

VESTIBULAR DISEASE: DIAGNOSIS AND TREATMENT

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The function of the vestibular system is to transduce the forces of gravity and movement into neurological signals that the brain can use to develop an awareness of the position of the head in space and to coordinate head movements with motor reflexes responsible for ocular and postural stability. Not surprisingly, lesions of the vestibular system commonly result in abnormal posture of the head and body, gait imbalance, and abnormal eye movements.

Peripheral components

Vestibular receptors are located within the fluid-filled membranous labyrinth, which is encased in the bony labyrinth of the inner ear. These structures are located in the petrous temporal bone in close association with CN VII, sympathetic innervation to the face, and, in horses, the guttural pouch.

There are three semicircular canals in the inner ear with each canal oriented in a different plane: (1) anterior-vertical, (2) posterior-vertical, and (3) lateral-horizontal. At one end of each canal is an enlargement (ampulla) containing the crista ampullaris. The crista ampullaris contains the specialized hair cells, responsible for transducing rotational movement into neuronal impulses.

The saccule and utricle contain maculae that are primarily responsible for transducing gravitational forces and linear acceleration.

Vestibular information is transmitted to the brain via the vestibulocochlear nerve (CN VIII).

Central components

The vestibulocochlear nerve synapses on the vestibular nuclei, located within the medulla oblongata, and on neurons in the rostral portion of the cerebellum. The vestibular nuclei have projection pathways (medial longitudinal fasciculus) to the nuclei of cranial nerves III, IV, and VI to control movement of the eyes. This system helps to provide conjugate gaze (both eyes looking in the same direction), especially when the head is in motion. Descending pathways (vestibulospinal pathways) influence neurons in the spinal cord that provide tone in the antigravity muscles in the neck and thoracic limbs to maintain posture.

Clinical signs of vestibular disease

Vestibular dysfunction can occur with damage to either the peripheral or central components. Most disorders affect the vestibular system in an asymmetric fashion (unilateral), but occasionally bilateral lesions occur. Different clinical signs are seen depending on whether the lesion affects peripheral or central components (Table).

Table Neurologic Signs of Peripheral vs. Central Vestibular Disease

| Sign | Peripheral Disease | Central Disease |
|-----------------------------------|--------------------|------------------------------|
| Head tilt | Same side | Either side |
| Ataxia | Yes | Yes |
| Conscious proprioceptive deficits | No | Yes, same side |
| Nystagmus | | |
| Horizontal | Yes | Yes |
| Rotary | Yes | Yes |
| Vertical | No | Yes |
| Changes direction | No | Yes |
| Horner's syndrome | Yes | Rare |
| Cranial nerve deficits | Facial | Trigeminal, Abducens, Facial |

Head tilt

Head tilt is the most consistent sign of unilateral vestibular dysfunction. This occurs due to the loss of antigravity muscle tone on one side of the neck. Peripheral vestibular lesions cause a head tilt towards the side of the lesion. For example, with a right inner ear lesion, the right ear is held lower than the left. Central lesions can cause a head tilt to either side. Animals with bilateral vestibular disease usually do not have a head tilt but typically stand crouched, low to the ground.

Pathophysiology

The utricle and saccule contain maculae that sense head position relative to gravity. Within the maculae are specialized hair cells embedded in a gelatinous substance containing calcium carbonate crystals (otoliths). The pull of gravity causes the otoliths to deflect the hair cells, which send neural impulses to the brain. The macula in the utricle is oriented in a horizontal plane and is primarily responsible for detecting gravitational pull when the head is upright. As the head leans farther forward or backward, the system is less sensitive. The maculae in the saccule are oriented in a vertical plane and are primarily responsible for detecting gravitational forces when the animal is lying down.

The vestibular neurons in the maculae are tonically active. When the head is in the horizontal position, the input from each side is equal. When the head is tilted to the left, the hair cells in the left are excited and those on the right inhibited. This results in stimulation of the left vestibulospinal pathways, which increases input to the antigravity muscles on the left, in the neck, trunk, and limbs. This serves to return the head and body to a level position.

A lesion in the left peripheral vestibular components will abolish the neuronal input from the left, while the baseline activity from the right remains. This stimulates the right vestibulospinal pathways, increasing tone to the antigravity muscles on the right. This causes the head and body to lean to the left.

The cerebellum provides tonic inhibition to the vestibular nuclei, via the caudal cerebellar peduncles. A lesion of the left -- will cause an increase in the tonic activity of the left vestibular nuclei, relative to the right. This results in increased activity of the left

vestibulospinal tract, increasing tone to the antigravity muscles on the left. This causes the head, and in some cases, the body, to tilt to the right. This syndrome is called the paradoxical vestibular syndrome, since the head tilt is to the opposite side of the lesion.

Ataxia, gait disturbances

Animals with vestibular disease may lean, fall, or even roll to one side. It is common for an affected animal to fall when it shakes its head. Peripheral vestibular disease does not cause weakness or deficits in proprioceptive positioning. The presence of proprioceptive positioning deficits indicates a central lesion that is affecting ascending conscious proprioception or descending motor pathways.

Nystagmus

Nystagmus is a rhythmic movement of the eyes. Jerk nystagmus is the most common form of nystagmus and is characterized by a fast and slow phase. The direction of the nystagmus refers to the direction of the fast phase and may be horizontal, vertical, or rotary.

Physiologic nystagmus is nystagmus that occurs in normal animals and pathologic nystagmus implies an underlying abnormality.

Physiologic nystagmus

Rotational-Induced nystagmus

The visual system performs optimally when images are held steady on the retina. Even very small movements of the head must be compensated for to avoid images “slipping” on the retina. Normally, rotation of the head will induce a compensatory eye movement in the direction opposite of head movement. This serves to stabilize images on the retina. The stimulus for this eye movement is vestibular information from the semicircular canals. This vestibuloocular reflex is effective in compensating for angular velocities up to 300°/sec; visual tracking mechanisms can compensate for angular velocities only up to 30°/sec.

Each semicircular canal on one side is paired with a canal on the other side by their common position in a parallel plane. The vestibular neurons are tonically active and their activity is increased or decreased by deflection of the hair cells in different directions. Movement in the direction of one of these three planes stimulates the hair cells on one side, and inhibits the hair cells on the other side. For example rotation of the head to the left causes the endolymph to flow in the left canal so that the hair cells bend toward the utricle, causing increased activity of vestibular neurons on the left side. In the right canal, the endolymph flows to deflect the hair cells away from the utricle, causing decreased activity of vestibular neurons on the right side.

Signals from the vestibular neurons are relayed to the appropriate motor nuclei of cranial nerves III, IV, and VI, which control the extraocular muscles. For the above example in which the head rotates to the left, the end result is contraction of the right lateral rectus muscle and the left medial rectus muscle, causing the eyes to move to the right. This is the slow phase of physiologic nystagmus. The presence of a slow

compensatory eye movement induced by head rotation (the so-called doll's eye maneuver) implies normal function of the vestibulo-ocular pathways.

With continued head rotation, the slow compensatory movements of the eyes are regularly interrupted by a corrective fast movement in the direction of rotation, the fast phase of physiologic nystagmus. This fast phase is a type of saccade and is induced by visual stimulus, usually an image in the visual periphery.

In summary, rotational-induced nystagmus is characterized by a slow phase in the direction opposite of head rotation and a fast phase in the same direction of head rotation. For example, rotation of the head to the left causes a horizontal nystagmus with the fast phase to the left. Vestibular disease may cause an asymmetry rotational-induced nystagmus when the head is moved in different directions. Animals with bilateral vestibular disease have lack rotational-induced nystagmus

Pathologic nystagmus

Spontaneous nystagmus

Spontaneous nystagmus refers to nystagmus that is present continuously when the head is motionless. Spontaneous nystagmus is always abnormal. Damage to a single semicircular canal results in a decrease in the baseline activity of action potentials from the affected canal. This results in spontaneous nystagmus in the plane of the damaged canal, with the slow phase toward the damaged side and a fast phase in the opposite direction. Since selective damage to only one semicircular canal is unusual, spontaneous nystagmus due to a peripheral lesion usually has horizontal, vertical, and rotary components because of the combined effects of altered input from the damaged canals and otoliths. The horizontal and rotary components are most prominent, because the components from the two vertical canals and otoliths tend to cancel out.

Spontaneous nystagmus of central origin is usually purely vertical or horizontal, since horizontal and vertical vestibuloocular pathways separate beginning at the vestibular nuclei.

Positional nystagmus

Positional nystagmus refers to nystagmus that is present only when the head is placed in an unusual position, for example extended or upside down. The presence of positional nystagmus indicates vestibular dysfunction but does not further localize the lesion. However, nystagmus that changes direction with different head positions is most commonly seen with central lesions.

In summary, the presence of either spontaneous or positional nystagmus is always abnormal and usually indicates vestibular dysfunction. With peripheral vestibular disease the nystagmus is either horizontal or rotary and the fast phase is directed away from the side of the lesion. With central vestibular disease, the nystagmus may be in any direction (including vertical) and may change direction with changes in the position of the head. In other words, vertical nystagmus or nystagmus that changes direction with different positions of the head indicate a central lesion. Animals with bilateral vestibular disease do not have spontaneous or positional nystagmus.

Pendular nystagmus

Pendular nystagmus refers to nystagmus that does not have a fast and slow phase; that is, the eyes move with equal speed in both directions. Spontaneous pendular nystagmus is often caused by a congenital abnormality in the visual pathways, most commonly in oriental breed cats (for example, Siamese and Himalayan) and dairy cattle.

Strabismus

Vestibular disease may cause one eye to be deviated ventrally or ventrolaterally when the neck is extended (positional strabismus, also called skew deviation). The ventrally deviated eye is usually on the side of the lesion. Occasionally, a constant ventral strabismus is present with vestibular disease. This strabismus is caused by the imbalance between the unopposed action of the contralateral utricle when the ipsilateral utricle is disrupted.

Cranial nerve deficits

Since the facial nerve and sympathetic innervation to the face travel very close to the inner ear, peripheral vestibular lesions may be associated with ipsilateral facial paralysis or Horner's syndrome. Horner's syndrome in the cat and dog is characterized by ipsilateral miosis, ptosis (drooping of the upper lid and sometimes elevation of the lower lid), enophthalmos, and protrusion of the third eyelid. In large animals, ptosis is usually the most apparent manifestation. Horses will also often have excessive, ipsilateral sweating of the face. With lesions proximal to the head, the sweating may extend down the neck. Ruminants with Horner's syndrome often have prominent vascular engorgement, most obvious in the ipsilateral pinna. There is an absence of sweating on the ipsilateral side of the nasal planum.

Central vestibular lesions may also affect other cranial nerves, such as the trigeminal or abducens nerve.

Compensatory mechanisms

A feature of the vestibular system is its ability to compensate for disorders provided the lesion is stable or changing slowly enough. This process results from modulation of activity in the brainstem and cerebellum. Basically, the brain utilizes visual and general proprioceptive information to compensate for the abnormal vestibular information. This compensation is enhanced by head movement. Drugs and procedures that inhibit the vestibular system may be counterproductive.

Peripheral Vestibular Diseases

Otitis media-interna

Otitis is the most common cause of peripheral vestibular disease in the dog and is also common in the cat, horse, and pig (especially after outbreaks of swine influenza).¹ Otitis can cause vestibular dysfunction by two mechanisms. Bacteria that infect the middle ear can produce toxins that inflame the cochlea or the vestibular system or both (serous labyrinthitis). Alternatively, bacteria may invade the labyrinth itself (suppurative

labyrinthitis), often as an extension of otitis externa and otitis media. However, signs of otitis externa may be absent. Common bacterial isolates include *Staphylococcus* spp., *Streptococcus* spp., and *Pseudomonas* spp. Lymphocytic-plasmacytic otitis media-interna, probably caused by immune-mediated reactions, can also occur.

Most affected animals have signs of otitis externa, including head shaking, rubbing or scratching at the ears, and pain. Frequent yawning may also be a feature. In addition to peripheral vestibular disease, otitis media-interna may be associated with ipsilateral facial paralysis (about 60% of dogs) and ipsilateral Horner's syndrome (about 5% of dogs). Early in the course of otitis media, there may be hyperirritability of the sympathetic pathway to the eye, resulting in mydriasis.

Diagnosis is based on a thorough otoscopic examination, which often requires anesthesia and cleaning of the ears by gently flushing with saline. Otoscopic examination allows visualization of only about 50% of the tympanic membrane in dogs. A small (2.5 mm) endoscope allows a more complete examination. The tympanic membrane may be absent, disrupted, or bulging. Samples for cytology and culture/sensitivity should be collected. Tympanography is also invaluable in assessing the tympanic membrane and middle ear. Radiographic changes may include fluid density within the tympanic cavity and sclerosis of the bulla, but radiographs are usually normal early in the course of disease.

Bacterial otitis interna should be treated with 4-6 weeks of systemic antibiotics chosen on the basis of culture/sensitivity. Pending culture results, a first generation cephalosporin (cephalexin, 10-15 mg/lb, twice daily) should be used. Surgery, to provide drainage and remove infected tissue may be necessary in cases refractory to medical therapy. A mild head tilt, facial paralysis, or Horner's syndrome may persist despite effective therapy because of permanent damage to neural structures.

Canine idiopathic vestibular syndrome

This is the second most common cause of peripheral vestibular disease in the dog. Compared to dogs with otitis, dogs with idiopathic vestibular disease tend to be older (mean age 12.5 years). There is an acute onset of ataxia (which can be severe), head tilt, rotary or horizontal nystagmus and, occasionally vomiting. Postural reactions are normal and dogs do not have facial paralysis or Horner's syndrome. The cause of this syndrome is unknown. A similar disease, vestibular neuronitis, occurs in people and may be caused by a virus. Clinical signs improve spontaneously within 2 weeks, although there may be a mild, persistent head tilt.

Vestibular suppressants, such as meclazine, lorazepam, or amitriptyline may be helpful in decreasing signs. These agents work by suppressing vestibular tone from the contralateral, normal vestibular apparatus, decreasing the imbalance in vestibular input to the brain. Long term use of these drugs is contraindicated as this may inhibit the compensatory mechanisms involved in recovery.

Feline idiopathic vestibular syndrome

Feline idiopathic vestibular syndrome is a common cause of peripheral vestibular dysfunction in cats. This disease is most common in summer months and can affect any age cat. It is characterized by a sudden onset of ataxia, nystagmus, and head tilt, consistent with a peripheral vestibular lesion. Vomiting is uncommon. Rarely, signs of

bilateral vestibular disease are observed. Facial paralysis, Horner's syndrome, and proprioceptive positioning deficits are not features of this disease. Neurologic deficits typically improve within about 2 weeks. In some cats, there is a mild persistent head tilt and ataxia. There is no firm evidence that corticosteroids, antibiotics, antihistamines, or any other treatment influences the outcome of this disease. Short-term administration of vestibular suppressants may be helpful. Relapse has been reported but is rare.

Nasopharyngeal polyps

Inflammatory polyps arise from the lining of the tympanic cavity or auditory tube in cats and, rarely, dogs. Affected cats are usually 1 to 5 years old. Signs may reflect upper respiratory (sneezing, respiratory stridor), pharyngeal (gagging, dysphagia), or inner ear disease (peripheral vestibular dysfunction, Horner's syndrome, facial paralysis). Diagnosis is based on careful oropharyngeal and otoscopic examination. Radiographic abnormalities are similar to those seen with otitis media. Some polyps can be removed by simple traction, but recurrence can occur. Definitive treatment may require bulla osteotomy to remove the portions of the polyp within the bulla cavity. The prognosis is generally good.

Neoplasia

Neoplasia originating in the ear canal is a rare cause of peripheral vestibular dysfunction in dogs and cats. Examples include squamous cell carcinoma, ceruminous gland adenocarcinoma and lymphoma. Neoplasia should be suspected in older animals and in animals with pain on opening the mouth. Lysis or active periosteal reaction involving the bulla or temporal bone is almost always due to neoplasia. The prognosis is poor.

Hypothyroidism

Hypothyroidism can cause peripheral vestibular dysfunction in dogs. Onset of signs may be acute or chronic. Affected dogs may also have unilateral or bilateral facial paresis, lethargy, and generalized weakness. However, vestibular dysfunction is often the only clinical sign and obvious signs of hypothyroidism are often absent. Diagnosis is based on laboratory evaluation of thyroid function and response to thyroid supplementation. Vestibular dysfunction typically resolves within 2 months of treatment.

Ototoxicity

Although many drugs and chemicals are potentially toxic to the inner ear, the prevalence of ototoxicity in dogs and cats appears to be low. In my experience, topical application of chlorhexidine has been associated with acute signs of peripheral vestibular disease, and occasionally deafness, in dogs and cats. The potential contribution of any underlying otitis and iatrogenic trauma in these cases is incompletely understood. If vestibular dysfunction is evident immediately after instillation of a potentially ototoxic substance, the ear canal should be immediately flushed with saline. Vestibular dysfunction tends to resolve in about 2 weeks, but any deafness may be permanent.

Bilateral vestibular dysfunction can be a complication of systemic administration of aminoglycosides or loop diuretics.

Central Vestibular Diseases

Inflammatory

Inflammatory disorders of the brain (encephalomyelitis) are common causes of central vestibular lesions in dogs and cats. Other neurological deficits can also be seen, depending on which areas of the nervous system are involved.

Canine distemper encephalomyelitis

Signs of systemic illness (pneumonia, gastroenteritis) are common in young dogs but are usually absent or mild in mature dogs. Vaccinated dogs can be affected. Diagnosis in mature dogs is difficult. Approximately 50% of affected dogs will have positive fluorescent antibody testing of conjunctival scrapings. Typical CSF findings consist of a mononuclear pleocytosis and increased protein. Detection of antibodies to the virus in CSF is probably the most definitive test, but false negatives are not uncommon. Many affected dogs will improve temporarily with corticosteroid administration (prednisone 0.5-2 mg/lb/day). The long-term prognosis is poor.

Feline infectious peritonitis (FIP)

FIP is caused by an immune-mediated response to a corona virus. Involvement of the CNS is usually associated with the parenchymatous (dry) form rather than with the effusive (wet) form. Vestibular dysfunction is common. Affected cats often have hyperglobulinemia and involvement of other organs, especially the eyes. Serum antibody titers that are currently available are nonspecific and often negative in cats with neurologic signs. A mixed (neutrophilic and mononuclear) pleocytosis with elevated protein concentration is the most common finding on CSF analysis. There is no effective treatment and prognosis is poor.

Rickettsial encephalitis

Neurologic abnormalities are seen in about 40% of dogs with Rocky Mountain Spotted Fever (RMSF) and 20% of dogs with ehrlichiosis. Many affected dogs also have lethargy, fever, and thrombocytopenia. Leukocytosis is more common with RMSF, while ehrlichiosis is more likely to cause leukopenia and anemia. On CSF analysis, RMSF may cause a neutrophilic pleocytosis and mildly elevated protein, while ehrlichiosis is more likely to cause a mononuclear pleocytosis and markedly elevated protein. Diagnosis of RMSF is based on a rise in serum antibody concentration in acute and convalescent samples. A single positive IgG titer is usually sufficient to diagnose ehrlichiosis. Treatment of either disease consists of administering doxycycline (5 mg/kg, orally, twice daily) or chloramphenicol (50 mg/kg, orally, every 8 hours) for 2 to 3 weeks. The prognosis is generally good with prompt treatment, although neurologic deficits may progress or persist despite treatment.

Fungal encephalitis

Cryptococcosis is the most common fungus to involve the nervous system. Affected animals may have involvement of other organ systems, such as the eyes, nose, or skin. CSF findings are variable and may be normal, but organisms are commonly identified on CSF cytology. Detection of cryptococcal capsular antigen in serum or CSF is also helpful in the diagnosis. The recommended treatment is fluconazole (5 mg/kg, orally, twice daily). Therapy should be continued for at least 6 months to prevent relapse.

Blastomycosis occasionally involves the central nervous system. Affected animals usually have evidence of involvement of other organs, such as the lungs, eyes, skin, or lymph nodes. There may be a neutrophilic pleocytosis on CSF analysis. Definitive diagnosis is best made by identifying organisms in extraneural tissue such as lymph nodes. Serum antibody titers are also helpful. Treatment with itraconazole or amphotericin B can be attempted but the prognosis for blastomycosis that involves the nervous system is poor.

Coccidiomycosis should be considered in animals with a history of being in the southwestern United States. Most affected dogs do not have obvious signs of extraneural involvement. On CSF analysis there may be a neutrophilic or mixed (mononuclear cells and neutrophils) pleocytosis. Serology is also helpful in the diagnosis of coccidiomycosis. Treatment consists of long-term administration of fluconazole (5 mg/kg, orally, twice daily). Many dogs with relatively mild signs will recover if treated early. The presence of severe neurological deficits warrants a guarded prognosis.

Granulomatous meningoencephalomyelitis

Granulomatous meningoencephalomyelitis (GME) is an idiopathic disease that results in inflammation of the central nervous system and, occasionally, the eyes. Adult dogs are affected and small breeds (terriers and poodles) may be predisposed. Signs consist of an acute or chronic onset of focal or multifocal neurological deficits or signs of meningitis. Tentative diagnosis is based on CSF findings and exclusion of infectious causes of meningoencephalitis but definitive antemortem diagnosis is difficult. A mononuclear pleocytosis with increased protein is the most common CSF finding but a predominantly neutrophilic response can also occur. Treatment with immunosuppressive doses of prednisone often results in temporary improvement but the long-term prognosis is poor as most dogs eventually become refractory to therapy.

Toxoplasmosis

Toxoplasma gondii can occasionally cause a nonsuppurative encephalitis in dogs and cats. Infected cats often have evidence of disease in other organs, such as uveitis, pancreatitis, and respiratory disease. Dogs with toxoplasmosis often also have other diseases, such as canine distemper. Diagnosis is based on identifying the organism in tissue or a 4-fold increase in IgG antibody in paired sera. In cats, high concentration of IgM antibody in serum or CSF is supportive. Clindamycin or sulfadiazine and pyrimethamine are recommended for treatment.

Neosporosis

Neospora caninum, a recently recognized protozoan, can cause a nonsuppurative encephalitis in dogs. The life cycle of this organism has not been defined. Many

previously reported cases of toxoplasmosis in dogs were probably actually neosporosis. Other organs, including muscle, liver, and lungs can be affected. Diagnosis is based on serology or identifying the organism in tissue samples. Early treatment with clindamycin or sulfadiazine and pyrimethamine may be effective but the prognosis is poor.

Neoplastic

In dogs, the most common tumors to cause central vestibular dysfunction are meningioma and choroid plexus papilloma. In cats, meningioma and lymphoma are the most common brain tumors. Clinical signs consist of progressive neurologic dysfunction. Hemiparesis is common. Diagnosis is based on imaging studies, such as computed tomography or magnetic resonance imaging. Surgery and/or radiation therapy is often helpful, but the long-term prognosis is guarded.

Toxic

Metronidazole toxicity

Signs of metronidazole toxicity in dogs consist of vertical nystagmus, generalized ataxia, anorexia and vomiting. Seizures and head tilt have also been seen. Acute development of neurological dysfunction may occur 3 to 14 days after starting administration of metronidazole at doses greater than 30 mg/lb/day. There appears to be much individual variation in susceptibility of dogs to adverse effects of this drug. Treatment consists of stopping medication and supportive care. Dogs typically recover within 1 to 2 weeks. In cats, metronidazole toxicity typically causes signs of forebrain involvement (disorientation, seizures, ataxia, and blindness) rather than vestibular dysfunction.