity caused by aminoglycoside, and idiopathic vestibular disease (La'Toya *et al*., 2014).

Regarding renal insufficiency in encephalitozoonosis, it could be differentiated from the causes of chronic azotemia. Ultrasonography may be the solution for the detection of chronic renal failure of rabbits (La'Toya *et al*., 2014). Ocular lesions associated with *E. cuniculi* infection in rabbits could be differentiated with lens-induced uveitis secondary to geriatric cataract formation, and bacterial uveitis (Lesion is usually bilateral and seen in *Pasteurella multocida* infection) (Tee *et al*., 2011).

Prevention

To prevent the risk of *E. cuniculi* infections in rabbits' farms, avoid or reduce the direct contact of commercial or farm rabbits with pet or wildlife rabbits with a strict and through cleaning and disinfection of the environment. Using the "all-in and all-out" system is important to remove the entire rabbits' population and apply restrict cleaning and disinfection regiment before introducing new rabbits. Despite *E. cuniculi* is very resistant to the harsh environmental conditions, its spores could be destroyed using some disinfectants including 1% sodium hydroxide, 0.3% formaldehyde, and 1% hydrogen peroxide for 30 minutes as well as 0.1% bleach for 10 minutes and 70% ethanol for 30 seconds (La'Toya *et al*., 2014). Also, using raised feeders and drinkers to decrease the urine contamination (Fukui *et al*., 2013). In addition, appropriate hygienic measures should be considered by handling animals by hand-washing and disinfection. Selection of encephalitozoonosis genetically resistant breeds such as Lop-eared and Rex Rabbits' could help in the disease eradication (Fukui *et al*., 2013). Periodical serological monitoring of young rabbits every 2 weeks for 2 months to isolate healthy sero-negative animals from the *E. cuniculi* sero-positive individuals in separate cages. Rabbits show negative serological tests for a month should be used for future breeding, followed by serological testing monthly to guarantee their freedom of encephalitozoonosis (Meredith and Richardson, 2015). The newly introduced rabbits should be administered prophylactic oral or feed fenbendazole for 28 days to reduce the risk of *E. cuniculi* spread (Meredith and Richardson, 2015). Dietary propbiotics play an important role in rising the immune response of rabbits and consequent prevention of many infections (Mancini and Paci, 2021).

Control and treatment

Since encephalitozoonosis has no specific treatment, especially in acute immunocompromised rabbits, successful treatment of the disease is a critical challenge (Csokai *et al*., 2009). The treatment of animals with chronic neurological or kidney affections shows bad prognosis (Harcourt-Brown and Holloway, 2003). Symptomatic and antiparasitic drugs could be used for acute cases of encephalitozoonosis, however no promise of a complete recovery (La'Toya *et al*., 2014).

The specific medicament should prevent spore migration of proliferation, decrease inflammation caused by cell rupture, and manage nervous signs and simultaneous infections (La'Toya *et al*., 2014). Antiprotozoa and antifungal drugs could be used for the treatment of *E. cuniculi* being sharing parasitic and fungal properties (Wei *et al*., 2022). Benzimidazoles and fumagillin are effectively used as anti-microsporidial or anti *E. cuniculi* therapy in humans (Wei *et al*., 2022). Benzimidazole showed *in vitro* efficacy against *E. cuniculi* as well as prevented and treated natural and experimental infections with *E. cuniculi* in immuno-suppressed rabbits (Suter *et al*., 2001; Abu-Akkada and Oda, 2016). Fenbendazole is also recommended for the better prevention and treatment of *E. cuniculi* in the infected rabbits with fewer side effects. Rabbits given fenbendazole as a prophylactic measure before *E. cuniculi* infection exhibited seronegative reactions 21 days post-infection with absence of spores in brain tissues (La'Toya *et al*., 2014; Fisher, 2021; Dobos *et al*., 2022). Fenbendazole gave successful results against acute or chronic encephalitozoonosis when orally administrated at 20 mg/kg body weight daily for 28 days (Meredith and Richardson, 2015). It is recommended that treatment with fenbendazole should be extend for 30-60 days as the drug is believed to inhibit the replication of parasite replication and spores persist long-time in in the environment (Suter *et al*., 2001). Fenbendazole inhibits β-tubulin polymerization that disturbs the formation of microtubule and damages the replication of parasite. Moreover, it can lower some inflammatory cytokines such as interleukin-1β, interferon-γ, and tumor necrosis factor-α (Cray and Altman, 2022). In addition, oxibendazole (15 mg/kg body weight) is also used for the treatment (Suter *et al*., 2001; Fisher and Graham, 2023). Albendazole is less used owing to developing hepatotoxicity with embryotoxic, teratogenic, and hepato-toxic effects (Capece *et al*., 2009; La'Toya *et al*., 2014). The efficacy of fumagillin, sparfloxacin, polyoxin D, and nikkomycin Z has been reported against encephalitozoonosis *in vitro*, however, their efficacy *in vivo* has not yet been tested (Meredith and Richardson, 2015).

Some anti-inflammatory drugs such as dexamethasone induced good results against *E. cuniculi* in infected rabbits when given intramuscularly at 2 mg/kg body weight for 3 doses every 6 hours. Despite this treatment can reduced inflammation induced by encephalitozoonosis, it may lead to increasing the severity of the disease due to the acute immunosuppression (La'Toya *et al*., 2014). Also, subcutaneous injection of dexamethasone (0.1–0.2 mg/kg body weight) for up to 3 doses once every 2 days induced complete cure of encephalitozoonosis (Meredith and Richardson, 2015). Non-steroidal anti-inflammatory substances could be used with caution as they act on the kidneys (La'Toya *et al*., 2014).

Injection of diazepam (0.5 mg/kg body weight) or midazolam (0.07-0.22 mg/kg body weight) in rabbits have neurological signs may act as sedative. Also, treatment of rabbits have nervous signs 3 times a day with metoclopramide (0.5 mg/kg body weight orally/subcutaneously), prochlorperazine (0.2-0.5 mg/kg body weight orally), or meclizine (12.5-25 mg/kg body weight orally) have been used as antiemetic drugs (Meredith and Richardson, 2015).

Broad spectrum antibacterial drugs could be used in cases with acute manifestations of encephalitozoonosis to treat any concomitant or secondary bacterial infection. Based on antibiotic stewardship, antibiotics are only indicated where there is evidence of a bacterial agent, and antibiotic

choice should be determined by culture and sensitivity results. Antibiotics are not indicated for the treatment of *E. cuniculi* but may be indicated where there is evidence of concurrent bacterial infection. Oral treatment with trimethoprim-sulfamethoxazole (15-30 mg/kg body weight, 2 times a day) or enrofloxacin (10 mg/kg body weight, 2 times a day) for 7-10 days is recommended (Meredith and Richardson, 2015).

Treatment of encephalitozoonosis using a combination of fenbendazole, enrofloxacin, oxytetracycline, and dexamethasone showed a 54.2% clinical recovery rate of infected rabbits (Künzel *et al*., 2008). However, there are no significant differences in alleviating the severity of neurologic signs of rabbits following fenbendazole, oxytetracycline, and steroid therapy (Sieg *et al*., 2012). Rabbits given fenbendazole were 1.6 times more likely to survive until day 10 when compared to non-treated individuals (Sieg *et al*., 2012).

Ocular lesions or uveitis in rabbits have encephalitozoonosis in rabbits have been treated conventionally with systematic and topical dexamethasone and oxytetracycline. Focal granuloma and cataract could be handled by surgical removal of the lens. Fusidic acid or dexamethasone+neomycin+polymyxin B is another topical ocular treatment (Harcourt-Brown and Holloway, 2003).

Rabbits should be monitored to avoid dehydration due to renal affection. The non-steroidal anti-inflammatory drugs is recommended in cases with normal renal function values (La'Toya *et al*., 2014). Herbal treatments can help in improving the renal function and reduce the disease progression in rabbits (An *et al*., 2014; Koh, 2018). Some herbs showed renal protective effects, and they can reduce creatinine, increase diuretic activity, enhance clearance of inulin, reduce proteinuria, improve the plasma levels of total cholesterol and albumin, and stimulate immunity (Koh, 2018). Lee *et al*. (1993) demonstrated that rehmanniae radix water extract showed ameliorating effects on the renal affections of rabbits. In addition, increase the amount of drinking water or feeding on greens freed feed. In addition, antioxidants such as vitamin C and vitamin E as well as omega-3 fatty acids showed beneficial effects in animals have renal insufficiencies (Paterno *et al*., 2009; Koh, 2018).

Fluid therapy, good feeding, prokinetic drugs, and stress-free environment could be another tools to assist rabbits with neurological manifestations (La'Toya *et al*., 2014).

Conclusion

The infection with *E. cuniculi* remains one of the most complex and persistent pathogens in lapine medicine. Its ability to maintain subclinical, lifelong infections makes it a "silent" threat that often only surfaces during periods of physiological stress. While advancements in serological testing and PCR have improved our ability to identify the parasite, the high prevalence of asymptomatic carriers means that a positive result must always be correlated with clinical signs. Current treatment protocols using fenbendazole are effective at reducing spore shedding and halting parasite replication, but they cannot reverse the permanent tissue damage (such as scarring in the kidneys or brain) that often occurs prior to diagnosis. Finally, regular screening of new arrivals and consistent monitoring of renal health in seropositive rabbits are essential to prevent outbreaks and manage chronic disease.

Conflict of interest

The author declares that there is no conflict of interest.

References

Abu-Akkada, S.S., Oda, S.S., 2016. Prevention and treatment of *Encephalitozoon cuniculi* infection in immunosuppressed rabbits with fenbendazole. Iranian Journal of Veterinary Research 17, 98-105.

Adaszek, Ł., Winiarczyk, S., Zi¸etek, J., Kalinowski, M., Dzi¸egiel, B., Bartnicki, M., Kalinowska, A., Jarosz, Ł., 2014. Diagnosis of the *Encephalitozoon cuniculi* infections in pet rabbits with neurological symptoms. Polish Journal of Veterinary Sciences 17, 361-363. https://doi.org/10.2478/pjvs-2014-0050

Addie, D.D., Tasker, S., Boucraut-Baralon, C., Belák, S., Egberink, H., Frymus, T., Hartmann, K., Hofmann-Lehmann, R., Marsilio, F., Lloret, A., 2020. *Encephalitozoon cuniculi* infection in cats: European guidelines from the ABCD on prevention and management. Journal of Feline Medicine and Surgery 22, 1084-1088. https://doi.org/10.1177/1098612x20941787

An, P., Dang, H.M., Shi, X.M., Ye, B.Y., Wu, X.L., 2014. Qufeng Tongluo" acupuncture prevents the progression of glomerulonephritis by decreasing renal sympathetic nerve activity. Journal of Ethnopharmacology 155, 277-284. https://doi.org/10.1016/j.jep.2014.05.019

Baldotto, S.B., Cray, C., Giannico, A.T., Reifur, L., Montiani-Ferreira, F., 2015. Seroprevalence of *Encephalitozoon cuniculi* infection in pet rabbits in Brazil. Journal of Exotic Pet Medicine 24, 435-440. https://doi.org/10.1053/j.jepm.2015.08.010

Bertram, A.C., Bertram, B., Bartel, A., Ewringmann, A., Fragoso-Garcia, A.M., Erickson, A.N., Müller, K., Klopfleisch, R., 2021. Neoplasia and tumor-like lesions in pet rabbits (*Oryctolagus cuniculus*): A retrospective analysis of cases between 1995 and 2019. Veterinary Pathology 58, 901-911. https://doi.org/10.1177/0300985820973460

Boot, R., Hansen, A.K., Hansen, C.K., Nozari, N., Thuis, H.C., 2000. Comparison of assays for antibodies to *Encephalitozoon cuniculi* in rabbits. Laboratory Animals 34, 281-289. https://doi.org/10.1258/002367700780384726

Capece, B., Alves, M., Cristofol, C., Hajovska, K., 2009. Comparative embriotoxicity of albendazole and fenbendazole in rabbits. Journal of Veterinary Pharmacology and Therapy 32, 131-132.

Coeuriot, C.T., Guise, L., Cazin, C.C., Meregalli, R., Fusellier, M.S., 2022. Tympanic bullae ultrasonography is feasible in nonsedated healthy rabbits (*Oryctolagus cuniculus*). Journal of the American Veterinary Medical Association 260, 1934-1940. https://doi.org/10.2460/javma.22.06.0235

Cox, J.C., Gallichio, H.A., 1978. Serological and histological studies on adult rabbits with recent, naturally acquired encephalitozoonosis. Research in Veterinary Science 24, 260-261.

Cray, C., Arcia, G., Schneider, R., Kelleher, S.A., Arheart, K.L., 2009. Evaluation of the usefulness of an ELISA and protein electrophoresis in the diagnosis of *Encephalitozoon cuniculi* infection in rabbits (USA). American Journal of Veterinary Research 70, 478-482. https://doi.org/10.2460/ajvr.70.4.478

Cray, C., McKenny, S., Perritt, E., Arheart, K.L., 2015. Utility of IgM titers with IgG and C-reactive protein quantitation in the diagnosis of suspected *Encephalitozoon cuniculi* infection in rabbits. Journal of Exotic Pet Medicine 24, 356-360. https://doi.org/10.1053/j.jepm.2015.06.017

Cray, C., Liebl, M.P., Arheart, K., Peschke, R., Künzel, F., Joachim, A., 2020. Comparison of enzyme-linked immunosorbent assay and immunofluorescence test for determination of anti-*Encephalitozoon cuniculi* antibodies in sera from rabbits with different clinical and histopathological presentations. Journal of Exotic Pet Medicine 32, 39-42. https://doi.org/10.1053/j.jepm.2019.11.003

Cray, C., Altman, N.H., 2022. An update on the biologic effects of fenbendazole. Comparative Medicine 72, 215-219. https://doi.org/10.30802/aalas-cm-22-000006

Csokai, J., Gruber, A., Kunzel, F., Tichy, A., Joachim, A., 2009. Encephalitozoonosis in pet rabbits (*Oryctolagus cuniculus*): Pathohistologi cal findings in animals with latent infection versus clinical manifestation. Parasitology Research 104, 629-635. https://doi.org/10.1007/s00436-008-1239-2

Desoubeaux, G., Piqueras, M.D.C., Pantin, A., Bhattacharya, S.K., Peschke, R., Joachim, A., Cray, C., 2017a. Application of mass spectrometry to elucidate the pathophysiology of *Encephalitozoon cuniculi* infection in rabbits. PLoS One 12, e0177961. https://doi.org/10.1371/journal.pone.0177961

Desoubeaux, G., Pantin, A., Peschke, R., Joachim, A., Cray, C., 2017b. Application of Western blot analysis for the diagnosis of *Encephalitozoon cuniculi* infection in rabbits: Example of a quantitative approach. Parasitology Research 116, 743-750. https://doi.org/10.1007/s00436-016-5343-4

Didier, E.S., Didier, P.J., Snowden, K.F., Shadduck, J.A., 2000. Microsporidiosis in mammals. Microbes and Infection 2, 709-720. https://doi.org/10.1016/s1286-4579(00)00354-3

Dipineto, L., Rinaldi, L., Santaniello, A., Sensale, M., Cuomo, A., Calabria, M., Menna, L.F., Fioretti, A., 2008. Serological survey for antibodies to *Encephalitozoon cuniculi* in pet rabbits in Italy. Zoonoses Public Health 55, 173-175. https://doi.org/10.1111/j.1863-2378.2007.01097.x

Doboși, A.A., Bel, L.V., Pașiu, A.I., Pusta, D.L., 2022. A review of *Encephalitozoon cuniculi* in domestic rabbits (*Oryctolagus cuniculus*) Biology, clinical signs, diagnostic techniques, treatment, and prevention. Pathogens, 11, 1486. https://doi.org/10.3390/pathogens11121486

Eatwell, K., Mancinelli, E., Hedley, J., Keeble, E., Kovalik, M., Yool, D., 2013. Partial ear canal ablation and lateral bulla osteotomy in rabbits. Journal of Small Animal Practice 54, 325-330. https://doi.org/10.1111/jsap.12042

Eidson, M., Matthews, S.D., Willsey, A.L., Cherry, B., Rudd, R.J., Trimarchi, C.V., 2005. Rabies virus infection in a pet guinea pig and seven pet rabbits. Journal of the American Veterinary Medical Association 227, 932-935. https://doi.org/10.2460/javma.2005.227.932

Espinosa, J., Ferreras, M.C., Benavides, J., Cuesta, N., Pérez, C., García Iglesias, M.J., García Marín, J.F., Pérez, V., 2020. Causes of mortality and disease in rabbits and hares: A retrospective study. Animals (Basel) 10, 158. https://doi.org/10.3390/ani10010158

Fisher, P.G., 2021. Neurologic and muscoskeletal diseases. In Ferrets, Rabbits, and Rodents: Clinical Medicine and Surgery, 4th ed.; Quesenberry, K., Orcutt, C., Mans, C., Carpenter, J.W., Eds.; WB Saunders: Philadelphia, PA, USA, pp. 233–249.

Fisher, P.G., Graham, J.E., 2023. Rabbits. In Carpenter's Exotic Animal Formulary, 6th ed.; Carpenter, W., Harms, C., Eds.; Elsevier: New York, NY, USA, pp. 575–626.

Fukui, D., Bando, G., Furuya, K., Yamaguchi, M., Nakaoka, Y., Kosuge, M., Murata, K., 2013. Surveillance for an outbreak of *Encephalitozoon cuniculi* infection in rabbits housed at a zoo and biosecurity countermeasures. Journal in Veterinary Medical Science 75, 55-61. https://doi.org/10.1292/jvms.12-0231

Gruber, A., Pakozdy, A., Weissenbock, H., Csokai, J., Kunzel, F., 2009. A retrospective study of neurological disease in 118 rabbits. Journal of Comparative Pathology 140, 31-37. https://doi.org/10.1016/j.jcpa.2008.09.009

Han, B., Moretto, M., Weiss, L., 2019. Encephalitozoon: Tissue culture, cryopreservation, and murine infection. Current Protocols in Microbiology 52, e72. https://doi.org/10.1002/cpmc.72

Harcourt-Brown, F.M., Holloway, H.K., 2003. *Encephalitozoon cuniculi* in pet rabbits. Veterinary Record 152, 427-431. https://doi.org/10.1136/vr.152.14.427

Hinney, B., Sak, B., Joachim, A., Kvá˘c, M., 2016. More than a rabbit's tale—Encephalitozoon spp. in wild mammals and birds. International Journal of Parasitology. Parasites and Wildlife 5, 76-87. https://doi.org/10.1016/j.ijppaw.2016.01.001

Isaac, I., Richardson, J., Liuti, T., Longo, M., 2022. Safety of intravenous iodinated contrast medium injection in rabbits undergoing conscious computed tomography. Veterinary Record Open 9, e31. https://doi.org/10.1002/vro2.31

Javadzade, R., Rostami, A., Arabkhazaeli, F., Bahonar, A., Rahimi, M.H., Mirjalali, H., 2021. Molecular detection and genotype identification of *E. cuniculi* from pet rabbits. Comparative Immunology, Microbiology and Infectious Diseases 75, 101616. https://doi.org/10.1016/j.cimid.2021.101616

Jeklova, E., Jekl, V., Kovarcik, K., Hauptman, K., Koudela, B., Neumayerova, H., Knotek, Z., Faldyna, M., 2010. Usefulness of detection of specific IgM and IgG antibodies for diagnosis of clinical encephalitozoonosis in pet rabbits. Veterinary Parasitology 170, 143-148. https://doi.org/10.1016/j.vetpar.2010.01.029

Jeklova, E., Levá, L., Kummer, V., Jekl, V., Faldyna, M., 2019. Immunohistochemical detection of *Encephalitozoon cuniculi* in ocular structures of immunocompetent rabbits. Animals (Basel), 9, 988. https://doi.org/10.3390/ani9110988

Jeklova, E., Leva, L., Matiasovic, J., Ondrackova, P., Kummer, V., Faldyna, M., 2020. Characterization of humoral and cell-mediated immunity in rabbits orally infected with *Encephalitozoon cuniculi*. Veterinary Research, 51, 79. https://doi.org/10.1186/s13567-020-00806-9

Kazacos, K.R., Reed, W.M., Kazacos, E.A., Thacker, H.L., 1983. Fatal cerebrospinal disease caused by *Baylisascaris procyonis* in domestic rabbits. Journal of the American Veterinary Medical

Association 183, 967-971.
Keeble, E.J., Shaw, D.J., 2006. Seroprevalence of antibodies to *Encephalitozoon cuniculi* in domestic rabbits in the United Kingdom. Veterinary Record 158, 539-544. https://doi.org/10.1136/vr.158.16.539
Koh, R., 2018. How to use acupuncture and herbal medicine for treatment of chronic renal failure. In Proceedings of the World Small Animal Veterinary Association Congress, Singapore, 25–28 September 2018.
Kimura, M., Aoki, M., Ichikawa-Seki, M., Matsuo, K., Yagita, K., Itagaki, T., 2013. Detection and genotype of *Encephalitozoon cuniculi* DNA from urine and feces of pet rabbits in Japan. Journal of Veterinary Medical Science 75, 1017-1020. https://doi.org/10.1292/jvms.12-0567
King, A., Posthumus, J., Hammond, G., Sullivan, M., 2012. Comparison of ultrasonography, radiography and a single computed tomography slice for the identification of fluid within the tympanic bulla of rabbit cadavers. Veterinary Journal 193, 493-497. https://doi.org/10.1016/j.tvjl.2012.02.006
Künzel, F., Gruber, A., Tichy, A., Edelhofer, R., Nell, B., Hassan, J., Leschnik, M., Thalhammer, J.G., Joachim, A., 2008. Clinical symptoms and diagnosis of encephalitozoonosis in pet rabbits. Veterinary Parasitology 151, 115-124. https://doi.org/10.1016/j.vetpar.2007.11.005
Künzel, F., Fisher, P.G., 2018. Clinical signs, diagnosis, and treatment of *Encephalitozoon cuniculi* infection in rabbits. Veterinary Clinics of North America. Exotic Animal Practice 21, 69-82. https://doi.org/10.1016/j.cvex.2017.08.002
La'Toya, V.L., Bradley, C.W., Wyre, N.R., 2014. *Encephalitozoon cuniculi* in pet rabbits: Diagnosis and optimal management. Veterinary Medicine, 5, 169-180. https://doi.org/10.2147/vmrr.s49842
Lee, H.S., Kim, S.T., Cho, D.K., 1993. Effects of rehmanniae radix water extract on renal function and renin secretion rate in unanesthetized rabbits. American Journal of Chinese Medicine 21, 179-186. https://doi.org/10.1142/s0192415x93000212
Liatis, T., Makri, N., Czopowicz, M., Richardson, J., Nuttall, T., Suñol, A., 2024. Otitis media/interna and encephalitozoonosis are the most common causes of head tilt in pet rabbits in the UK: 73 cases (2009–2020). Veterinary Record 195, e4267. https://doi.org/10.1002/vetr.4267
Mäkitaipale, J., Järvenpää, E., Bruce, A., Sankari, S., Virtala, A.M., Näreaho, A., 2022. Seroprevalence of *Encephalitozoon cuniculi* and *Toxoplasma gondii* antibodies and risk-factor assessment for *Encephalitozoon cuniculi* seroprevalence in Finnish pet rabbits (*Oryctolagus cuniculus*). Acta Veterinaria Scandinavica 64, 2. https://doi.org/10.1186/s13028-022-00622-5
Maestrini, G., Ricci, E., Cantile, C., Mannella, R., Mancianti, F., Paci, G., D'Ascenzi, C., Perrucci, S., 2017. *Encephalitozoon cuniculi* in rabbits: Serological screening and histopathological findings. Comparative Immunology, Microbiology and Infectious Diseases 50, 54-57. https://doi.org/10.1016/j.cimid.2016.11.012
Mancinelli, E., 2015. Diagnosing *Encephalitozoon cuniculi* infection in rabbits. Vet Times, 3 August 2015
Mancini, S., Paci, G., 2021. Probiotics in rabbit farming: Growth performance, health status, and meat quality. Animals (Basel) 11, 3388. https://doi.org/10.3390/ani11123388
Meredith, A.L., Richardson, J., 2015. Neurological diseases of rabbits and rodents. Journal of Exotic Pet Medicine 24, 21-33. https://doi.org/10.1053/j.jepm.2014.12.007
Morsy, E.A., Salem, H.M., Khattab, M.S., Hamza, D.A., Abuowarda, M.M., 2020. *Encephalitozoon cuniculi* infection in farmed rabbits in Egypt. Acta Veterinaria Scandinavica. 62, 11. https://doi.org/10.1186/s13028-020-0509-6
Montiani-Ferreira, F., Joachim, A., Künzel, F., Mello, F.R., Keeble, E., Graham, J., Martorell, J., Quinton, J.-F., Gottenger, A., Cray, C., 2024. *Encephalitozoon cuniculi* infection in rabbits (*Oryctolagus cuniculus*): Data from an international survey of exotic and small animal veterinarians. Animals (Basel), 14, 3295. https://doi.org/10.3390/ani14223295
Müller, K., Fuchs, W., Heblinski, N., Teifke, J.P., Brunnberg, L., Gruber, A.D., Klopfleisch, R., 2009. Encephalitis in a rabbit caused by humanherpesvirus-1. Journal of the American Veterinary Medical Association 235, 66-69. https://doi.org/10.2460/javma.235.1.66
Neumayerová, H., Juránková, J., Jeklová, E., Kudlá˘cková, H., Faldyna, M., Kova˘r˘cík, K., Jánová, E., Koudela, B., 2014. Seroprevalence of *Toxoplasma gondii* and *Encephalitozoon cuniculi* in rabbits from different farming systems. Veterinary Parasitology, 204, 184-190. https://doi.org/10.1016/j.vetpar.2014.04.020
Ozkan, O., Karagoz, A., Kocak, N., Alcigir, M.E., 2018. The first molecular detection and genotyping of *Encephalitozoon cuniculi* in rabbit's eye in Turkey. Kafkas Üniversitesi Veteriner Fakültesi Dergisi 24, 607-611. https://doi.org/10.9775/kvfd.2018.19696
Ozkan, O., Karagoz, A., Kocak, N., 2019a. First molecular evidence of ocular transmission of Encephalitozoonosis during the intrauterine period in rabbits. Parasitology International 71, 1-4. https://doi.org/10.1016/j.parint.2019.03.006
Ozkan, O., Yucesan, B., Pekkaya, S., Alçi¨gir, E., Gürcan, S., 2019b. Relationship between seropositivity of *Encephalitozoon cuniculi* and renal biochemical markers in clinically healthy rabbits. Ankara Üniversitesi Veteriner Fakültesi Dergisi 66, 197-204. https://doi.org/10.33988/auvfd.433457
Paterno, J.C., Freire, A.O., Soares, M.F., Franco, M.F., Schor, N., Teixeira, V.P.C., 2009. Electroacupuncture and moxibustion attenuate the progression of renal disease in 5/6 nephrectomized rats. Kidney and Blood Pressure Research 31, 367-373. https://doi.org/10.1159/000176189
Richardson, J., Longo, M., Liuti, T., Eatwell, K., 2019. Computed tomographic grading of middle ear disease in domestic rabbits (Oryctolagus cuniculi). Veterinary Record 184, 679. https://doi.org/10.1136/vr.104980
Rodríguez-Tovar, L.E., Villarreal-Marroquín, A., Nevárez-Garza, A.M., Castillo-Velázquez, U., Rodríguez-Ramírez, H.G., Navarro Soto, M.C., Zárate-Ramos, J.J., Hernández-Vidal, G., Trejo-Chávez, A., 2017. Histochemical study of *Encephalitozoon cuniculi* spores in the kidneys of naturally infected New Zealand rabbits. Journal of Veterinary Diagnostic Investigation 29, 269-277. https://doi.org/10.1177/1040638716668559
Sadeghi-Dehkordi, Z., Norouzi, E., Rezaeian, H., Nourian, A., Noaman, V., Sazmand, A., 2019. First insight into *Encephalitozoon cuniculi* infection in laboratory and pet rabbits in Iran. Comparative Immunology, Microbiology and Infectious Diseases 65, 37-40. https://doi.org/10.1016/j.cimid.2019.04.005
Santaniello, A., Dipineto, L., Rinaldi, L., Menna, L.F., Cringoli, G., Fioretti, A., 2009. Serological survey of *Encephalitozoon cuniculi* in farm rabbits in Italy. Research in Veterinary Science 87, 67-69. https://doi.org/10.1016/j.rvsc.2008.12.008
Sieg, J., Hein, J., Jass, A., Sauter-Louis, C., Hartmann, K., Fischer, A., 2012. Clinical evaluation of therapeutic success in rabbits with suspected encephalitozoonosis. Veterinary Parasitology 187, 328-832. https://doi.org/10.1016/j.vetpar.2011.12.014
Škrbec, M., Dov˘c, A., Hrženjak, N.M., Slavec, B., Žlabravec, Z., Ko˘car, N., Rojs, O.Z., Ra˘cnik, J., 2023. *Encephalitozoon cuniculi* infection of domestic rabbits (*Oryctolagus cuniculus*) in Slovenia between 2017 and 2021. Pathogens 12, 516. https://doi.org/10.3390/pathogens12040516
Suter, C., Müler-Doblies, U., Deplazes, P., Hatt, J.M., 2001. Prevention and treatment of *Encephalitozoon cuniculi* infection in rabbits with fenbendazole. Veterinary Record 148, 478-480. https://doi.org/10.1136/vr.148.15.478
Tee, K.Y., Kao, J.P., Chiu, H.Y., Chang, M.H., Wang, J.H., Tung, K.C., Cheng, F.P., Wu, J.T., 2011. Serological survey for antibodies to *Encephalitozoon cuniculi* in rabbits in Taiwan. Veterinary Parasitology 183, 68-71. https://doi.org/10.1016/j.vetpar.2011.06.011
Valencakova, A., Balent, P., Petrovova, E., Novotny, F., Luptakova, L., 2008. Encephalitozoonosis in household pet Nederland Dwarf rabbits (*Oryctolagus cuniculus*). Veterinary Parasitology 153, 265-269. https://doi.org/10.1016/j.vetpar.2008.01.047
Wang, Y., Qin, X., Diao, X., Liu, Y., Liu, J., 2022. Serological survey for antibodies to *Encephalitozoon cuniculi* and *Toxoplasma gondii* in pet rabbits in eastern coastal areas of China. Journal of Veterinary Medical Science, 84, 777-783. https://doi.org/10.1292/jvms.21-0660
Wasson, K., Peper, R.L., 2000. Mammalian microsporidiosis. Veterinary Pathology 37, 113-128. https://doi.org/10.1354/vp.37-2-113
Wei, J., Fei, Z., Pan, G., Weiss, L.M., Zhou, Z., 2022. Current therapy and therapeutic targets for microsporidiosis. Frontiers in Microbiology 13, 835390. https://doi.org/10.3389/fmicb.2022.835390
Wright, J.H., Craighead, E.M., 1922. Infectious motor paralysis in young rabbits. Journal of Experimental Medicine 36, 135-140. https://doi.org/10.1084/jem.36.1.135
Zanet, S., Palese, V., Trisciuoglio, A., Alonso, C.C., Ferroglio, E., 2013. *Encephalitozoon cuniculi*,-*Toxoplasma gondii* and *Neospora caninum* infection in invasive Eastern Cottontail Rabbits Sylvilagus floridanus in Northwestern Italy. Veterinary Parasitology 197, 682-684. https://doi.org/10.1016/j.vetpar.2013.05.014