**Syringohydromyelia and chiari-like malformations**

The term syringohydromyelia encompasses hydromyelia, which is dilatation of the central canal of the spinal cord, and syringomyelia, which is cavitation and fluid accumulation within the parenchyma of the spinal cord. These conditions may be of developmental origin, or may occur secondary to a number of other conditions, including trauma, vascular accidents, myelitis or chronic compressive lesions (e.g., intervertebral disk disease, neoplasia). There are a number of different theories to explain the specific physiologic origins of syringohydromyelia, although it is generally agreed that a disturbance of cerebrospinal fluid (CSF) flow dynamics plays an important role in many cases. In other cases, necrotic spinal cord tissue may just be passively replaced by CSF (e.g. infarction).

One cause of syringohydromyelia that has been increasingly recognized over the last few years is related to overcrowding of the caudal cranial fossa and foramen magnum, with resulting alterations in CSF flow dynamics. In veterinary medicine, this condition has been termed Chiari-like malformation or caudal occipital malformation syndrome (COMS). The former term is used to draw a parallel to Arnold-Chiari syndrome in humans, which is a developmental anomaly resulting in cerebellar herniation through the foramen magnum. In dogs, a number of abnormalities can be seen, including malformation of the occipital bone, cerebellar herniation, kinking of the medulla and dorsal compression at the atlanto-axial junction.

Chiari-like malformation has been recognized in small and toy breed dogs, and is particularly prevalent in the Cavalier King Charles spaniel breed. Clinical signs vary from mild dysfunction to profound neurologic deficits. Scratching at the neck or shoulder region is particularly common, and may be the only presenting complaint, mimicking a dermatological condition. Other signs include ataxia, tetraparesis, cervical pain or hyperesthesia, torticollis, and scoliosis. Clinical signs may be elicited with stimulation of the neck or shoulder regions (e.g., brushing, petting, or tugging on a leash), with changes in neck position, or with straining to urinate or defecate. Some dogs with Chiari-like malformation may not show clinical signs.

Although myelography and computed tomography (CT) may occasionally identify syringohydromyelia, this disorder is best diagnosed with magnetic resonance imaging (MRI), and the diagnosis of Chiari-like malformation generally requires this modality. Syringohydromyelia associated with Chiari-like malformation usually involves the cervical spinal cord, and may extend caudally to involve the thoracic and even the lumbar spinal cord.

Therapy for Chiari-like malformation may involve medical or surgical management. Some dogs may improve with glucocorticoids administered at anti-inflammatory doses. Gabapentin or pregabalin may be effective for the control of pain or paresthesia. Surgical management can be effective for this condition, and involves decompression of the caudal fossa with a craniectomy and C1 dorsal laminectomy.

**Meningoencephalitis and meningomyelitis**

Inflammation of the meninges, brain and spinal cord is a common condition in small animal medicine, and may present with a variety of clinical signs, including seizures, altered mentation, cranial nerve deficits, neck or back pain, ataxia and paresis. Neurologic examination often indicates a multifocal localization. A number of infectious organisms may cause meningoencephalomyelitis, including canine distemper virus, rabies, pseudorabies, feline infectious peritonitis virus, *Toxoplasma gondii*, *Neospora caninum*, *Cryptococcus* spp., *Aspergillus* spp., *Ehrlichia canis, Rickettsia rickettsii*, and a variety of bacterial organisms. However, the majority of canine patients with meningoencephalomyelitis do not have an identifiable infectious disease. This may be because the disease involves a sterile and likely immune-mediated process, because our current tests are not sensitive enough to detect small numbers of organisms, because serological testing may be performed before a patient has had a chance to seroconvert, or because we are not testing for the right organisms. A number distinct conditions have been described in dogs that have no identifiable infectious cause, including steroid-responsive meningoitis-arteritis (SRMA), granulomatous meningoencephalitis (GME), necrotizing meningoencephalitis (NME), necrotizing leukoencephalitis (NLE) and eosinophilic meningoencephalitis. Some of these terms were originally described for patients with a specific response to therapy (e.g., SRMA) or with a characteristic histologic pattern (GME, NME). The term meningoencephalitis of unknown etiology (MUE) has also been proposed to describe dogs with an antemortem clinical diagnosis of meningoencephalitis and negative infectious disease testing. Recently, NME in pugs has been shown to be associated with specific genetic haplotypes within the MHC II (DLA) region of chromosome 12. Interestingly, these genetic associations do not seem to be consistent across different breeds with histologically similar disease (e.g., Maltese, Chihuahuas).

A diagnosis of meningoencephalomyelitis is usually made following advanced diagnostic imaging (preferably MRI) and examination of CSF. Most animals have an elevated white blood cell count (pleocytosis) and protein level in the CSF. Serum and CSF blood titers for infectious disease organisms are often evaluated, although these tend to be low-yield, particularly in canine
patients. Traditionally, most of these tests have evaluated an antibody (IgG or IgM) response to the infectious organism, although some measure organism antigen and polymerase chain reaction (PCR) based testing is available for a number of organisms.

Therapy for animals with suspected immune-mediated meningoencephalomyelitis has traditionally revolved around glucocorticoids. Although many animals may respond to anti-inflammatory doses, an immunosuppressive dose may be required in some patients (e.g., those with GME). To achieve better control and to reduce the dose and side effects of glucocorticoids, many clinicians have utilized additional immunosuppressive and cytotoxic medications in these animals, including azathioprine, cyclosporine, cytosine arabinoside, lomustine (CCNU), procarbazine, leflunomide, and mycophenolate mofetil. These protocols have been successful in some anecdotal reports, although some animals remain refractory to all therapy.

### Newer anticonvulsant medications

Maintenance anticonvulsant therapy in dogs has traditionally consisted of phenobarbital and potassium bromide (KBr), either alone or in combination. In cats, oral diazepam has also been used for chronic therapy. Other traditional drugs used for humans with epilepsy are typically not effective or practical for small animal patients, usually due to unfavorable pharmacokinetics. No new anticonvulsant medications were licensed for use in humans between 1978 and 1993. However, between 1993 and 2014, a plethora of new drugs have been approved for seizure treatment in human patients in the United States. Unfortunately, many of these suffer from the same pharmacokinetic limitations, usually a short elimination half-life, making dosing impractical or impossible in small animals. In addition, some (e.g., lamotrigine, vigabatrin) have serious side effects in the dog. However, despite these shortcomings, a number of these medications may be suitable for use in small animal epileptics, and have been used successfully by veterinary practitioners.

Gabapentin (Neurontin) was developed as an analogue to gamma-aminobutyric acid (GABA), the most prominent inhibitory neurotransmitter within the brain. Although effective in preventing seizure activity, it appears that its effects are mediated mainly through mechanisms other than its intended effect, and likely involve voltage-gated calcium channels. Although not hepatically metabolized in humans, gabapentin is partly metabolized in the dog, followed by renal excretion. Gabapentin has been used successfully as a third drug in addition to phenobarbital and KBr in the dog and anecdotally as first-line therapy in dogs and cats. It also has a major role in the treatment of neuropathic pain in both human and veterinary patients. Gabapentin is available as a generic drug in Canada and the United States. More recently, pregabalin (Lyrica) has been developed, which acts in a similar mechanism to gabapentin, but with greater potency. Anecdotal reports of the use of pregabalin in dogs and cats with seizures are available.

Felbamate (Felbatol) has been available in the United States since 1993, has been used successfully for both focal and generalized seizures in dogs. Rare but devastating side effects in humans include acute aplastic anemia and liver failure, which have prevented widespread use of this drug. Felbamate is metabolized by the liver, and there are concerns associated with hepatotoxicity when this drug is used in combination with phenobarbital in veterinary patients. Because of its limited use, this drug has been fairly expensive for a number of years, although recently a generic version has been marketed.

Levetiracetam (Keppra) is a newer “broad spectrum” anticonvulsant that works through a novel mechanism of action. It is not extensively metabolized, has a large therapeutic index and a very beneficial side effect profile (mild sedation only). Its main disadvantages are expense, and the fact that it is usually administered every 8 hours. Levetiracetam has been used successfully as a third line drug in both dogs and cats with refractory epilepsy, and in limited use as monotherapy. It is available in generic formulation in Canada and the United States. In addition, an extended release formulation of levetiracetam has recently been released as a generic, and appears to be suitable for administration in dogs every 12 hours.

Zonisamide (Zonegran) is a sulfa drug with anticonvulsant properties. It has been available in Japan for some time, but has been only relatively recently introduced in North America. It is hepatically metabolized, but has a relatively favorable side effect profile. An advantage to this drug is that it can be administered every 12 hours. It has been successfully used as both an add-on therapy to phenobarbital and/or KBr and in limited use as monotherapy in dogs with epilepsy and is available as a generic in the United States.

Several newer drugs with anticonvulsant properties have recently been developed or are currently in development (e.g., lacosamide, rufinamide, brivaracetam, seletracetam, fluorofelbamate). No reports of their use in animals with epilepsy are available at this time.

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<thead>
<tr>
<th>Medication</th>
<th>Elimination half-life (hours)</th>
<th>Dose</th>
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<tbody>
<tr>
<td>Felbamate</td>
<td>5-6</td>
<td>15-20 mg/kg q 8 h</td>
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<tr>
<td>Gabapentin</td>
<td>2-4</td>
<td>10-30 mg/kg q 8 h</td>
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<tr>
<td>Levetiracetam (standard</td>
<td>4-6</td>
<td>20 mg/kg q 8 h</td>
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<td>intermediate release)</td>
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<tr>
<td>Levetiracetam (extended</td>
<td></td>
<td>20-30 mg/kg q 12 h</td>
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<tr>
<td>release)</td>
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<tr>
<td>Zonisamide</td>
<td>15-20</td>
<td>5-10 mg/kg q 12 h</td>
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In addition to new anticonvulsant medications, novel routes of administration are also being investigated. Of particular interest is the intranasal route, which allows rapid absorption of the delivered medication through the nasal mucosa. Preliminary studies have shown that this route results in rapid drug absorption, and avoids some of the problems associated with rectal administration, such as the substantial first pass effect (hepatic metabolism) that occurs with this latter method of delivery. Preliminary clinical evidence has also been positive, and this method may have a role in the treatment of animals in status epilepticus where intravenous access is not available, and in at-home therapy for animals with cluster seizures.

Pharmacologic intervention for acute spinal cord injury
Pharmacologic therapy of acute spinal cord injury in veterinary patients has traditionally centered around the administration of glucocorticoids; either dexamethasone or the rapid acting drugs prednisolone sodium succinate or methylprednisolone sodium succinate. These drugs have often been given at very high doses based on evidence in experimental studies for the prevention of free radical based oxidation injury of nervous system tissue, and on the National Spinal Cord Injury Study (NASCIS) trials in human patients. However, critical review of this evidence has cast serious doubt on the validity of these studies conclusions, and on the perceived benefits of these drugs in this scenario. As a result, the use of glucocorticoids in spinal cord injury patients remains very controversial.

Recently, the use of polyethylene glycol (PEG) has been evaluated in dogs with acute spinal cord injury. This compound acts to repair disrupted cell membranes (axons), ideally allowing the restoration of nerve conduction across the site of injury, and showed some promise in initial studies. The results of a large, multicenter clinical trial in dogs with acute spinal cord injury would suggest that both glucocorticoids and PEG may not be as effective as originally believed for canine patients.