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TOXOPLASMOSIS IN PALLAS' CATS (*OTOCOLOBUS FELIS MANUL*) AT THE DENVER ZOOLOGICAL GARDENS

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Abstract: In May 1996 the Denver Zoological Gardens obtained two male and two female Pallas' cats (*Otocolobus felis manul*) that were wild-caught in the Ukraine. These animals were part of a group of 16 wild-caught adults (eight male and eight female) imported to the United States and Canada between 1995 and 1996. The Denver Zoological Gardens cats were quarantined at the zoo hospital for approximately 1 mo. During the quarantine period they were immobilized for physical examination, and sera were obtained from them to evaluate for exposure to *Toxoplasma gondii*. All cats were positive for *T. gondii* antibodies by latex agglutination (titers from 1:512 to 1:1024). After being paired for breeding, one pair produced two litters, and another pair produced four litters, a total of 17 kittens between 1997 and 2001. Four kittens and two young adults died from a disseminated granulomatous and necrotizing inflammation consistent with toxoplasmosis. *Toxoplasma gondii* infection was confirmed in all six deceased cats by polymerase chain reaction performed on formalin-fixed tissues. An additional five kittens disappeared and were not available for necropsy. The fatality rate from toxoplasmosis was 35.3% (6/17) for cats that were available for necropsy and could have been as high as 64.7% (11/17) if it were assumed that the disappeared kittens were also affected. The Pallas' kitten survival rate at the Denver Zoological Gardens was 35.3%. This article describes the clinical and pathologic features of toxoplasmosis in a group of Pallas' cats at the Denver Zoological Gardens.

Key words: Pallas' cat, *Otocolobus felis manul*, *Toxoplasma gondii*, toxoplasmosis.

CASE REPORT

The Denver Zoological Gardens obtained four (two male [Ivan and Vasil] and two female [Olena and Katya]) adult, wild-caught Pallas' cats (*Otocolobus felis manul*). The cats were born in the Ukraine and were imported through Russia as part of a shipment to several North American institutions in 1996. The Denver Zoological Gardens cats were examined under sedation after 3 wk in quarantine. In addition to a physical examination, blood was collected to determine the status of *Toxoplasma gondii* infection. Latex agglutination antibody titers (LAT) to *T. gondii*, with the use of a commercial kit (Tanabe USA Inc., San Diego, California 92111, USA), for the four cats ranged from 1:512 to 1:1024 (Tables 1, 2). LAT titers of 1:32 or more are considered as evidence of *T. gondii* exposure, whereas a fourfold increase in titer over a period of 2–3 wk is considered to indicate acute infection. The results of this assay compare favorably with those of enzyme-linked immunosorbent assay for the detection of IgG using domestic cat sera.[12] The titers were most probably indicative of past exposure because the quarantine examinations were conducted within 3 wk of arrival. The cats appeared to be in good health otherwise and were subsequently relocated to a small feline building.

After release from quarantine the founder cats remained healthy except for the development of recurrent anterior uveitis in the left eye of one cat (Olena), first noted approximately 6 mo after quarantine. The first episode of anterior uveitis was clinically resolved after a subconjunctival injection of atropine sulfate (Vedco Inc., St. Joseph, Missouri 64504, USA) and an anti-inflammatory ophthalmic preparation (Celestone® Soluspan®, Schering Corporation, Kenilworth, New Jersey 07033, USA). Anterior uveitis recurred in the same eye 1 mo later, and it was treated topically with one drop of 1% atropine sulfate ophthalmic solution (Vedco), another subconjunctival injection of Celestone® Soluspan®, and clindamycin (Pharmacia & Upjohn Co., Kalamazoo, Michigan 49001, USA) dosed at 25 mg/kg i.m. q 12 hr for 7 days. Anterior uveitis was not documented again.

The cats were paired for breeding 1 yr later, and four kittens were born to one pair (Katya and Vasil) on 16 April 1997 (Table 1). A 20-day-old kitten disappeared and so was unavailable for necropsy. It is unknown if the queen cannibalized the kitten because it might have been unhealthy, possibly affected by toxoplasmosis. When 48 days old, the remaining three kittens (Pat, Stoli, and Kamchatka) were given their first neonatal evaluations and sex determination (two male and one female). At this time vaccines were administered (1 ml s.q., Fel-O-Vax® IV, Fort Dodge Lab., Fort Dodge, Iowa 50501, USA; 1 ml s.q., Imrab® 3 killed rabies vac-

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Table 1. Group, name, sex (M = male, F = female), date of birth (DOB), date of toxoplasmosis titers, and titer results for wild-caught Pallas' cats founders (Katya and Vasil) and offspring from two litters.

Group	Name/sex	DOB	Date of titer	Result
Founder	Katya/F	wild-caught	19 Jun 1996	1:1,024
			14 May 1998	1:1,024
Founder	Vasil/M	wild-caught	19 Jun 1996	1:512
			25 Mar 1998	>1:2,048
			6 Dec 1996	>1:2,048[a]
Litter 1	Pat/F	16 Apr 1997	3 Jun 1997	1:64
			3 Jul 1997	<1:32
			4 Sep 1997	>1:2,048
Litter 1	Stoli/M	16 Apr 1997	3 Jun 1997	1:32
			deceased 16 Jun 1997	
Litter 1	Kamchatka/M	16 Apr 1997	3 Jun 1997	1:32
			deceased 16 Jun 1997	
Litter 1	unnamed/?	16 Apr 1997	deceased 6 May 1997	
Litter 2	Tanya/F	20 Apr 1998	12 May 1998	1:256
			15 Jun 1998	1:128[a]
			13 Jul 1998	<1:32
			6 Apr 1999	>1:1,024
Litter 2	unnamed/?	20 Apr 1998	deceased 30 Apr 1998	

[a] IgG was evaluated for this titer to toxoplasmosis; all other samples were polyclonal titers.

Table 2. Group, name, sex (M = male, F = female), date of birth (DOB), date of toxoplasmosis titers, and titer results for wild-caught Pallas' cats founders (Olena and Ivan) and offspring from four litters.

Group	Name/sex	DOB	Date of titer	Results
Founder	Olena/F[a]	wild-caught	20 Jun 1996	1:512
			14 Jan 1997	>1:2,048
Founder	Ivan/M	wild-caught	20 Jun 1996	1:512
			14 Apr 1998	1:2,048
Litter 1	Mary/F	30 Apr 1998	25 Jun 1998	1:32
			23 Jul 1998	<1:32
			25 Oct 1999	>1:1,024
Litter 1	Marina/F	30 Apr 1998	25 Jun 1998	1:32
			23 Jul 1998	<1:32
			6 Apr 1999	>1:1,024
Litter 1	unnamed/?	30 Apr 1998	deceased 3 May 1998	
Litter 1	unnamed/?	30 Apr 1998	vanished 17 May 1998	
Litter 1	unnamed/?	30 Apr 1998	vanished 17 May 1998	
Litter 2	Rosie/F	5 May 1998	30 Jun 1999	1:256[b]
			22 Mar 2000	<1:32
Litter 3	Bela/M	16 Apr 2000	13 Jun 2000	<1:32
			21 Nov 2001	1:256
Litter 3	Karloff/M	16 Apr 2000	13 Jun 2000	<1:32
			21 Nov 2001	1:256
Litter 3	unnamed/M	16 Apr 2000	deceased 22 Apr 2000	
Litter 3	unnamed/F	16 Apr 2000	deceased 16 May 2000	
Litter 4	Chun Li/F	24 Apr 2001	11 Jul 2001	<1:32
			21 Nov 2001	<1:32

[a] This cat had two episodes of anterior uveitis on 12 Dec 1996 and 14 Jan 1997.

[b] IgG was evaluated for titer to toxoplasmosis; all other samples were polyclonal titers.

cine, Rhone Merieux Inc., Athens, Georgia 30601, USA), and the blood was collected for *T. gondii* antibody titers (Table 1). The keeper also reported during the examination that one of the male kittens (Kamchatka) had been less active and less responsive for the past 2 days. Kamchatka had a weak positive titer to *T. gondii* (1:32). It continued to decline in health and was taken the next day to the zoo hospital for evaluation. Thoracic radiographs showed a faint interstitial infiltrate. The abdomen had mildly distended large- and small-bowel intestinal loops. While under anesthesia, barium sulfate (Humco™, Texarkana, Texas 75501, USA) was administered using a gastric tube. There was no gastric emptying for 45 min. Barium was then administered directly through a tube into the colon, with no movement for 20 min. Because gastrointestinal obstruction was a consideration, an exploratory laporatomy was performed, with the only abnormality noted being an enlarged (2 cm) ileocecal lymph node. The lymph node was surgically removed and biopsied. Histopathologic evaluation demonstrated a mild, multifocal, granulomatous lymphadenitis. The next day, the kitten was taken to a veterinary ophthalmologist for the evaluation of potential visual abnormalities because it did not appear to be tracking movements in it's environment. No abnormalities were noted by the ophthalmologist. The kitten was subsequently evaluated by two veterinary neurologists during the next 48 hr and was thought to have clinical findings consistent with cortical disease. Computed tomography (CT) under isoflurane (Isoflo®, Abbott Laboratories, North Chicago, Illinois 60064, USA) anesthesia demonstrated a moth-eaten appearance in the cortex that could be compatible with encephalitis. A cerebrospinal fluid sample was obtained, and it showed normal cell counts and protein concentrations. Magnetic resonance imagery (MRI) was recommended as a diagnostic technique that might provide better detail of the brain. The kitten was sedated with 0.45 mg (0.5 mg/kg) of xylazine (Xyla-Ject®, Phoenix Pharmaceutical Inc., St. Joseph, Missouri 64506, USA) and 0.01 mg (0.005 mg/kg) atropine sulfate (Vedco) i.m. and was maintained on isoflurane administered by a face mask. It was transported on isoflurane from the zoo hospital to the University of Colorado Health Sciences Center's Department of Radiology. Anesthesia during the MRI was maintained with a propofol drip (Propoflo™, Abbott Laboratories) made up of 1.5 mg propofol/ml in normal saline and was delivered at a rate of one drop for every 3–5 sec. The results of the MRI were similar to those of the CT scan; a small hypodense area was identified in the left cerebellum and throughout the cerebrum. The hypodense areas probably represented malacia and could be associated with a nonsuppurative encephalitis. The kitten was found dead 2 days later when it was 61 days old.

Histopathology showed granulomatous and necrotizing inflammation in the liver, kidney, spleen, adrenals, and stomach. Two protozoal cysts filled with bradyzoites morphologically consistent with *T. gondii* were noted within the myocardium. Formalin-fixed, paraffin-embedded tissues were obtained for assay in a polymerase chain reaction (PCR). Using a different scalpel blade for each sample, approximately 25 mg of tissue was cut from the paraffin blocks. The samples were placed in PCR-ready 1.7-ml microcentrifuge tubes (QIAGEN Inc., Valencia, California 91355, USA), were deparaffinized, and had their DNA extracted by a commercially available kit (DNeasy Tissue Kit, QIAGEN Inc.). For an internal negative control, water was digested for every 10 samples using the tissue extraction method, minus the deparaffinizing steps. The positive control was the fresh brain tissue from a *T. gondii*–infected mouse.

PCR was performed on the DNA extractions with primers TOX4 and TOX5 as previously described, with the following modifications.[10] The 50-μl reaction mix consisted of 10 mM Tris–HCl (pH 8.3), 50 mM KCl (Perkin–Elmer Inc., Wellesley, Massachusetts 02481-4078, USA), 2.5 mM $MgCl_2$, 0.5 μM of each primer, 200 μM of each dNTP (Promega Corp., Madison, Wisconsin 53711, USA), and 2 U of gold *Taq* polymerase (Perkin–Elmer.). Amplification was performed on a Perkin–Elmer 480 thermal cycler using a time-release PCR assay protocol as follows: 95°C for 5 min, then 40 cycles of 95°C for 1 min, 55°C for 1 min, 72°C for 30 sec with an extra 1 sec added to each cycle, and a final extension of 72°C for 5 min and a 4°C hold. The amplified products (529 base pairs) were observed by electrophoresis in a 1.5% agarose gel containing ethidium bromide. *Toxoplasma gondii* DNA was amplified from several tissues.

The next day, the male sibling (Stoli) was found to be depressed and tachypneic. The kitten had radiographic evidence of pneumonia, was placed in an oxygen cage, and was started on clindamycin 25 mg/kg i.m. q 12 hr. It was found dead later that evening. Stoli had a weak positive LAT of 1:32 for toxoplasmosis. Histopathologic findings were similar to those of the previously described case, except that no organism compatible with toxoplasmosis was noted on the sections evaluated. In addition, the histopathology in this case included a marked, widespread, subacute, fibrinosuppurative, granulomatous pneumonia. PCR was performed as

described, and it amplified *T. gondii* DNA from multiple tissues.

Although there were no signs of active toxoplasmosis infection in the remaining female kitten (Pat), it was moved to the zoo hospital for hand rearing and observation when it was 62 days old. It was later transferred to another zoo, where it died at age four during an emergency ovariohysterectomy for a dystocia (Dr. William Swanson, Cincinnati Zoo & Botanical Garden, Cincinnati, Ohio 45220, USA, pers. comm.). Although no organisms compatible with toxoplasmosis were seen histologically, granulomatous encephalitis, myocarditis, hepatitis, and acute pneumonitis were observed, which were very compatible with toxoplasmosis. Perhaps the dystocia caused a recrudescence of the organisms from cysts that were acquired as a kitten.

The next year, both founder pairs produced litters; Katya and Vasil had a second litter of two kittens on 20 April 1998, and Olena and Ivan had their first litter of five kittens on 30 April 1998 (Tables 1, 2). One unsexed kitten disappeared from the Katya–Vasil litter, and three unsexed kittens disappeared from the Olena–Ivan litter. The surviving kittens (Tanya, Mary, and Marina) were moved to the zoo hospital for hand rearing when they were 18 days old (eyes just beginning to open). There were no clinical episodes compatible with toxoplasmosis for the 4 mo the kittens were at the zoo hospital. At approximately 1 yr of age, Tanya and Marina were transferred to another zoo. Six weeks after arrival and quarantine examination, Tanya developed anterior uveitis in the left eye (Della Garell, Cheyenne Mountain Zoo, Colorado Springs, Colorado 80906-5728, USA, pers. comm.). It was successfully treated with topical atropine sulfate and 1% prednisolone acetate suspension (Alcon Laboratories, Fort Worth, Texas 76134, USA) q 8 hr for 10 days and with oral clindamycin dosed at 15 mg/kg q 12 hr for 16 days. Tanya had a >1:1,024 LAT titer for toxoplasmosis on preshipment exit examination. Paired *T. gondii* IgG titers were performed at a different laboratory during the uveitis episode and were not considered supportive (less than fourfold rise) of an active infection by this laboratory (first sample 1:4,096; second sample, 2 wk later, 1:8,192).

The remaining offspring housed at the Denver Zoological Gardens (Mary) was introduced to an unrelated founder male (Vasil) in August 1999 when 15 mo old, after the founder female (Katya) was killed in an accident. Seven weeks later, Mary died after a 4-day history of anorexia and ambulatory difficulties. Radiographs taken the day before death showed a diffuse infiltrate pattern with a pleural effusion. Generally, there was a bloody pleural effusion, the lungs had multifocal yellow foci, and the visceral lymph nodes appeared enlarged and necrotic. Histopathologically, there was granulomatous and pleocellular inflammation in the brain, liver, lungs, stomach, adrenals, visceral lymph nodes, and heart that contained bradyzoite-containing cysts morphologically consistent with *T. gondii*. Multiple tissues were positive for *T. gondii* DNA by PCR, as described previously.

On 5 May 1999, Olena and Ivan had a second litter with a single female kitten (Rosie) (Table 2). This kitten was housed with the queen and did not exhibit episodes consistent with toxoplasmosis as a kitten. When 11 mo old, it presented itself to the hospital with a history of inappetence and mild ataxia. On physical examination, the most significant finding was an alveolar pattern present on radiography (Figs. 1, 2). The cat died 48 hr later despite treatment with clindamycin (25 mg/kg q 12 hr) and fluid therapy. Serum was negative for *T. gondii* antibodies by LAT. Histopathology results showed granulomatous and necrotizing inflammation. A single protozoal tissue cyst, consistent with *T. gondii*, was noted within the skeletal muscle myofiber. Several tissues were positive for *T. gondii* DNA by PCR testing, as previously described.

On 16 April 2000, Olena and Ivan produced a third litter of four kittens (Table 2). A 6-day-old male kitten was found dead, and a 30-day-old female kitten died within 24 hr of presenting with lethargy. Granulomatous and necrotizing inflammation affecting multiple organs, but no organisms consistent with *T. gondii*, was noted in the tissue sections evaluated. Several tissues were positive for *T. gondii* DNA by PCR testing. Both surviving male kittens had episodes of lethargy and apparent neurologic dysfunction (one kitten acted as if blind, and the other appeared to the keeper to be ''dull'' for approximately 24 hr). In addition, these two kittens were positive for *Giardia* cysts and were treated with 20 mg/kg p.o. q 24 hr metronidazole for 5 days and with 25 mg/kg i.m. q 24 hr clindamycin for 2 wk. Because of concerns that the stress of handling for vaccination might cause clinical toxoplasmosis, the surviving kittens were prophylactically treated with 25 mg/kg q 24 hr clindamycin a week before and a week after the second and third vaccinations at 9 and 13 wk of age.

On 24 April 2001, this same pair produced a single kitten named Chun Li (Table 2). At the suggestion of the Feline Advisory Group, we administered the oral anticoccidial agent diclazuril (not available in the United States) at 1 mg/kg q 24 hr for 7 days before and 7 days after the neonatal examinations.[19]

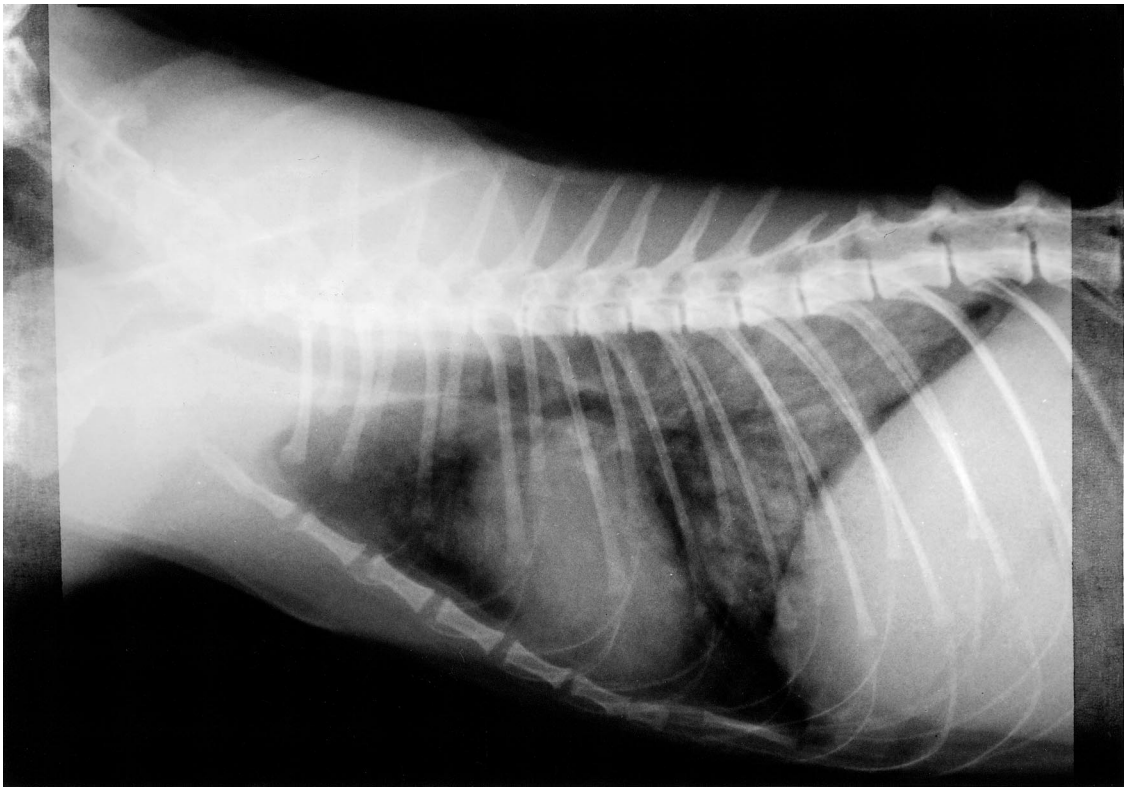

Figure 1. Right lateral radiograph of Pallas' cat, Rosie, revealing a diffuse, bilateral lung infiltrate with extensive air bronchograms, primarily in the pattern of alveolar infiltrates.

We reverted to the clindamycin prophylactic program previously described for the second and third neonatal examinations because the volume of diclazuril to be administered was too large to be given to a rapidly growing kitten. The blood was obtained at each examination for *T. gondii* evaluation. To date (1 yr of age), the kitten has not had any symptoms compatible with toxoplasmosis.

DISCUSSION

Between 1997 and 2001, 17 Pallas' kittens were born in six different litters to two pairs of wild-caught Pallas' cats at the Denver Zoological Gardens. The classical histopathologic findings[6,8] and the detection of *T. gondii* DNA in multiple tissues of the six necropsied cats established disseminated toxoplasmosis as the cause of death. The mortality rate for the kittens available for necropsy was 35.3% (6/17). Five kittens disappeared and were unavailable for necropsy. If it is assumed that the disappeared kittens were also affected by toxoplasmosis, the mortality rate will increase to 64.7% (11/17). Six kittens (two male and four female) survived, resulting in a 35.3% survival rate (6/17).

Toxoplasma gondii is an obligate intracellular coccidian.[7] Domestic cats and probably other members of the family Felidae are the definitive hosts for the organism and shed oocysts in feces.[7] The primary routes of transmission are ingestion of sporulated oocysts in contaminated food or water and ingestion of tissue cysts in undercooked meat.[7] Toxoplasmosis is of zoonotic concern, but proper hand-washing hygiene after handling cat feces samples and uncooked meat products is thought to reduce the risk of acquiring *T. gondii* infection.[7]

Transplacental or lactational transmission also occurs in some cases of domestic cat and can result in subclinical or clinical infections in kittens.[9,13–15,17] In the Pallas' cats described here, there is evidence for both transplacental and lactational transmissions and for transmission in the postnatal period by ingestion of tissue cysts or oocysts. It appears likely that the founder cats were all infected before arrival because of the presence of antibodies in serum, which were unlikely to have developed during the 3-wk time period between arrival and testing. Additionally, the cats were housed in isolation and fed a commercially produced exotic feline diet during

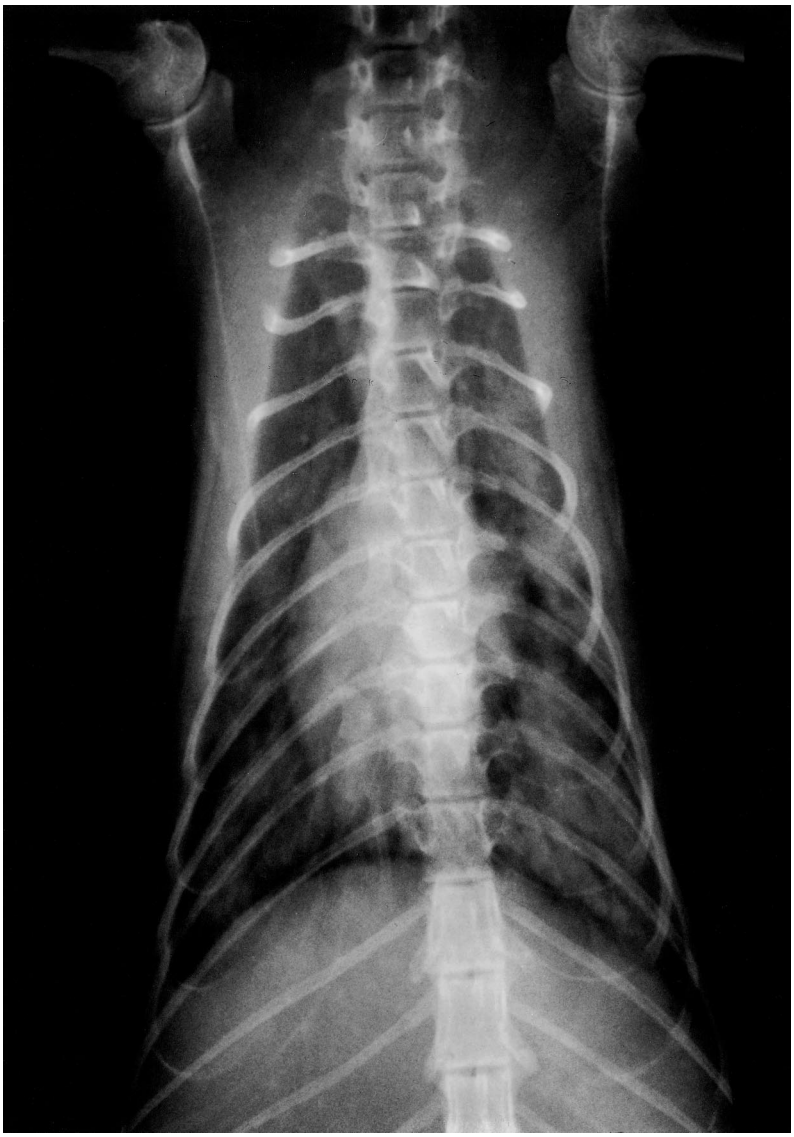

Figure 2. Ventrodorsal radiograph of Pallas' cat, Rosie, revealing a diffuse, bilateral lung infiltrate with extensive air bronchograms, primarily in the pattern of alveolar infiltrates.

the initial testing period. The four kittens that died from toxoplasmosis when they were between 1 and 8 wk of age were probably infected transplacentally or lactationally as a result of limited to no access to *T. gondii* in the environment because the kittens were either not weaned or had not been out of the building. There have been other reports of toxoplasmosis being likely acquired transplacentally in Pallas' cats. A stillborn Pallas' kitten from a pair originating from the same 1996 import group as the Denver Zoological Gardens founder cats was found to have multiorgan inflammatory lesions with an intralesional protozoan consistent with *T. gondii* (Drs. Mark Campell and Philip Long, Cincinnati Zoo & Botanical Garden, Cincinnati, Ohio 45220, USA, pers. comm.). The transmission in this case could only have occurred transplacentally. In a separate report, one Pallas' cat either aborted or resorbed several fetuses, and another produced a litter of two kittens that died from toxoplasmosis at 6 wk of age.[16] The infection occurred transplacentally or lactationally, or through infection of pigeons that were trapped at the zoo.

If the kittens described here were infected trans-

placentally or lactationally through chronically infected queens, it would be notable. In humans, transplacental infection of the fetus through seropositive mothers usually does not occur.[2] Most experimental studies on transplacental or lactational infection have used *T. gondii*–naive queens, and so little is known about transplacental or lactational transmission by the previously infected queen.[10,16,18] The source of *T. gondii* resulting in the death of the two adult Pallas' cats described here cannot be definitely determined.

Five kittens had detectable low levels of serum antibodies between 2 and 8 wk of age, which at a later age became undetectable (Pat, Tanya, Mary, Marina, and Rosie; Tables 1, 2). Antibodies detected at 2–8 wk of age were likely maternally derived because seropositivity was not maintained. These kittens were likely *T. gondii* naive for the first several months of their life. Four of the five kittens (Pat, Tanya, Mary, and Marina) later developed high serum antibody levels indicative of past exposure or asymptomatic infection. The fifth kitten (Rosie; Table 2) had an acute episode of ataxia and alveolar lung disease in the face of a negative antibody titer, suggesting acute infection rather than exacerbation of chronic infection due to stress. The antibody titer patterns of Mary (Table 2) also suggested maternal transfer of antibodies that waned with time followed by exposure sometime in the postnatal period. Whether Mary had an overwhelming primary infection just before death or whether the stress associated with being introduced to a new male activated chronic toxoplasmosis cannot be determined because there was an interval of a year between the antibody titers. There were no other obvious medical problems in these two cats, emphasizing that even healthy adult Pallas' cats appear to be susceptible to fatal toxoplasmosis. Additionally, fatal toxoplasmosis was reported in a 6-yr-old captive Pallas' cat at another zoological institution.[5] But none of the adults and not all the kittens exposed to *T. gondii* died, evidence that not all Pallas' cats exposed to *T. gondii* die of toxoplasmosis. None of the four seropositive founder cats developed fatal toxoplasmosis, and three kittens (Marina, Tanya, and Pat) had antibody patterns consistent with postnatal infection but did not die while at the Denver Zoo. As mentioned previously, Pat died at another institution (during surgery for dystocia), presumably from toxoplasmosis. Tissue PCR DNA testing for toxoplasmosis will be performed at a future date and will hopefully confirm the diagnosis.

Fatal toxoplasmosis usually results from replication of the organism in the tissues, resulting in granulomatous inflammation and necrosis. Lesions are most common in the lungs, liver, heart, spleen, pancreas, and mesenteric lymph nodes.[8,14] Histopathologic results from the cats described here are consistent with those previously described for disseminated toxoplasmosis. Because of severity of inflammation, organisms are not always detected in tissues histologically by the use of hemotoxylin and eosin stain. All living affected Pallas' cats that were radiographed at the Denver Zoological Gardens had a radiographic alveolar infiltrate pattern. There are other tissue protozoans that infect cats, but in the cases described here, PCR amplification of toxoplasmal DNA was used to confirm the diagnosis of toxoplasmosis.[4]

In domestic cats, clinical illness that does not result in death has been described.[11] Some of the most common clinical manifestations are fever, anterior uveitis, retinochoroiditis, hyperesthesia attributed to muscle pain, and neurologic dysfunction. Lethargy and neurologic dysfunction were present in several Pallas' cats described here. In addition, recurrent anterior uveitis clinically similar to that induced by *T. gondii* was detected in one of the seropositive founder females and was reported in a 1-yr-old seropositive female that recently had been transferred to another institution. Some Pallas' cats described here were seropositive for *T. gondii* antibodies but were clinically normal, suggesting subclinical infection. The results of this study document that there are many similarities associated with *T. gondii* infection between Pallas' cats and domestic cats.

Currently, treatment for clinical toxoplasmosis in domestic cats consists of supportive care and antibiotics. To our knowledge, there are no antibiotics that are completely effective in clearing the body of tissue cysts.[7] Clindamycin has been prescribed most frequently with a variety of dosing regimens. The drug is currently used at 10–12 mg/kg q 12 hr for a minimum of 4 wk.[7,11] Most cats with acute disseminated toxoplasmosis die in spite of antibiotic therapy.[3] It appears that the same finding is true for Pallas' cats because none of the four acutely ill kittens or cats described here that were treated with clindamycin survived. In one study of acutely infected domestic research cats, clindamycin therapy was associated with increased mortality; in this case, *T. gondii* infection was induced by intracarotid injection.[1] There have been multiple reports of the successful use of clindamycin in the management of domestic cats with more chronic toxoplasmosis, particularly those with fever and uveitis.[7,11] In the cats described here, it is possible that clindamycin therapy was beneficial in the two surviving kittens from the 2,000 litters, which experienced brief periods of lethargy and neurologic dysfunction, and in both adult cats treated for anterior uveitis.

A February 1999 survey sent to the institutions that received the 16 wild-caught founder Pallas'

cats revealed that 13 of the 16 (81.25%) deceased kittens that were available for necropsy were suspected to have died from toxoplasmosis.[18] It is apparent that fatal disseminated toxoplasmosis is a limiting factor in the successful propagation of this species in captivity. But it is currently unknown why this species has such a high mortality rate for toxoplasmosis compared with other felids. Because *T. gondii* has a worldwide distribution, it seems unlikely that the Pallas' cat is a naive felid species for this organism. But the toxoplasmosis status for free-ranging adult Pallas' cats and the level of toxoplasmosis mortality in free-ranging kittens are unknown. During periods of stress, *T. gondii* tissue cysts may rupture, and the replication of released organisms can cause clinical disease.[7] It is possible that *T. gondii*–associated disease is exacerbated in captivity during periods of stress, i.e., weaning, examinations, vaccinations, and breeding activity.

CONCLUSIONS

The Denver Zoological Gardens experienced high morbidity and mortality from toxoplasmosis in the offspring of recently imported, wild-caught Pallas' cats. The Denver Zoo kittens consistently demonstrated radiographic evidence of diffuse, bilateral, alveolar infiltrates and air bronchograms. Unfortunately, these signs were also associated with high mortality despite treatment. High mortality from toxoplasmosis in Pallas' cats has also been reported by several other institutions. Because domestic and many exotic cats are recognized as the definitive hosts for this parasite, it is unclear why Pallas' cats are afflicted with such high morbidity and mortality. A better understanding of this disease, as it affects Pallas' cats, will be needed for captive management and treatment of clinical disease. The felid TAG has been pursuing some research projects in this vein. Toxoplasmosis currently presents a serious impediment to the successful reproduction of Pallas' cats in captivity.

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