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Features

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Encephalitozoon cuniculi-Associated Phacoclastic Uveitis in the Rabbit: A Review

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In 1993, Wolfer et al[1] diagnosed spontaneous lens capsule rupture and resultant phacoclastic uveitis (lens rupture uveitis) in eight dwarf rabbits. On histopathology, the lenses of six of the eight dwarf rabbits contained intralenticular organisms interpreted to be *Encephalitozoon cuniculi*, a microsporidian parasite. Case reports since 1993 have described phacoclastic uveitis due to *E. cuniculi* in young (<2 years of age) dwarf rabbits (with no apparent sex predilection) without a history of ocular trauma.[2–5] Meyer-Breckwoldt[6] reviewed case histories of 200 pet dwarf rabbits brought to the Small Animal Clinic of the Hannover Veterinary School, Germany, in 1995 and 1996. She found 84 rabbits (42%) had antibodies to *E. cuniculi*, and 50 (25%) had various disorders, while the remaining rabbits were healthy. Eighteen positive rabbits (43%) showed torticollis and ataxia characteristic of encephalitozoonosis. All of the rabbits in the control group of 100 were seronegative. Ewringmann and Gobel[7] tested 227 pet rabbits brought to the Berlin Veterinary School Small Animal Clinic for *E. cuniculi*. Of these rabbits, 125 (45%) had a positive antibody titer, and 152 (55%) were seronegative. They found that 51 seropositive rabbits (41%) had clinical signs of encephalitozoonosis: 23 (45%) had central nervous system (CNS) disorders, 16 (31%) had kidney failure, seven (14%) had phacoclastic uveitis, and three (6%), with both CNS and renal disorders, had phacoclastic uveitis.

We now know that *E. cuniculi* infection (even subclinical infection) produces hyperimmune sera to the parasite that persists for approximately 7 years, and it also induces foreign body inflammatory responses to implanted biomaterials. Recent studies by Sobottka et al[8] showed that SC immunization with *E. cuniculi* can generate highly active rabbit hyperimmune sera. They found during a 3-year follow-up of experimentally *E. cuniculi*-immunized rabbits that the decay curves for antibody titers against the parasite (when fitted using mathematical modeling) resulted in a predicted duration for specific immune responses of 7 years. In 1988, Ansbacher et al[9] found that *E. cuniculi* infection of rabbits altered their response to neural device biomaterials (i.e., brain-implanted platinum wires coated with various polymers). Normally we would not expect to see a reaction to the neural device biomaterials but in *E. cuniculi* seropositive rabbits, these researchers found edema, neuronal and glial reactions, and inflammatory responses to the coated wires at all implant sites in the brain.

What we do not know is why phacoclastic uveitis develops predominantly in young dwarf rabbits with *E. cuniculi* when we rarely see it in other rabbits, despite a high seropositive incidence in nonlaboratory rabbits. In two important but unrecognized papers, Kunstyr et al[10,11] examined non-dwarf and dwarf strains of rabbits showing a common clinical sign of either head tilt

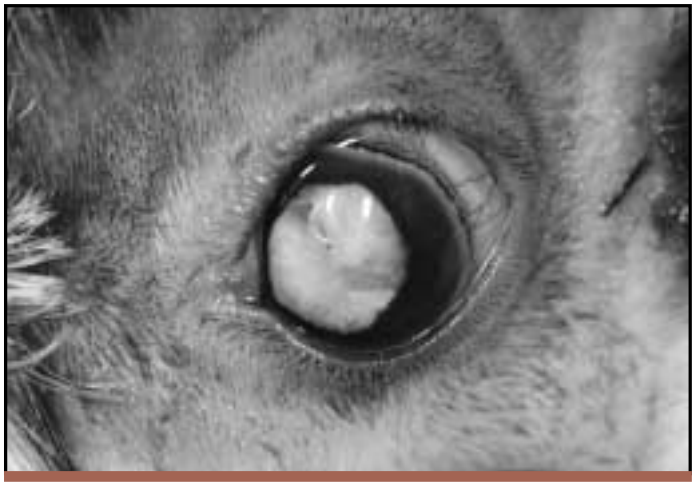

Figure 1. Ocular appearance of mature phacoclastic uveitis and cataract in a rabbit. (Courtesy of John Sapienza, DVM, DACVO, Plainview, New York)

or torticollis. With one exception, they found all the nondwarf rabbits had otitis and empyema of either one or both middle ears. They isolated *Pasteurella multocida* from pus and from the nose of all but one of these rabbits and on occasion also isolated it from the brain. By contrast, they confirmed the presence of *E. cuniculi* both histologically and serologically in all the dwarf rabbits, proving that it did not affect the ears of the animals but the CNS instead. They assumed that the different exposure to both agents, rather than the susceptibility, was responsible for the differences found between the two types of rabbits.

Pathologists frequently report encephalitozoonosis in rabbits as an incidental finding at necropsy. Granulomatous encephalitis and renal lesions are typical microscopic findings. There are no predilection sites, and lesions occur in all areas of the brain, most often with a perivascular and periventricular distribution. Although many rabbits infected with *E. cuniculi* are asymptomatic, clinicians have occasionally reported neurologic signs including convulsions, tremors, torticollis, paresis, and coma.[12] Feaga[13] examined ten rabbits with wryneck and found that nine had encephalitis. He identified lesions, including small granulomas consistent with encephalitozoonosis, in seven of the nine rabbits. He compared this group with ten control rabbits and found nine rabbits had no histologic evidence of encephalitic granulomas. Feaga suggested that wryneck is an inflammatory reaction caused by rupture of the brain cells from multiplying *E. cuniculi*.

The incidence of reported phacoclastic uveitis in rabbits has a similar distribution of age and breed that Kunstyr et al saw in rabbits showing head tilt or torticollis. The ocular lesion in phacoclastic uveitis appears as a white, sometimes fluffy mass in the anterior chamber of the eye. On biomicroscopic examination, the mass originates at the lens capsule, and the inflammation is centered on the break in the capsule. The lesion occurs after rupture of the lens capsule releases lens protein into the anterior chamber, resulting in granulomatous uveitis. The posterior segment of the eye (i.e., vitreous, retina, choroid) is unaffected.

Whether we can treat phacoclastic uveitis is controversial. Treatment involves phacoemulsification to remove the lens and granuloma, or enucleation of the eye.[4,14,15] However, phacoemulsification is difficult to perform due to the granulomatous nature of infection. Without treatment, most affected eyes become phthisical (atrophied) and require enucleation. Rabbits, like rodents, have an extensive orbital venous plexus, and severe hemorrhage during the procedure is a possible complication, making enucleation of the eye more difficult when compared with species such as the dog.

If the phacoclastic uveitis lesion is mild, topical corticosteroids (e.g., Pred Forte, Allergan) and long-term oral dosing with albendazole may be effective. Fenbendazole is effective in preventing experimental infection of *E. cuniculi* and for eliminating the spores from the CNS of naturally infected rabbits. Suter et al[16] gave fenbendazole (20 mg/kg daily) for 7 days before they experimentally infected rabbits with *E. cuniculi* and continued the fenbendazole for 2 or 21 days after infection. They found fenbendazole was effective in preventing the establishment of the parasites. In addition, in naturally infected, seropositive rabbits, they successfully isolated *E. cuniculi* from seven of nine untreated animals but not from the brain tissue of eight animals treated with fenbendazole-medicated pellets for 4 weeks. Dosing with albendazole is also controversial, and scientists have not clearly established the effectiveness of treatment.[17,18] In experimental rabbits given albendazole and infected with *E. cuniculi*, all albendazole-treated rabbits (100%) were seronegative 7 days after infection, while 43% of the control rabbits (no albendazole) were seropositive. On day 21 postinfection, all the control rabbits (100%) were positive, while 43% of the albendazole-treated rabbits were seropositive. All the control rabbits remained positive until the end of the experiment on day 120. The researchers observed an increase in the number of positive animals in the albendazole-treated group on day 21. The number of seropositive rabbits increased until day 60 and culminated at 71%, after which it started to fall gradually to 57%. In summary, these researchers concluded that albendazole gives some protection against *E. cuniculi* infection compared with rabbits not treated with albendazole.

The author believes treatment with an antiprotozoal agent such as fenbendazole or albendazole is critical even with enucleation because affected rabbits most likely have *E. cuniculi* in the brain and are at risk of developing encephalitis. Stiles et al[4] successfully used phacoemulsification to remove an *E. cuniculi*-positive lens and granuloma in a 5-month-old rabbit. Four months after surgery there was recurrence of a granuloma in the anterior chamber. They treated the rabbit with oral albendazole (30 mg/kg PO daily for 30 days, then 15 mg/kg PO daily for another 30 days) and daily topical prednisolone on the affected eye. Over 8 weeks the granuloma gradually resolved. The

author always treats young *E. cuniculi*-seropositive dwarf rabbits with fenbendazole (20 mg/kg daily) for up to 8 weeks whether the animals have clinical signs or ocular lesions. The author recommends the same treatment regimen in any rabbit with phacoclastic uveitis and also recommends phacoemulsification. If the owner cannot afford or does not want phacoemulsification, clinicians may attempt to treat the eye topically with corticosteroids and recommend regular follow-ups to monitor the uveitis. Topical treatment nearly always results in the same outcome—atrophy of the eye. Consulting ophthalmologists have said that if the phacoclastic uveitis is detected early and immediate topical treatment and oral fenbendazole is initiated, the eye may be saved.

Other veterinarians have reported success with different treatments. Ewringmann and Gobel[7] treated 20 *E. cuniculi*-seropositive rabbits with CNS symptoms with oxytetracycline, dexamethasone, vitamin B, and infusions. Eleven rabbits (55%) showed complete recovery, and five (25%) showed an improvement of clinical signs. They also treated seven rabbits with phacoclastic uveitis with oxytetracycline and dexamethasone parenterally and topical ocular tetracycline and dexamethasone ointment and found that signs of ocular inflammation disappeared after this therapy. Feaga[13] had good success treating rabbits with *E. cuniculi* encephalitis with prednisolone (11 mg/kg IM). Felchle and Sigler[14] gave no antiprotozoal medication but used only phacoemulsification to treat a New Zealand white rabbit with slowly progressive unilateral phacoclastic uveitis and cataract formation due to *E. cuniculi* (positive PCR on collected irrigating solution with lenticular contents). More than 1 year following surgical therapy, they found the rabbit could see and was comfortable without medication.

The author recommends treating with topical ophthalmic corticosteroids on a case-by-case basis depending on the severity of the clinical signs and the response of the rabbit to initial antiprotozoal therapy. The author will follow up with fenbendazole after phacoemulsification and/or topical ocular treatment.

SUMMARY

Phacoclastic uveitis is a recently recognized disease of rabbits, particularly dwarf rabbits, with no apparent sex predilection but a propensity to affect younger individuals. Pasteurella granulomas in the iris can mimic *Encephalitozoon* phacoclastic uveitis. Serum ELISA antibody titers against *E. cuniculi* and *P. multocida* are useful in distinguishing the two diseases. At present, serum samples must be sent to the United States or Europe.

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A Message From the President

The AEMV officers and past president Michael Dutton have been busy creating *Exotic Mammal Medicine and Surgery*, which you now hold in your hand. Our goal is to provide you with usable and interesting information on small exotic mammals. We've scanned the available literature looking for articles that would be of interest to the practitioner working with small mammals.

Our short-term plans are to provide readers with abstracts from the scientific literature that pertain to exotic mammals. It's amazing what's out there! This issue contains abstracts of articles from *Lab Animal*, *Comparative Medicine*, *Veterinary Pathology*, the *American Journal of Veterinary Research*, and others. We also have included a book review, a species natural history piece, and an overview of ocular *Encephalitozoon cuniculi* in rabbits.

Our long-term goal is to add original scientific papers, research results, and original case reports to the above format. ***Submission guidelines can be found on the AEMV Web site at* www.aemv.org.** ***We encourage members or other interested veterinarians to submit something of interest.***

The AEMV has also been active in organizing "First Step" in association with the International Conference for Exotics. This half-day seminar serves as an introduction to exotic mammal medicine. Our plan is to expand the content and length of this pre-ICE continuing education opportunity in 2004.

I want to thank all the officers for their support, hard work, and enthusiasm. Special thanks go to Michael Dutton for his commitment to this publication, both in its development and long-term design. I am also very grateful to all the AEMV members who have volunteered their time to write abstracts or have made other contributions. The active support of our membership is very welcome, so be sure to let us know if you want to get involved.

Please contact me (peter.g.fisher@verizon.net) with any comments, suggestions, questions, or concerns. Our profession and the welfare of small exotic mammals will only continue to advance through the exchange of information and member camaraderie.

Peter G. Fisher, DVM
President, AEMV

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Lab Animal magazine, which is free in the United States, has just increased its U.S. circulation to 11,000 issues every month. Right now is the very best time for AEMV members to go to the *Lab Animal* Web site and fill in the online subscription request to receive the journal. Follow these instructions to get your free subscription!

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The IVIS Web site provides a convenient way to access information on veterinary medicine and is offered as a free service to clinicians, researchers, librarians, educators, and veterinary students.

Check out the Veterinary Librarian Citation Database

The Veterinary Librarian Citation Database has been valued by animal health professionals since 1989 and has grown on all levels. The entire database now covers more than 60,000 citations with about 5,000 new additions each year. Many private practitioners, institutions, and zoos worldwide use the program to save time and improve the quality of the animal health care they deliver. To enable veterinary specialists to only focus on articles within their specialty, they provide five species groupings: Zoo Package (comprehensive), Small Animal, Equine, Avian/Exotic, and Food Animal. The database is updated twice each year. Users have the following update options:

- One-time-only purchase
- Twice each year
- Once per year

Each update CD contains all previous information plus any additional citations that have been added. Each species grouping is approximately 20 MB in size, except the Zoo Package, which is approximately 120 MB.

Marty Page, publisher of the *Veterinary Journal* Index, is offering AEMV members a discount on the initial purchase of the Avian/Exotic software package that allows access to the citation database. The package is available to AEMV members for $95 (normally $145) and can be returned for a full refund if it does not meet your expectations. This package can be a real time saver when doing a literature search—check it out at **www.vjindex.com**!

Natural History of the Rabbit (*Oryctolagus cuniculus*)

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ORIGIN AND DOMESTICATION

During the last ice age, the geographic distribution of the Old World rabbit was limited to what are now Spain, Portugal, and northwest Africa. Today, humans have introduced rabbits to nearly every part of the globe. Rabbits belong to the order of Lagomorpha; this order consists of two families, which contain 13 genera and 69 species. The rabbit is a member of the Leporidae family, which includes 11 genera and 47 species. The species of *Oryctolagus cuniculus* is the only species of the genus *Oryctolagus*. The Phoenicians arrived on the Iberian Peninsula about 3,000 years ago and, having noticed the abundance of rabbits, called the area "the land of the rabbit," from which the words *Hispania* and consequently *Spain* evolved. The Romans can be credited with introducing rabbits outside of the western Mediterranean area. They valued rabbits for their meat, and domestication of the rabbit is thought to have started during the Roman Empire. Special rabbit gardens or *leporata* were constructed and maintained to ensure a good meat harvest. Further documentation of the rabbit's role in society is available through study of 16th-century art, literature, and society. Elizabeth I and Henry IV had large, enclosed gardens dedicated solely to rabbit hunting as a social event. A work of art on exhibit at the Louvre, *Madonna and Child With St. Catherine and a Rabbit,* was painted by Titian around 1530 and shows a pure white rabbit in the center of the composition. The fact that the rabbit is completely white suggests that different breeds were already present in the mid 1500s. However, significant breeding success in rabbits has only been achieved since the start of the 19th century, and today the American Rabbit Breeder Association officially recognizes 42 breeds. One of the newest additions to this list is the mini rex, recognized as a distinct breed in 1990. The domestic rabbit of today bears little physical resemblance to its original wild ancestor.

HABITAT AND BEHAVIOR

Today, wild rabbits and their relatives, hares and pikas, can be found in a variety of environments: deserts, forests, and even the tundra. They usually prefer a substrate ideal for digging, such as sandy soil, but some species are at home in a marsh or swamp. Rabbits can be found at elevations of up to 5,000 meters above sea level, with the range of the pika reaching up to 6,000 meters above sea level. The burrow systems dug by the rabbit can be complex structures, reaching dimensions of up to 3 meters in depth and 45 meters in length.

Rabbits are very social (gregarious) and territorial animals. They usually live in groups of six to eight with a strict social hierarchy. This social structure is extremely important for the males, as it determines which male will have access to mate the females. Juvenile males will be driven out of the group and have to establish or join another warren. Males mark their territory with scent glands located under the chin and in the genital area, or by urine spraying. Rabbits spend most of the day in their burrows and come out to eat during the early evening and morning hours. As is typical in prey species, they are always alert to their surroundings and will alarm others if they perceive danger. Sometimes a vocal warning will be uttered, or more commonly the rabbit will stomp the ground with its hind feet to serve as a warning to other rabbits. The size of the rabbit's home range and the social group is usually determined by the abundance of food in the area. In general, the range for the males is larger than females and can be up to 50 acres.

RABBITS AND MYTHOLOGY

Rabbits are usually associated in mythology with the moon and the cycle of life and death. This is probably due to their very prolific nature as well as their nocturnal behavior. In China, the rabbit is a symbol of longevity and reproductive power. People thought female rabbits became pregnant by looking at the moon. The Easter bunny myth is probably derived from the medieval belief that the rabbit ushered in the dawn and was a creator of life. This originated from the Anglo-Saxon moon goddess Eostre (Easter) who was portrayed with a rabbit's head, symbolizing springtime and the renewal of a new moon.

In Christianity, the rabbit was considered the personification of timidity, lust, and promiscuity. In Titian's previously mentioned painting, the rabbit is placed at the feet of the Madonna and symbolizes moral triumph over more basic instincts. As well, the rabbit often assumes the role of the trickster, able to fool those who wish it harm.

The ancient Britons were forbidden to eat rabbits and used them in divination, using their actions, feeding patterns, and sometimes their entrails to predict the future. As a good omen, the Britons released a rabbit before battle.

From ancient times rabbits have been intimately associated with human society and continue to provide a lasting interest through their fascinating habits and behaviors.

SUGGESTED READING

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The Exotic Guidebook: Exotic Companion Animal Procedures

By Lucy Bartlett and Teresa Lightfoot
Published by Zoological Education Network

The Exotic Guidebook: Exotic Companion Animal Procedures is compact and presented in a sturdy two-ring binder. Sections can be arranged as desired, and the thick card-style pages open to lay flat, facilitating easy reference during surgery. Each section presents common surgeries for a particular species, and sections are color coded for easy reference. The initial offering includes common ferret, guinea pig, prairie dog, and rabbit surgeries. The *Guidebook* is designed to easily accommodate additional species and procedures as they become available.

ON THE PLUS SIDE

The concept of an all-in-one illustrated guide to the more common exotic animal surgeries is an attraction in itself. Information included goes far beyond simple step-by-step instructions for procedures such as small mammal castration and ferret adrenalectomy. Guidelines for presurgical patient evaluation are thorough and include suggestions for selection of surgical instruments and suture materials. Guidelines for administration of preanesthetic drugs and induction of anesthesia are discussed for each species covered. A generous number of photographic illustrations accompany the text and nicely demonstrate such things as the proper administration of an intramuscular injection to the guinea pig. I found the section on evaluation of the ferret with adrenal or pancreatic neoplasia to be exceptionally informative.

The "Surgical Steps" sections begin with the location of the initial incision site and conclude with the selection of suture type and pattern for surgical closure. In between, the surgical procedures are described step-by-step in great detail, and photographic illustrations accompany the detailed surgical description.

Each surgical description concludes with a section on postoperative considerations. Many of these are of critical importance and have not always been emphasized in previous descriptions of exotic surgical procedures. Prime examples include the importance of a rapid return to eating post-surgery for prevention of herbivorous gastrointestinal stasis and postoperative pain control. Of less importance, but certainly of great concern to practitioners new to these species, are informational gems such as the occurrence of postoperative abdominal skin bruising following ferret celiotomy. Each section contains similar valuable hints, tricks, and suggestions accumulated over years of the authors' experience with these species.

ON THE MINUS SIDE

While most surgical photographic images are excellent, a few defy rapid comprehension. Several would have benefited dramatically from side-by-side line drawings to help newcomers distinguish between similarly appearing tissues. Recommendations for diagnosis of insulinoma in the ferret are a bit of an enigma. Blood glucose below 70 mg/dl is considered to suggest insulinoma, while 90 to 120 mg/dl is normal. The inexperienced practitioner is given no suggestions as to what to do with those pesky ferrets with blood glucose between 70 and 90 mg/dl.

As thorough as the sections on exotics anesthesia are, it is a bit surprising no mention is given to anesthetic monitoring. While this is obviously not the primary duty of the surgeon, the *Guidebook* is geared toward veterinarians who are new to exotic animal surgeries, and guidelines for this critical aspect would have been of great benefit. Along those lines, conspicuously absent are recommendations for maintenance of intraoperative body heat for those species discussed other than the rabbit.

ADD TO THE BOOKSHELF

The Exotic Guidebook is a worthy addition for all practitioners who regularly perform or expect to perform exotic animal surgeries. While experienced practitioners may not find a lot of new information in the *Guidebook*, it is an excellent reference to have on hand for visiting veterinary students and veterinary technicians as they help prepare patients for surgery. Many portions can even be used when discussing surgical options with clients considering surgery for their exotic pets. Future offerings of surgical procedures for additional exotic pets will only increase the value of the *Guidebook*.

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Selected Abstracts on Exotic Mammal Medicine and Surgery

Hepatobiliary Inflammation, Neoplasia, and Argyrophilic Bacteria in a Ferret Colony

Garcia A, Erdman SE, Xu S, et al: *Vet Pathol* 39(2):173–179, 2002.

ABSTRACT

Eight genetically unrelated pet domestic ferrets *(Mustela putorius furo)* from a colony of 34 were diagnosed with hepatobiliary disease over a 7-year period. Affected ferrets ranged from 5 to 8 years of age and included two neutered males and six spayed females. The primary initial complaint was weight loss but affected ferrets also exhibited anorexia, lethargy, and diarrhea.

All 34 ferrets in the colony were negative for Aleutian disease virus (ADV) by counterimmunoelectrophoresis (CIEP) and polymerase chain reaction (PCR). Aleutian disease in ferrets can cause bile duct hyperplasia, periportal fibrosis, and hepatitis. PCR analysis of fecal bacterial isolates from one ferret generated a sequence isolate with 98% similarity to *Helicobacter cholecystus* and 97% similarity to *Helicobacter* sp strain 266-11. PCR also amplified an isolate of *Campylobacter mucosalis* from one affected ferret that had hepatic cystadenoma. All eight ferrets had chronic cholangiohepatitis and biliary hyperplasia. Two ferrets had cholangiocellular cystadenoma and two had cholangiocellular carcinoma. One ferret also had multicentric lymphoblastic lymphoma with hepatic involvement. Curved or spiral-shaped organisms (argyrophilic bacteria) were identified in liver samples of three ferrets by silver stain, including both ferrets with carcinoma.

The authors proposed that the clustering of lesions in this colony suggested an infectious agent. The hepatic lesions observed in these ferrets were similar to those in mice infected with *Helicobacter hepaticus* and a novel *Helicobacter* sp. Hepatocellular neoplasms and hemangiosarcomas were observed in infected mice. Neoplastic transformation of chronic infectious and/or inflammatory hepatic disease documented in other mammalian species, including humans, was discussed.

COMMENTARY

Liver disease is common in middle-aged to older ferrets and has been linked to infectious agents, toxins, inappropriate nutrition, and metabolic conditions. The authors did not report any results (liver or fecal bacterial isolates or histopathology) on clinically unaffected ferrets, and the population studied was too small to draw definitive conclusions. Concurrent disease, such as* Campylobacter *and lymphoma, might also have played a role.

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Seven Cases of Vaccination Site Fibrosarcomas in Ferrets

Munday J, Richey L, Stedman NL: *Vet Pathol* 39:5, 2002.

ABSTRACT

Ten ferrets were diagnosed with cutaneous fibrosarcomas at the University of Georgia over a 6-year period. Seven of these tumors were located in vaccination sites (interscapular, dorsal thorax, neck area) and three were elsewhere (ventral abdomen, base of tail, paw). Five of the seven ferrets with vaccination site fibrosarcomas were given canine distemper and rabies vaccines in the preceding 12 months. The vaccination history of the other two ferrets was unknown.

Histologically, all the vaccination site fibrosarcomas were well demarcated and were located in the hypodermis, adjacent to the panniculus muscle. There was a mild to moderate lymphoplasmacytic inflammation with peripheral lymphoid aggregates in five of the seven tumors, and four of the tumors also contained rare to numerous giant cells. There was intracellular basophilic granular material present in two of the neoplasms. Immunohistochemistry demonstrated muscle cytoskeletal proteins in four of the seven vaccination site fibrosarcomas. The three non-vaccination site fibrosarcomas did not contain muscle proteins and did not have basophilic material, giant cells, or lymphoplasmacytic inflammation. In feline vaccine-induced sarcomas, intratumoral lymphoplasmacytic inflammation, giant cells, intracellular basophilic material, and myoblast differentiation are reported features. The high proportion of vaccination site fibrosarcomas observed in this study suggests a relationship between vaccinations and the development of fibrosarcomas in the ferret.

COMMENTARY

Vaccine-induced fibrosarcomas have not been previously diagnosed in nonfeline species and should be considered rare in the ferret. As the number of ferrets seen in clinical practice

increases, there may be a corresponding increase in vaccination site reactions. At this time, the benefits of vaccination in the ferret exceed the risk of vaccine-associated sarcoma; however, it would be prudent to separate and document vaccination sites as a preventive measure.

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Evaluation of Fentanyl Transdermal Patches in Rabbits: Blood Concentrations and Physiologic Response

Foley PL, Henderson AL, Bissonette EA, et al: *Comp Med* 51(3):239–244, 2001.

ABSTRACT

Fentanyl is a synthetic opioid with predominately mμ receptor agonistic activity. Transdermal fentanyl patches (TFP) (Duragesic, Janssen Pharmaceutica) are available in 25, 50, 75, and 100 μg/hour strengths, which continuously release fentanyl over a 72-hour period. Two studies were carried out using 25-μg TFP on adult, intact New Zealand white rabbits, and the ability to attain plasma fentanyl concentrations associated with analgesia was evaluated. The study also assessed the drug's effect on basic physiologic and behavioral parameters.

The studies demonstrated that fentanyl patches are safe and well tolerated by rabbits and result in plasma fentanyl concentrations consistent with analgesia. After application, plasma fentanyl levels gradually increased in the first 12 to 24 hours. After patch removal, the plasma fentanyl levels rapidly decreased. One study measured fentanyl plasma levels in rabbits comparing clipping versus depilatory cream (Neet for Sensitive Skin) for preparation of the patch application site. In rabbits in which the fur was clipped, plasma fentanyl levels gradually increased in the first 24 hours and then plateaued over the next 48 hours. After patch removal, the plasma fentanyl rapidly decreased. No apparent adverse effects were noted during treatment. In the rabbits in which depilatory cream was used for hair removal, the skin became erythematous but diminished after 24 hours. This group had a rapid increase in plasma fentanyl concentrations during the initial 12-hour period at which time the concentrations peaked. Plasma fentanyl concentrations then decreased at a steady rate until the time of patch removal. Two rabbits in this group appeared moderately to heavily sedated in the first 4 to 8 hours after patch application but returned to normal alertness the following morning. The initial 12-hour surge in fentanyl concentration in this group would account for the sedation and could be the result of the increased dermal vascularity associated with the use of depilatory cream.

An interesting finding associated with the study involved the pattern of cyclic hair growth. In rabbits with slow hair regrowth, plasma fentanyl concentrations followed pharmacokinetic patterns similar to other species. However, if hair follicles are in the anagen phase at the time of patch application, it should be noted that rapid hair regrowth may cause a problem with drug absorption.

COMMENTARY

The use of TFP in rabbits provides an additional modality of pain relief. Other studies have indicated its cost is approximately one-fourth that of buprenorphine. Limitations as outlined by this study must be considered before using the patch. Fentanyl is a class II drug, thereby necessitating proper storage and appropriate record keeping. Fentanyl is not an approved drug for rabbits, so its use in private practice would follow off-label drug usage guidelines. This study did not address different strengths of TFP for varying body weights of rabbits as would be seen in private practice. It may be prudent to use one-half of a 25-μg/hour patch for smaller breeds such as the dwarfs and mini lops.

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Plasma Concentrations of Adrenocorticotrophic Hormone and α-melanocyte-stimulating Hormone in Ferrets *(Mustela putorius furo)* With Hyperadrenocorticism

Schoemaker NJ, Mol JA, Lumeij JT, Rijnberk A: *Am J Vet Res* 63(10):1395–1399, 2002.

ABSTRACT

The objective of this study was to determine plasma concentrations (measured by radioimmunoassay) of adrenocorticotrophic hormone (ACTH) and α-melanocyte-stimulating hormone (α-MSH) in normal healthy ferrets *(Mustela putorius furo)* and in ferrets with clinical hyperadrenocorticism. The diagnosis of hyperadrenocorticism was based on history, clinical signs, ultrasonography of the adrenal glands, and urinary corticoid:creatinine ratios.

The clinical signs associated with hyperadrenocorticism (alopecia, muscle wasting, and skin atrophy) in humans, dogs, cats, and horses are the result of increased levels of plasma cortisol. A disparate situation occurs in the ferret where increases in plasma levels of estradiol, androstenedione, 17 α-hydroxyprogesterone, and dehydroepiandrosterone sulfate (not cortisol) result in physical changes dominated by features of excessive production of these sex hormones. Alopecia, vulva swelling in ovariohysterectomized jills, and recurrence of sexual behavior after neutering may result in ferrets with hyperadrenocorticism.

In humans, dogs, and cats, the most common form of hyperadrenocorticism is pituitary dependent, where excessive ACTH is secreted by pituitary gland adenomas. As well, there is the possibility that neoplastic transformation of melanotrophic cells of the pars intermedia, primarily producing the ACTH derivative α-MSH, causes hyperstimulation of the adrenal cortices and a resulting hypersecretion of cortisol. In ferrets, it is suggested that hyperadrenocorticism may be luteinizing hormone (LH) dependent based on the observations that hyperadrenocorticism is seen almost exclusively in neutered ferrets, and these ferrets can be treated successfully with leuprolide acetate.

The study found that plasma concentrations of ACTH and α-MSH in ferrets with hyperadrenocorticism are essentially identical to those of healthy neutered ferrets. As a result, it is believed that the adrenocortical changes and clinical signs cannot be ascribed to hypersecretion of ACTH. In addition, it is likely that there was no primary hypercortisolism because this finding should be associated with either decreased or increased plasma ACTH concentrations. Thus, hyperadrenocorticism in ferrets should probably be regarded as a normo-cortisolemic and corticotrophin-independent hypersection of primarily androgens. In ferrets with adrenocorticol hyperfunction, involvement of the LH-receptor is likely. Recent preliminary immunohistochemistry studies by Wagner et al and this group have revealed that adrenal tumors possess cells with LH receptors.

COMMENTARY

This study provides another piece in the ferret adrenal disease puzzle. Unlike dogs, ferrets with adrenal disease appear to be ACTH and α-MSH independent, and clinical signs are not related to hypercortisolism. This work is supportive of adrenal LH-receptor involvement in ferret hyperadrenocorticism.

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Dental Disease in Chinchillas in the U.K.

Crossley DA: *J Small Anim Pract* 42(1):12–19, 2001.

ABSTRACT

Dental abnormalities are a common medical problem in pet chinchillas; however, detailed descriptions of dental lesions are lacking in the literature. This paper is the culmination of Dr. David Crossley's doctoral thesis and a comprehensive study of dental disease in chinchillas in England. Data were recorded from visual, clinical, radiographic, and postmortem examinations of chinchillas from pet homes, rescue centers, breeding colonies, and participating veterinarians. Over 600 presumed healthy chinchillas were subjected to visual and external examination, and a more detailed investigation was performed in 56 chinchillas. Gross postmortem examination was performed on 104 chinchillas.

Dental abnormalities, particularly those related to tooth root elongation, were detected in 35% of apparently healthy chinchillas. Of the 56 individuals presented for clinical signs of dental disease, common findings included weight loss, palpable deformity of the ventral mandible, overgrown incisor teeth, abnormal cheek tooth occlusion, discomfort on facial palpation, and ocular discharge. Interestingly, salivation ("slobbers") was not a common finding.

Findings observed on 16 lateral skull radiographs included incisor coronal elongation (100%), cheek teeth root elongation (94%), coronal elongation of cheek teeth (69%), and cheek

teeth occlusal irregularities (44%). Asymmetry of dental arcades was a common finding on dorsoventral and rostrocaudal skull radiographs. In addition to these findings, postmortem examination of 104 individuals revealed caries and resorptive lesions (37%), adrenal hyperplasia (32%), and periodontal pocketing or bone loss (14%). Oral ulceration and abscessation were less common findings, being observed in only 13 individuals (7 with ulcers and 6 with abscesses).

Results of this study indicate that "malocclusion," as defined by abnormality of jaw relationship or tooth position, poorly describes dental disease in chinchillas in the United Kingdom. Rather, chinchillas suffer from a wide range of dental pathologies, particularly those involving tooth root and crown elongation. It appears that the lack of attrition is probably the most important factor in the development of this problem, with stress and nutritional imbalances being possible cofactors. Provision of a high-roughage diet that mimics the natural diet of chinchillas in the wild may reduce or prevent many of the dental problems seen in captive chinchillas.

COMMENTARY

The chinchilla has evolved in arid mountain conditions where vegetation is fibrous and coarse, low in energy, and high in abrasive silicates. Captive chinchillas are often fed a processed diet of pellets, raisins, alfalfa, and treats that require minimal chewing and are low in abrasive phytoliths. This low-roughage diet dramatically reduces tooth wear and is thought to be a major contributing factor in most of the dental abnormalities seen in chinchillas. Offering a diet high in "chew factor" like grass hay may help slow down the development of dental disease in chinchillas.

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Spontaneous Tumors in Captive African Hedgehogs: *(Atelerix albiventris)* A Retrospective Study

Raymond JT, Garner MM: *J Comp Pathol* 124(2–3):128–133, 2001.

ABSTRACT

This article presents a retrospective study of spontaneous tumors diagnosed in domesticated African hedgehogs *(Atelerix albiventris)* by Raymond and Garner, pathologists at Northwest ZooPath (NZP). Out of 66 captive African hedgehogs, 40 tumors were diagnosed in 35 (53%) of the necropsies. Of the 40 tumors, 34 (85%) were found to be malignant, and only six (15%) were benign. There was no gender preference observed.

Despite neoplasia being a relatively common diagnosis in hedgehogs, there are only a handful of reported cases. This comprehensive, retrospective study on hedgehog tumors indicated an 85% occurrence of malignant neoplasms, with 3½ years being the median age of affected hedgehogs. The most commonly diagnosed tumors were mammary gland neoplasia (8), lymphosarcoma (6), oral squamous cell carcinoma (5), cutaneous mastocytoma (3), uterine leiomyosarcoma (2), and myelogenous leukemia (2). The most commonly involved body systems were integumentary (15), hemolymphatic (8), digestive (7), endocrine (5), genital (3), nervous (1), and musculoskeletal (1). Sites where tumors were not observed were the ears, eyes, male genitalia, respiratory system, and urinary system.

The majority of tumors from tissue of epithelial or mesenchymal origin were malignant. The most common tumor location was the integument (37.5%), with the majority of these tumors being of mammary gland origin. Multicentric and alimentary lymphosarcomas represented 15% of the total cases. The third most common site of neoplasia was the oral cavity, with oral tumors representing another 15% of the study's total. The majority of the oral tumors were squamous cell carcinomas.

COMMENTARY

This article presents a concise listing of the tumor types and tissue origins a practitioner is most likely to encounter in the captive African hedgehog. The high percentage of malignant tumors gives the clinician a useful prognostic indicator for hedgehogs diagnosed with tumor masses. The article also details the systemic effects and sequelae associated with various hedgehog neoplasias. The reference section lists the known reports (at the time of publication) of hedgehog neoplasia and serves as a useful resource.

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Chocolate, an Effective Means of Oral Drug Delivery in Rats

Huang-Brown KM, Guhad FA: *Lab Anim* 31(10):34–36, 2002.

ABSTRACT

An effective method of oral drug administration has been developedfor rats by mixing drugs with chocolate. Premixed drug–chocolate pellets were made by measuring an amount of medication equal to 10 doses (in this study, indomethacin, an NSAID, and celecoxib, a COX-2 inhibitor, were used) and mixing this powdered form of medication into approximately 500 mg of softened chocolate, the amount of four mini chocolate chips (Minichips, Hershey Foods). This softened chocolate–medication mixture was then divided into 10 aliquots, which were allowed to solidify for storage. The estimated chocolate consumption per rat was

<0.17 g/kg body weight per day. This amount of chocolate correlates with a daily theobromine dose of <0.02 mg/kg per day that is well below documented theobromine or chocolate toxicity in any species.

The rats required a training period of about 8 days before readily accepting the chocolate. After this learning period, 95% of the animals readily accepted the chocolate-feeding regimen, and results from this technique demonstrated appropriate levels of drug absorption. We believe that this method of drug administration provides consistent, reliable, easy, and accurate dosing. This method obviates the problem of lack of water solubility with oral gavage in that chocolate mixes well with both water-soluble and nonsoluble drugs.

COMMENTARY

Chocolate provides an economical, nontoxic, readily available material that can be used with large groups of animals. Limitations of the method include the 8-day acceptance learning period and the initial drug–chocolate mixing and preparation.

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An exotic pet is a rare or unusual animal pet: an animal kept within human households which is relatively unusual to keep or is generally thought of as a wild species rather than as a pet. The definition is an evolving one; some rodents, reptiles, and amphibians have become firmly enough established in the world of animal fancy to sometimes no longer be considered exotic. Sometimes any unique or wild-looking pet (including common domestic animals such as the ferret and the fancy rat) is considered an Will exotic animals make great pets? You'll be surprised that the answer to that question is a resounding yes. The next question is this: are exotic mammals low maintenance pets? That should be on the top of your list if you are looking for exotic and best mammal pets. Well, some exotic mammals are low maintenance while some are not. You just have to know which is which. And that is why we have this little guide. Exotic Mammals. What others are saying. The Wolf's mona monkey (Cercopithecus wolfi), also called Wolf's guenon, is a colorful Old World monkey in the Cercopithecidae family. It is found in central Africa, primarily between the Democratic Republic of the Congo and Uganda. It lives in primary and secondary lowland rainforest and swamp forest. See more. Unbelievably Cute Mammal With Teddy Bear Face Rediscovered.