Neurologic disease is increasingly recognized in pet rabbits. Many causes are similar to those found in traditional pet species. Signs of CNS disease include behavioral changes, changes in mentation, head tilt (usually vestibular disease), nystagmus, paresis, paralysis and seizure. True CNS disease should be distinguished from lethargy and/or the typical “freezing” response of a prey animal to stress.

**Vestibular Disease**

The most common CNS disease encountered in pet rabbits is vestibular disease. As in other animals, vestibular disease can be peripheral (affecting the inner ear, peripheral axons of the vestibular division of cranial nerve VIII) or central (affecting the vestibular portions of the medulla, cerebellum, spinal cord and/or brainstem). Signs common to both central and peripheral vestibular disease can include head tilt, nystagmus, strabismus, and asymmetric ataxia. Distinguishing between the two can be challenging in rabbits; however, careful examination may reveal the presence of Horner’s syndrome, or facial paralysis involving cranial nerve VII (facial nerve), which only occurs in peripheral vestibular disease.

Central vestibular disease abnormalities can include abnormal mentation, hemiparesis, and postural deficits. These can be difficult to evaluate in the rabbit. Vestibular disease can appear as an acute onset; however, many rabbits with vestibular disease have gradually acclimated to increasing balance issues, and can actually represent more chronic disease. These patients will eventually present when ataxia becomes obvious to owners. Careful questioning may reveal the rabbit has been less willing to move about or is displaying altered behavior patterns, such as avoid upper levels of the cage, or taking paths along the outside of the enclosure in order to balance, and less trips across the center of the enclosure. Some rabbits may be eating or drinking less and may present with mild to marked loss of condition. While a few disease conditions may be over-represented in rabbits with vestibular disease, such as *Encephalitozoon cuniculi* (ECUN) infections and otitis media, other diseases documented in rabbits include suppurative encephalitis, lymphoma, *Baylisascaris* infection, toxoplasmosis, and trauma, toxin exposure, cardiovascular disease and Herpes simplex virus.

In the emergency setting, diagnostic testing should focus on secondary conditions that might require immediate intervention, such as dehydration and secondary renal insufficiency. Supportive care includes the following: correcting of fluid deficits, nutritional support, and prevention from continued injury, including protection of the “down” eye which is
susceptible to corneal damage. Some rabbits may benefit from low dose sedation to prevent continuous thrashing and rolling within the enclosure. The author recommends a combination of midazolam: 0.2-0.5 mg/kg and butorphanol: 0.1-0.3 mg/kg administered IM. It should be kept in mind that rabbits with milder vestibular disease may worsen temporarily after sedation due to relaxation and decreased muscle tone. Other supportive care includes the use of anti-motion sickness medications such as meclizine.

Treatment of the primary cause of vestibular disease requires a precise diagnosis, which is challenging, especially in those cases with central disease. Computed tomography (CT) and magnetic resonance imaging (MRI) are well described in pet rabbits and can be extremely useful for identification of lesions of the middle ear (otitis media), and space occupying central lesions. Treatment of ECUN is described below. Rabbits with otitis media may benefit from long-term antibiotic therapy, but true efficacy is under debate due to the thick nature of rabbit pus and inability of antibiotics to penetrate. A number of reports describe various surgeries of the ear, including bulla ostectomy with or without surgery of the external ear canal. Retrospective studies for techniques and outcomes are currently unavailable. It should be noted that spontaneous improvement/recovery have been seen in rabbits suspected to have either ECUN or otitis media, further complicating evaluation of treatment efficacy.

Other infectious causes may be difficult to impossible to identify ante-mortem. ECUN infection in rabbits is described in detail below.

Encephilitozoon cuniculi (ECUN)

The exact nature of the organism ECUN is currently under debate, with protozoal and fungal origins proposed. After initial exposure, the organisms invade host cells; multiplication occurs and the cells eventually rupture, releasing spores. Spores released from kidney tubules can be expelled in urine for up to two months in the rabbit. Cell rupture is associated with granuloma formation and inflammation, which is the cause of most clinical symptoms. In most animals, ECUN becomes dormant, and disease expression is a result of stress and immunosuppression incidence is most common in the young, aged, and otherwise immunosuppressed patients. The target organs for the organism include the lens of the eye, CNS and kidney. Rabbits with granulomatous nephritis related to ECUN may present with chronic renal failure. The most consistent sign appears to be weight loss. Antemortem diagnosis can be challenging, as blood parameters (BUN/creatinine) do not change until late in the disease. Ocular lesions include lens disease or rupture and anterior uveitis. It should be noted that ocular infections in rabbits can be acquired in utero. Many rabbits have been exposed to ECUN, which is demonstrated by high percentage of apparently normal animals with elevated IgG levels (over 75% in various studies). In addition, naturally infected animals have been found with severe inflammatory lesions and no clinical disease, as well as clinical disease in the face of mild lesions. In one study of rabbits with inflammatory CNS lesions and histopathologically demonstrated organisms, some rabbits also had otitis media, suppurative encephalitis, and lymphoma.
Another study indicated Herpes simplex virus as a cause of CNS disease. This indicates that even in rabbits with ECUN-related inflammation, clinical signs still may not be due to ECUN.

Similarly, for patients presented with suspected ECUN related kidney disease, other differential diagnoses for renal disease include nephritis, nephrosis, urolithiasis, toxin exposure and others. Ophthalmic lesions of ECUN are not unique to the condition, and ocular lesions typical of ECUN can also be caused by bacterial uveitis or keratitis.

Testing at this point may be the ECUN panel offered by University of Miami, www.cpl.med.miami.edu, which currently includes analysis of IgG, IgM, and CRP. Again, all rabbits with signs and symptoms suggested ECUN should be evaluated for other disease processes known to cause similar signs and symptoms.

Without definitive ante-mortem diagnostic testing, recommending treatment is problematic. It should also be kept in mind that disease may be a result of inflammation caused by the organisms, which may be absent at the time of presentation. Spontaneous recoveries can also be seen even without treatment. These factors all complicate evaluation of response to any treatment protocol.

Treatments suggested for elimination of organisms include albendazole, fenbendazole and oxibendazole. Adjunct therapy for inflammation includes steroids, NSAIDS and other drugs including cyclophosphamide. A 2012 study compared neurologic scores in 95 suspect ECUN rabbits treated with oxytetracycline or oxytetracycline plus fenbendazole, with or without dexamethasone. Increased survival rates were seen in the group that included fenbendazole, with or without the addition of dexamethasone. While there is only a single study demonstrating the use of fenbendazole for this purpose in rabbits, albendazole is also used in practice. Benzimidazole toxicity has been reported in humans and other species, and is apparently now identified in rabbits undergoing treatment for ECUN. Benzimidazole damages rapidly dividing cells, in particular those in the bone marrow and the crypt epithelium cells of the intestinal tract. Patients typically present with non-specific clinical signs that may include lethargy, and decreased appetite. Pancytopenia is often identified. Graham reported 3 rabbits with histopathologically confirmed lesions of benzimidazole toxicity. 10 rabbits had signs suggesting toxicity and were considered suspect. Rabbits were given either albendazole (doses ranged from 9-41 mg/kg PO SID for 13-42 days) or fenbendazole (doses ranged from 20-225 mg/kg PO SID for 30 days).

While benzimidazoles may be useful for the treatment of ECUN in rabbits, conservative dosing strategies are recommended. Owners should be informed of possible risks associated with therapy.

References: