Feline intralenticular Encephalitozoon cuniculi: three cases from California

Joie Lin1, Barbara Nell2, Taemi Horikawa3, and Mitzi Zarfoss4

Abstract
Case series summary Three domestic shorthair cats from California presented to veterinary ophthalmologists with immature cataracts. Other presenting clinical signs included corneal edema, anisocoria, anterior uveitis, elevated intraocular pressure, blepharospasm and/or lethargy. All patients were immunocompromised due to concurrent diseases and/or immunomodulatory drugs. Diagnostics included serial comprehensive ophthalmic examinations with tonometry, ocular ultrasound, electroretinogram and testing for other causes of feline uveitis. Testing for Encephalitozoon cuniculi included serology, histopathology and/or PCR of aqueous humor, lens material or paraffin-embedded whole eye. Treatments included antiparasitic medication, anti-inflammatory medication and supportive care in all three cases. Surgical treatment included enucleation (one case), bilateral phacoemulsification and unilateral intracocular lens placement (one case) and bilateral phacoemulsification with bilateral endolaser ciliary body ablation and bilateral intracocular lens implantation (one case). Both cats for which serologic testing for E cuniculi was performed were positive (1:64–1:4096). In all cats, diagnosis of intracocular E cuniculi was based on at least one of the following: lens histopathology or PCR of aqueous humor, lens material or paraffin-embedded ocular tissue. The clinical visual outcome was best in the patient undergoing phacoemulsification at the earliest stage of the cataract.

Relevance and novel information Encephalitozoon cuniculi should be considered as a differential cause of cataracts and uveitis in cats in California, the rest of the USA and likely worldwide.

Keywords: Encephalitozoon cuniculi; uveitis; cataracts; phacoemulsification

Accepted: 25 May 2022

Introduction
Encephalitozoon cuniculi is a worldwide microsporidian.1,2 Spores can be transmitted via respiratory, oral,3 conjunctival,4 intranasal, intraovarial or transplacental routes.5 In veterinary ophthalmology, E cuniculi is predominantly known as a cause of cataracts and phacoelastic uveitis in rabbits;6,7 after transplacental transmission, spores are speculated to enter the lens via the lenticular blood supply while it is still present.8 However, a recent study with immunohistochemical evidence of intralenticular E cuniculi after oral infection in 4-month-old, immunocompetent, specific pathogen-free rabbits9 suggested that alternative mechanisms for lens infections are possible. Reports of ocular involvement in other species are limited and include cataract and uveitis in a snow leopard in France,10 cataract, uveitis and chorioretinal lesions in dogs in Europe,11 keratitis and uveitis in an American cat,12 polyarteritis nodosa and cataract in a blue fox,13 cataract and neurologic lesions in mink in Norway14 and keratoconjunctivitis in an American cockatoo.15 In addition, E cuniculi has been thoroughly investigated in dogs in Europe,11 keratitis and uveitis in an American cat,12 polyarteritis nodosa and cataract in a blue fox,13 cataract and neurologic lesions in mink in Norway14 and keratoconjunctivitis in an American cockatoo.15

1School of Veterinary Medicine, University of California-Davis, Davis, CA, USA
2Department for Small Animals and Horses, Veterinary University of Vienna, Vienna, Austria
3Ophthalmology for Animals, Apts, CA, USA
4Pets Referral Center, Berkeley, CA, USA

Corresponding author: Joie Lin DVM, School of Veterinary Medicine, University of California-Davis, 1 Garrod Drive, Davis, CA 95616, USA
Email: jvlin@ucdavis.edu

Creative Commons CC BY: This article is distributed under the terms of the Creative Commons Attribution 4.0 License (https://creativecommons.org/licenses/by/4.0/) which permits any use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage).
as a cause of feline cataract in Austria. This report includes the clinical data from three feline cases of intra-
lenticular E cuniculi in California, USA; one case is
discussed at length (case 1), while the other two cases
cases 2 and 3) are summarized in Table 1.

Case series description

Case 1

A 3-year-old male castrated domestic shorthair cat
presented to an emergency service for blepharospasm,
anisocoria and lethargy. The patient had a history of
chronic upper respiratory infections and diarrhea. It had
been rescued from a southern Californian shelter and
lived indoors in San Francisco.

On initial emergency examination, the patient’s intra-
ocular pressure was 26 mmHg OD and 33 mmHg OS,
with mild corneal edema OU. Treatment included robe-
nacoxib (2 mg/kg SC once [Onsior; Elanco]), ofloxacin
(OU q8h) and 2% dorzolamide/0.5% timolol (OU q12h).
See Table 1 for the diagnostic testing results (testing for
E cuniculi was not immediately performed).

Initial ophthalmic examination revealed menace
response and pupillary light reflex (PLR) positive OU,
mild corneal edema with moderate keratic precipitates
OU, aqueous flare OU (trace OD and 1/4 + OS), focal
posterior synechiae OS and focal anterior cortical cata-
ракты OU (Keeler PSLClassic). Intraocular pressure was
20 mmHg OD and 12 mmHg OS (Icare Tonovet; Icare
Finland). Retinal examination (Keeler Vantage Indirect)
was normal except for numerous, punctate, gray, slightly
hyporeflective lesions in the dorsal retina OU. Treatment
with topical diclofenac 0.1% ophthalmic solution OU q12h
(Bausch and Lomb) was initiated. Treatment with fluco-
nazole (10.7 mg/kg PO q12h long-term for Cryptococcus
neofor mans) and doxycycline (4.3 mg/kg PO q12h for
21 days for Bartonella species) was initiated.

One week after initial presentation, aqueous flare was
unimproved. Treatment with topical 1% prednisolone
acetate suspension (OU q12h; Pacific Pharma) and topi-
cal 0.5% cidofovir (OU q12h; Wedgewood Compounding
Pharmacy) were added.

One month after initial presentation, the patient
developed a large superficial corneal ulcer OS, suspected
to be related to herpes exacerbated by topical steroids.
Prednisolone acetate was discontinued, and bacitracin
neomycin gentamicin ophthalmic ointment (AC Pharma-
ceuticals, Arroyo Grande CA) was added OU q8h.

Approximately 2 months after the initial examination,
the corneal ulcer OS persisted. Aqueous flare was trace
OD and 1/4 + OS, with an intraocular pressure (IOP) of
19 mmHg OD and 44 mmHg OS. Aqueocentesis was
performed OS, and aqueous humor was submitted for
PCR to determine if C neoformans, Bartonella species or
feline coronavirus (FCoV) were the cause of uveitis.
Because the patient’s cataracts appeared to be similar to
those described in a previous report, a special request
was made to IDEXX to add an E cuniculi PCR test. A
contact lens (PureVision BC 6.6; Bausch and Lomb) was
placed, and a partial lateral temporary tarsorrhaphy
was performed for 2 weeks. Medication administered
immediately after the procedures included bacitracin
neomycin gentamicin ophthalmic ointment (OU q8h)
and dorzolamide HCl/timolol maleate (OS q8h; Bausch
and Lomb). Oral medications included rifampin (for
diarrhea), buprenorphine (Hikma 0.5 mg/ml), roben-
coxib (6 mg PO q24h for 3 days [Onsior; Elanco]) and famiciclovir (250 mg PO q12h; Neogen). Aqueous humor
cytology (Veterinary Diagnostics) showed increased cel-
ularity, with 68% mixed (mostly mature) lymphocytes,
15% quiescent to vacuolated macrophages and 17% non-
degenerate to slightly poorly preserved neutrophils
(see Tables 1 and 2). Given the positive aqueous humor
PCR result for E cuniculi, treatment with fenbendazole
(50 mg/kg PO q24h for 3 weeks) was initiated.

Three months after initial presentation, ophthalmic
examination indicated similar signs of uveitis with
punctate fluorescein positivity OS only, and IOP was
16 mmHg OD and 8 mmHg OS. Topical 0.1% nepafenac
ophthalmic suspension (OU q12h; Nevanac Alcon) was
initiated.

Four months after initial presentation, aqueous flare
had resolved with normal IOP without any dorzolamide/
timolol in the previous 3 days. Given the anticipated
difficulty in controlling uveitis medically and the like-
lihood that cataracts would progress in the long term,
cataract surgery was considered. Owing to the patient’s
positive FCoV status, thoracic radiographs (unremarkable),
adrenal ultrasound (splenomegaly and mild mesen-
teric lymphadenopathy) and ultrasound-guided aspiration
of a mesenteric lymph node (cytologically normal) were
performed (see also Table 1).

Five months after initial presentation, E cuniculi
serology was 1:64 (University of Miami Avian & Wildlife
Laboratory; see Table 2 for the full list of E cuniculi tests).
Electroretinogram (ERG Retinographics BNP200) was
normal with b-wave amplitudes >300 µV OU. Ocular
ultrasound (Toshiba AplioMX) was normal OU except
for multifocal capsular/cortical lens irregularities OU
(Figure 1). Phacoemulsification was performed OU
(Acrivet Alexos). An intraocular lens was placed OS
only (An-lens MC1-13) due to excision of a peripheral
capsular plaque necessitating excess capsule removal
OD. Immediate postoperative medications included
0.3% ofloxacin ophthalmic solution (OU q6h; Bausch
and Lomb), 0.5% cidofovir (OU q12h), 0.1% Nevanac
(OU q6h), 1% prednisolone acetate (OU q6h), 2% dorzo-
lam ide ophthalmic solution (OU q8h; Micro Labs) and
Opticare (OU q12h; Opticare Eye Lube Plus Aventix)
Ocular medications included fenbendazole (50 mg/kg PO
q24h for 3 weeks), fluconazole, amoxicillin trihydrate/
clavulante potassium (62.5 mg PO q12h; Zoetis), trans-
mucosal buprenorphine (0.02 mg/kg q8h; Wedgewood
### Table 1 Case summaries

| Case 1 | Case 2 | Case 3 |
|--------|--------|--------|
| **Signalment** | 3-year-old MN DSH | 15-year-old FS DSH | 1.75-year-old FS DSH |
| **Presenting clinical signs** | Blepharospasm, anisocoria, lethargy | Rapid-onset cataracts, 6 months after diagnosis of intestinal lymphoma | Upper respiratory signs, ocular discharge, cloudy opacity OS |
| **Description of initial cataract** | Focal anterior cortical cataracts OU (see Figure 1) | Immature cataracts OU | Incipient peripheral cortical cataracts OU (see Figure 2) |
| **Degree of uveitis at presentation** | Mild corneal edema OU, moderate keratic precipitates OU, aqueous flare OU (trace OD and 1/4 + OS) | No flare, rubeosis or episcleral injection OU | OD: no aqueous flare, mild keratic precipitates |
| **IOP, lowest to highest** | • 16–37 mmHg OD | • 9–70 mmHg OD | OS: rubeosis iridis, 3–4/4 + aqueous flare, keratic precipitates |
| **Systemic testing: negative, normal results** | • CBC and serum chemistry | • 8–44 mmHg OS | • 11–30 mmHg OD |
| | • Seronegative: *T. gondii* IgG/IgM, FeLV antigen (IDEXX Reference Laboratory) | • Aqueous humor PCR was negative: FHV-1, FCoV, FeLV, *Bartonella* species, *C. neoformans*, *T. gondii*, FIV | • 15–62 mmHg OS |
| | • Thoracic radiographs | • Normal cytology of a mesenteric lymph node | • *Bartonella* species = 4 + strong positive (Western blot, National Veterinary Laboratory) |
| | • Upper respiratory PCR panel (IDEXX Reference Laboratory): *C. felis*, feline calicivirus, *M. felis* and influenza A | • FIP PCR (blood): negative | • FeLV-positive (Antech Diagnostics) |
| | • Seronegative: FCoV IFA < 1:400 | • FCoV titer 1:3200 | Systemic diagnoses |
| **Systemic testing positive results** | • *C. neoformans* titer 1:8 | • B henselae and B *cliamdigeae* titer = 1:128 | • *Intestinal lymphoma* |
| | • Fecal testing positive: *Giardia* (ELISA), *T. foetus*, *Cryptosporidium* species, *Giardia* species, FCoV and *C. perfringens* alpha toxin gene (PCR; IDEXX Reference Laboratory) | • Upper respiratory PCR panel, FHV-1 positive at 0.160 thousands/swab (latent infection; IDEXX Reference Laboratory) | • *FeLV* |
| | • Abdominal ultrasound (splenomegaly and mild mesenteric lymphadenopathy) | • Abdominal ultrasound (splenomegaly and mild mesenteric lymphadenopathy) | *Bartonella* species serologic positive |
| | • Repeat coronavirus titer 1:1600 | • Repeat coronavirus titer 1:1600 | |
| **Medical treatment for *E. cuniculi*** | Fenbendazole 50 mg/kg PO q24h for 3 weeks, repeated twice | Fenbendazole 70 mg/kg PO q24h for 3 weeks | Fenbendazole 50 mg/kg PO q24h for 10 days (multiple courses) |
| **Surgical treatment** | Phacoemulsification OU | Phacoemulsification OU | Enucleation OS |
| | Intraocular lens OS | Intraocular lens OU | |
| | | Endoscopic cyclocryocoagulation OU | |

(Continued)
|                      | Case 1                                                                 | Case 2                                                                 | Case 3                                                                 |
|----------------------|------------------------------------------------------------------------|------------------------------------------------------------------------|------------------------------------------------------------------------|
| **Glaucma treatment**| 2% dorzolamide/0.5% timolol OU q12h                                    | 2% dorzolamide OU q6h                                                   | Methazolamide (Wedgewood Compounding Pharmacy) 15 mg PO q24h–q12h       |
|                      | 2% dorzolamide OU q8h                                                  | 7.5 mg PO q24h                                                         |                                                                                                                                   |
| Uveitis treatment    | Onsior (robenacoxib; Elanco)                                          | 2% dorzolamide OU q12h–q6h                                            | Dexamethasone 0.1% (Bausch and Lomb) OS q24h–q12h                        |
|                      | Diclofenac 0.1% ophthalmic solution (Bausch and Lomb) OU q12h          | 0.5% timolol OU q12h                                                   |                                                                                                                                   |
|                      | Topical 1% prednisolone acetate suspension (Pacific Pharma) OU q24h–q12h| Neomycin polymyxin B sulfates and dexamethasone OU three times weekly   |                                                                                                                                   |
|                      | 0.1% nepafenac ophthalmic suspension (Nevanac Alcon) OU q24h–q6h       | 1% prednisolone acetate OU q8h                                        |                                                                                                                                   |
| Keratitis treatment  | Bacitracin neomycin gentamicin ophthalmic ointment (AC Pharmaceuticals) | Bacitracin neomycin gentamicin ophthalmic suspension (AC Pharmaceuticals) |                                                                                                                                   |
|                      | OU q8h                                                                 | OU q8h                                                                 |                                                                                                                                   |
|                      | Famciclovir (Neogen) 250mg PO q6h                                      | Ofloxacin 0.1% (Bausch and Lomb) OS q12h                               |                                                                                                                                   |
|                      | Ofloxaclin 0.3% OU q24h                                                | Opticogard (Opticare Eye Lube Plus; Aventix) OU q12h                   |                                                                                                                                   |
|                      | Opticare (Opticare Eye Lube Plus; Aventix) OU q12h                     | 0.5% cidofovir (Wedgewood Compounding Pharmacy) OU q12h                 |                                                                                                                                   |
|                      | 0.5% cidofovir (Wedgewood Compounding Pharmacy) OU q12h                 |                                                                       |                                                                                                                                   |
| Medical treatment    | Fluconazole 10.7 mg/kg PO q12h                                         | Prednisolone 5 mg PO q24h                                              | Doxycycline (Road Runner Compounding Pharmacy) 6mg/kg PO q12h for 25 days (multiple courses)                                  |
| for other conditions | Doxycycline 4.3 mg/kg PO q12h for 3 weeks                               | Chlorambucil 2 mg PO q12h for four doses q2weeks                       |                                                                                                                                   |
|                      | Ronidazole (for diarrhea)                                             | Vitamin B12/cobalamin 250 µg monthly                                   |                                                                                                                                   |
|                      | Buprenorphine (0.5 mg/ml; Hikma)                                       | SC fluids for hyporexia                                                |                                                                                                                                   |
| Duration of          | 14 years post-phacoemulsification                                      | 1 year post-phacoemulsification                                        |                                                                                                                                   |
| follow-up            |                                                                       |                                                                       |                                                                                                                                   |
| Outcome              | OS: pseudophakic                                                      | OU: pseudophakic, menace negative but patient navigated the room well, |                                                                                                                                   |
|                      | OD: aphakic                                                           | PLR and dazzle positive, comfortable, no flare, mild retinal degeneration |                                                                                                                                   |
|                      | OU: menace and PLR positive, comfortable, no aqueous flare, mild capsular opacity, numerous, punctate, gray, slightly hyporefective retinal lesions | IOP 18/17 mmHg OD/OS                                                   |                                                                                                                                   |
|                      | IOP 18/17 mmHg OD/OS                                                  |                                                                       |                                                                                                                                   |

MN = male neutered; DSH = domestic shorthair; FS = female spayed; IOP = intraocular pressure; CBC = complete blood count; T. gondii = Toxoplasma gondii; FIV = feline immunodeficiency virus; FeLV = feline leukemia virus; C felis = Chlamyphila felis; M felis = Mycoplasma felis; FHV-1 = feline herpesvirus-1; FCoV = feline coronavirus; C neoformans = Cryptococcus neoformans; FIP = feline infectious peritonitis; IFA = immunofluorescence; B henselae = Bartonella henselae; B clarridgeiae = Bartonella clarridgeiae; T foetus = Tritrichomonas foetus; C perfringens = Clostridium perfringens; NA = not available; E cuniculi = Encephalitozoon cuniculi; SC = subcutaneous; EOD = every other day; PLR = pupillary light reflex
Table 2  Encephalitozoon cuniculi testing

|                  | Case 1                                      | Case 2                                      | Case 3                                      |
|------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|
| Serology (IgG)   | 1:64*                                       | NA                                          | 1:4096 (2014) then 1:256 (2018)*           |
| PCR              | • Aqueocentesis fluid, positive†            | • Phacoemulsified lens fluid, positive§     | Paraffin scrolls of enucleated eye (OS), positive† |
|                  | • Lens material, positive, strain II‡       | • Urine negative¶                           |                                             |
| Histopathology   | Lens capsule: Gram-positive, Ziehl–Neelsen acid-fast positive∞ | NA                                          | Globe: intralenticular organisms, Gram-positive, variably acid-fast, Luna stain positive (see Figure 3)† |

*University of Miami Avian & Wildlife Laboratory
†IDEXX Reference Laboratories
‡Department for Pathobiology, Veterinary University Vienna
§Athens Veterinary Diagnostic Laboratory, University of Georgia
¶Comparative Pathology Laboratory, University of California, Davis
∞Comparative Ocular Pathology Laboratory of Wisconsin
NA = not available

Figure 1  Case 1: (a,b,d) clinical photos and (c) ultrasound image. Pupils were pharmacologically dilated with 1% tropicamide ophthalmic in (a), (b) and (d) (Akorn). (a,b) OD focal anterior subcapsular to anterior cortical cataract and focal pigment on lens capsule. The lens capsule appeared focally wrinkled at the site of the cataract clinically, but no capsular tears were visible on slit-lamp examination. (c) OS: vertical ultrasound image showing echoic dorsal anterior subcapsular cataract with anterior cortical to nuclear extension. The lens capsule was interpreted to be intact via ultrasound. Other than lens abnormalities, anterior and posterior segments were within normal limits. (d) OS: clinical photo showing retro-illumination of focal subcapsular to anterior cortical cataract (dark lenticular opacities). Images courtesy of Dr Mitzi Zarfoss
Compounding Pharmacy) and robenacoxib (6 mg PO q24h for three doses [Onsior; Elanco]). One day post-operatively, IOP was 37 mmHg OD and 43 mmHg OS but normalized after two extra doses of 2% dorzolamide/0.5% timolol OU. Perincisional superficial corneal ulcers and 1/4+ aqueous flare were present OU.

Lens capsule plaques were submitted to the Comparative Ocular Pathology Laboratory of Wisconsin. Histopathology of the right lens capsule presented moderate numbers of foamy-to-epithelioid macrophages with numerous 1–3 µm, rod-shaped microsporidia consistent with *E cuniculi*. The organisms were strongly Gram positive and lightly Ziehl–Neelsen acid-fast positive (see Table 2).

Postoperatively, topical anti-inflammatories were tapered over several months, and dorzolamide/timolol was eventually discontinued. On ophthalmic recheck 17 months postoperatively, the patient was visual, comfortable, normotensive and PLR positive OU. There was mild anisocoria, dyscoria and mydriasis OD, aphakia OD, pseudophakia OS, no aqueous flare OU, minimal capsular opacity and an unchanged retinal examination with numerous punctate gray lesions in the dorsal retina OU. Medications consisted of 0.1% Nevanac (OU q24h). At home, vision was reportedly very good.

**Discussion**

This case series demonstrates that intralenticular *E cuniculi* is a potential cause of cataracts, uveitis and secondary glaucoma in domestic cats in California, USA.

Although *E cuniculi* is found worldwide, feline ocular encephalitozoonosis has only been reported in Austria,16 France10 and the USA (feline cornea).12 Factors including climate and animal reservoirs may affect *E cuniculi*’s prevalence and risk to cats. Specifically, environmental spore viability varies by temperature.3 Given that encephalitozoonosis in rodents has been documented worldwide,5, 17–22 rodents likely spread disease, as corroborated by case 1 and several Austrian cases that tested positive for the mouse strain (strain II).16

Although *E cuniculi* is an opportunistic pathogen in immunocompromised people,23 the role of immunosuppression in feline ocular encephalitozoonosis remains unclear. The cases in this study were immunocompromised due to concurrent diseases (see Table 1) and immunomodulatory drugs (prednisolone and chlorambucil in case 2). This aligns with the current understanding that immunosuppression exacerbates rabbit encephalitozoonosis.4 However, in the 2011 study published by Benz et al,16 11 systemically healthy European Shorthair cats also developed cataracts and uveitis from *E cuniculi*, though 4/11 cats had positive titers for *Toxoplasma gondii* (IgG 1:4000). In the same study, 2/100 ophthalmologically healthy cats had a positive antibody titer for *E cuniculi*. Research conducted in North America,24,25 Europe16,26,27 and Asia28–30 has found that *E cuniculi* prevalence range from 0% to 26.8%, with one paper demonstrating a seroprevalence of 6.1% (18/295)30 in healthy, asymptomatic cats.

The mechanism by which *E cuniculi* causes uveitis is unknown. *E cuniculi* antigens may contribute to the inflammatory response;31 this is supported by Nell et al31 and cases 1 and 3, which suggest that focal anterior cataracts due to *E cuniculi* may be more inflammatory relative to focal cataracts due to other etiologies. Alternatively, *E cuniculi* may replicate and physically disrupt the lens, leading to lens-induced uveitis.7 In case 1, aqueous humor PCR screening failed to show any evidence of other intraocular infections and supported *E cuniculi* being the causative agent for uveitis.

Currently, phacoemulsification surgery, antiparasitic medication and symptomatic treatment are employed.
to treat intralenticular *E. cuniculi* infections. Phacoemulsification treats cataracts, removes microsporidia and minimizes further pathogen replication and intraocular inflammation. Fenbendazole, often prescribed at ranges of 20–50 mg/kg q24h for 3 weeks (extra-label), targets various pathogen stages. Symptomatic treatment often includes oral and ophthalmic anti-inflammatories to address anterior uveitis. Since systemic immunosuppression facilitates *E. cuniculi*, corticosteroids should be employed at anti-inflammatory doses. The literature and this report suggest that surgical management of intraocular *E. cuniculi* via phacoemulsification, especially early phacoemulsification, can successfully maintain vision and comfort, while medical management alone may more commonly lead to blindness, discomfort and enucleation.

Various diagnostic testing is available for *E. cuniculi* (see Table 2). Serology is a non-invasive, low-risk screening tool that is expected to be weakly or strongly positive for *E. cuniculi* in cats with intraocular *E. cuniculi*; however, PCR positivity of ocular fluid/tissues provides more definitive evidence of intraocular involvement. PCR detection of *E. cuniculi* varies based on sample location. In Benz et al, aqueous humor from 10/19 affected cats was PCR positive, whereas lens material was PCR positive in one or both eyes in 11/11 of these cats.

Histopathology with hematoxylin and eosin stains can help guide the diagnosis of *E. cuniculi*; the preferred histologic stains for *E. cuniculi* spore detection are modified trichrome and Gram stain with light microscopy and calcofluor white stain with ultraviolet light microscopy, though acid fast trichrome can be effective (see Figure 3d); in case 3, Luna stain was helpful.

When feline cataracts are identified, possible causes include chronic uveitis (most common), trauma (especially penetrating trauma), *E. cuniculi*, secondary to glaucoma or lens luxation, congenital, possibly hereditary,
Conclusions
This study highlights *E cuniculi* as a cause of feline cataracts in the USA (and likely worldwide). Study limitations include low case numbers and heterogeneous, incomplete patient data with limited follow-up. Although this series provides clinically relevant information, it does not necessarily represent optimal treatment of feline ocular *E cuniculi*. Because the literature on feline encephalitozoonosis is somewhat lacking, future studies should more thoroughly evaluate systemic involvement, pathophysiology and/or best treatment practices. *E cuniculi* should be considered in cats presenting with cataracts, especially those with concurrent anterior uveitis. The authors hope that increased awareness and testing will lead to earlier diagnosis of feline intraocular *E cuniculi* and improved clinical outcomes.

Author note Case 3 of this series was presented at a specialty conference in 2015.37

Acknowledgements The authors would like to recognize the work of Christopher M Reilly DVM, DACVP of Specialty VETPATH for his pathology expertise and work in characterizing case 3, as well as significant contributions to the manuscript. In addition, Leandro BC Teixeira DVM, DACVP (Comparative Ocular Pathology Laboratory of Wisconsin) provided histopathology expertise. Holly Hamilton DVM, DACVO primarily managed case 3 and provided valuable feedback on the manuscript. The authors thank Dr Carolyn Cray for providing valuable expert consultation in case 1 and in preparation of the manuscript. The authors thank Dr Patty Smith for her clinical assistance with case 3, Drs Lana Linton and Kristina Gronkiewicz for their support in treatment of case 2 and Dr Marcella Harb-Hauser for her clinical support with case 1. The authors would also like to thank Dr Klaas-Ole Blohm for assistance with PCR testing for case 1.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding The authors received no financial support for the research, authorship, and/or publication of this article.

Ethical approval The work described in this manuscript involved the use of non-experimental (owned or unowned) animals. Established internationally recognized high standards (‘best practice’) of veterinary clinical care for the individual patient were always followed and/or this work involved the use of cadavers. Ethical approval from a committee was therefore not specifically required for publication in *JFMS Open Reports*. Although not required, where ethical approval was still obtained it is stated in the manuscript.

Informed consent Informed consent (verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (experimental or non-experimental animals, including cadavers) for all procedure(s) undertaken (prospective or retrospective studies). For any animals or people individually identifiable within this publication, informed consent (verbal or written) for their use in the publication was obtained from the people involved.

ORCID iD Joie Lin https://orcid.org/0000-0001-7803-5121
Taemi Horikawa https://orcid.org/0000-0002-7388-0999

References
1 Bohne W, Böttcher K and Groß U. The parasitophorous vacuole of *Encephalitozoon cuniculi*: biogenesis and characteristics of the host cell-pathogen interface. *Int J Med Microbiol* 2011; 301: 395–399.
2 Ashton N, Cook C and Clegg F. Encephalitozoonosis (nosematosis) causing bilateral cataract in a rabbit. Br J Ophthalmol 1976; 60: 618–631.
3 Harcourt-Brown F. Infectious diseases of domestic rabbits. In: Harcourt-Brown F (ed). Textbook of rabbit medicine. St Louis, MO: 2002, pp 361–385.
4 Jeklova E, Leva L, Kovarcik K, et al. Experimental oral and oocural Encephalitozoon cuniculi infection in rabbits. Parasitology 2010; 137: 1749–1757.
5 Hinney B, Sak B, Joachim A, et al. More than a rabbit’s tale – Encephalitozoon spp. in wild mammals and birds. Int J Parasitol Wildl 2016; 5: 76–87.
6 Künnel F and Fisher PG. Clinical signs, diagnosis, and treatment of Encephalitozoon cuniculi infection in rabbits. Vet Clin North Am Exot Anim Pract 2018; 21: 69–82.
7 Giordano C, Weigt A, Vercelli A, et al. Immunohistochemical identification of Encephalitozoon cuniculi in phacoclastic uveitis in four rabbits. Vet Ophthalmol 2005; 8: 271–275.
8 Ozkan O, Karagoz A and Kocak N. First molecular evidence of oocural transmission of Encephalitozoonosis during the intrauterine period in rabbits. Parasitol Int 2019; 71: 1–4. DOI: 10.1016/j.parint.2019.03.006.
9 Jeklová E, Levá L, Kummer V, et al. Immunohistochemical detection of Encephalitozoon cuniculi in ocular structures of immunocompetent rabbits. Animals 2019; 9: 988. DOI: 10.3390/ani9110988.
10 Scurrell EJ, Holding E, Hopper J, et al. Bilateral lenticular Encephalitozoon cuniculi infection in a snow leopard (Panthera uncia). Vet Ophthalmol 2015; 18 Suppl 1: 143–147.
11 Nell B, Csokai J, Fuchs-Baumgartinger A, et al. Encephalitozoon cuniculi causes focal anterior cataract and uveitis in dogs. Tierarztl Prax Ausg K Kleintiere Heimtiere 2015; 43: 337–344.
12 Buyukmihci N, Bellhorn R, Hunziker J, et al. Encephalitozoon (Nosema) infection of cornea in a cat. J Am Vet Med Assoc 1977; 171: 355–357.
13 Arnesen K and Nordstoga K. Ocular encephalitozoonosis (nosematosis) in blue foxes: polyarteritis nodosa and cataract. Acta Ophthalmol 1977; 55: 641–651.
14 Bjerkås I. Brain and spinal cord lesions in encephalitozoonosis in mink. Acta Vet Scand 1990; 31: 423–432.
15 Phalen DN, Logan KS and Snowden KF. Encephalitozoon hellem infection as the cause of a unilateral chronic keratoconjunctivitis in an umbrella cockatoo (Cacatua alba). Vet Ophthalmol 2006; 9: 59–63.
16 Benz P, Maaß G, Csokai J, et al. Detection of Encephalitozoon cuniculi in the feline cataractous lens. Vet Ophthalmol 2011; 14 Suppl 1: 37–47.
17 Hofmannová L, Sak B, Jék V, et al. Lethal Encephalitozoon cuniculi genotype III infection in Steppie lemmings (Lagurus lagurus). Vet Parasitol 2014; 205: 357–360.
18 Meredith AL, Cleaveland SC, Brown J, et al. Seroprevalence of Encephalitozoon cuniculi in wild rodents, foxes and domestic cats in three sites in the United Kingdom. Transbound Emerg Dis 2015; 62: 148–156.
19 Kitz S, Grimm F, Wenger S, et al. Encephalitozoon cuniculi infection in Barbary striped grass mice (Lemmuscomys barbarus). Schweiz Arch Tierheilkd 2018; 160: 394–400.
20 Sak B, Kváč M, Kvitěnová D, et al. The first report on natural Enterocytozoon bieneusi and Encephalitozoon spp. infections in wild East-European house mice (Mus musculus musculus) and West-European house mice (M. m. domesticus) in a hybrid zone across the Czech Republic–Germany border. Vet Parasitol 2011; 178: 246–250.
21 Perek-Matysiak A, Lesnianka A, Buikowska-Gawlik K, et al. The opportunistic pathogen Encephalitozoon cuniculi in wild living Murinae and Arvicolinae in Central Europe. Eur J Protistol 2019; 69: 14–19.
22 Tsukada R, Tsuchiyama A, Sasaki M, et al. Encephalitozoon infections in Rodentia and Soricomorpha in Japan. Vet Parasitol 2013; 198: 193–196.
23 Mathis A, Weber R and Deplazes P. Zoonotic potential of the microsporidia. Clin Microbiol Rev 2005; 18: 423–445.
24 Kourgelis C, Reilly C, Von Roedern M, et al. Serological survey for antibodies to Encephalitozoon cuniculi in cats within the United States. Vet Parasitol Reg Stud Rep 2017; 9: 122–124.
25 Hsu V, Grant DC, Zajac AM, et al. Prevalence of IgG antibodies to Encephalitozoon cuniculi and Toxoplasma gondii in cats with and without chronic kidney disease from Virginia. Vet Parasitol 2011; 176: 23–26.
26 Piekar ska J, Kicia M, Wesolowska M, et al. Zoonotic microsporidia in dogs and cats in Poland. Vet Parasitol 2017; 246: 108–111.
27 Lorens B, del Aguila C and Arias C. Enterocytozoon bieneusi (Microsporidia) in faecal samples from domestic animals from Galicia, Spain. Mem Int Oswaldo Cruz 2002; 97: 941–945.
28 Jamshidi S, Tabrizi AS, Bahrami M, et al. Microsporidia in household dogs and cats in Iran; a zoonotic concern. Vet Parasitol 2012; 185: 121–123.
29 Askari Z, Mirjalali H, Mohebali M, et al. Molecular detection and identification of zoonotic Microsporidia spore in fecal samples of some animals with close-contact to human. Iran J Parasitol 2015; 10: 381–388.
30 Tsukada R, Osaka Y, Takano T, et al. Serological survey of Encephalitozoon cuniculi infection in cats in Japan. J Vet Med Sci 2016; 78: 1615–1617.
31 Wolfer J, Grahn B, Wilcock B, et al. Phacoclastic uveitis in the rabbit. Prog Vet Comp Ophthalmol 1993; 3: 92–97.
32 Addie DD, Tasker S, Bourcraut-Baralon C, et al. Encephalitozoon cuniculi infection in cats: European guidelines from the ABCD on prevention and management. J Feline Med Surg 2020; 22: 1084–1088.
33 Kotkova M, Sak B, Kvetonova D, et al. Latent microsporidiosis caused by Encephalitozoon cuniculi in immunocompetent hosts: a murine model demonstrating the ineffectiveness of the immune system and treatment with albendazole. PLoS One 2013; 8. DOI: 10.1371/journal.pone.0060941.
34 Felchle LM and Sigler RL. Phacoemulsification for the management of Encephalitozoon cuniculi-induced phacoclastic uveitis in a rabbit. Vet Ophthalmol 2002; 5: 211–215.
35 Rodríguez-Tovar LE, Villarreal-Marroquín A, Nevárez-Garza AM, et al. Histochemical study of Encephalitozoon cuniculi spores in the kidneys of naturally infected New Zealand rabbits. J Vet Diagn Investig 2019; 29: 269–277.
36 Stiles J. Feline ophthalmology. In: Gelatt KN (ed). Veterinary ophthalmology. 5th ed. Chichester: Wiley-Blackwell, 2014, pp 1477–1559.
37 Reilly CM, Hamilton HL, Cray C, et al. Naturally occurring lenticular encephalitozoonosis in a domestic cat [abstract]. Vet Ophthalmol 2015; 18: E17–E34.