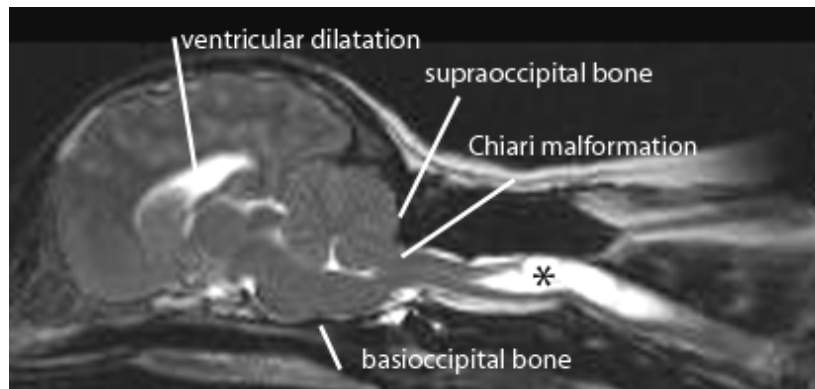
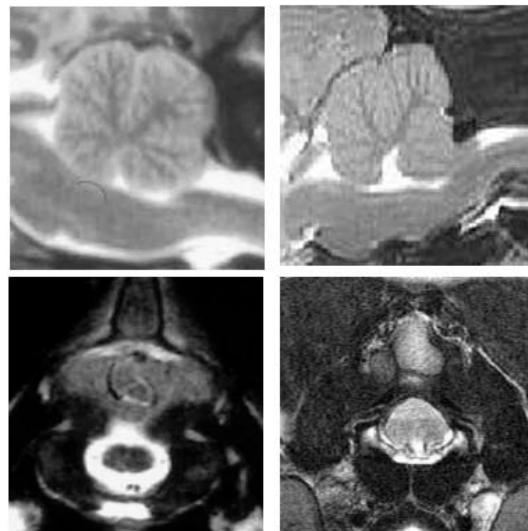


CANINE CHIARI-LIKE MALFORMATION AND SYRINGOMYELIA

Syringomyelia (SM) is characterised by fluid filled cavities within the spinal cord. SM occurs secondary to obstruction of cerebrospinal fluid (CSF) especially if that obstruction is at the foramen magnum. The most common predisposing cause in the dog is Chiari-like malformation (CM) (Rusbridge and others 2006). The primary clinical sign of CM/SM is pain, either due to obstruction of the CSF pulse pressure and/or a neuropathic pain syndrome due to damage to the spinal cord dorsal horn.



Midsagittal T2 weighted MRI of the brain and upper cervical spinal cord from 3 year old female CKCS with syringomyelia (asterisk) and Chiari-like malformation. She first developed signs of pain at 1.7 years old and clinical signs included shoulder scratching at exercise and when excited. She would not tolerate her right ear to shoulder area to be touched or groomed. She frequently vocalised and her owners were not able to exercise without her becoming distressed. She also had mild pelvic limb weakness. She was managed with a foramen magnum decompression and despite persistence of the syrinx, made a satisfactory post operative that was maintained for 1.8 years. Following this deterioration she was managed medically for a further 4 years.



Comparison between the cauda fossa and foramen magnum in a Staffordshire bull terrier (left) and a CKCS (right). The images on the top are midsagittal T2 weighted images of the caudal fossa and C1. The Staffordshire bull terrier has a well defined cisterna magna and unobstructed foramen magnum. In the CKCS the foramen magnum is obstructed by herniated cerebellar vermis. The images on the bottom are transverse T1 weighted images at the level of craniocervical junction. In the Staffordshire bull terrier an unobstructed subarachnoid space around the spinal cord can be appreciated. In the CKCS the CSF space cannot be appreciated and the neural tissue sectioned is the medulla and vermis – structures which are normally within the skull.

Chiari-like malformation (CM)

Chiari-like malformation (CM) is a condition characterised by disparity in size between the brain (too big) and the caudal fossa (too small) such that the cerebellum and brain stem are herniated into or through the foramen magnum (Cross and others 2009). Studies in the Griffon Bruxellois (Rusbridge and others 2009) have suggested that CM is characterised by a shortening of the basicranium and supraoccipital bone with a compensatory lengthening of the cranial vault especially the parietal bone. This has led to the hypothesis that the condition may be due to insufficiency of the bone and /or craniosynostosis of the lambdoid (occipitoparietal) and cranial base sutures. However the condition does not appear to be confined to a simple reduction in skull volume. Investigations comparing skull volumes and brain volumes between SM affected and unaffected dogs have found that caudal fossa volume is significantly smaller for CKCS with early onset SM (less than 2 years only) compared to CKCS that are MRI clear of SM at 5 years or greater. However in addition the parenchyma (i.e. brain) within the caudal fossa is significantly greater for CKCS with SM especially in CKCS with early onset SM (Driver and others 2010). Driver and others (2010) also demonstrated that increased parenchyma within the caudal fossa was positively correlated with syrinx size and that ventricle dimensions are positively correlated with syrinx dimensions i.e. dogs with SM tended to have ventriculomegaly and dogs with wide syringes tended to have greater ventriculomegaly.

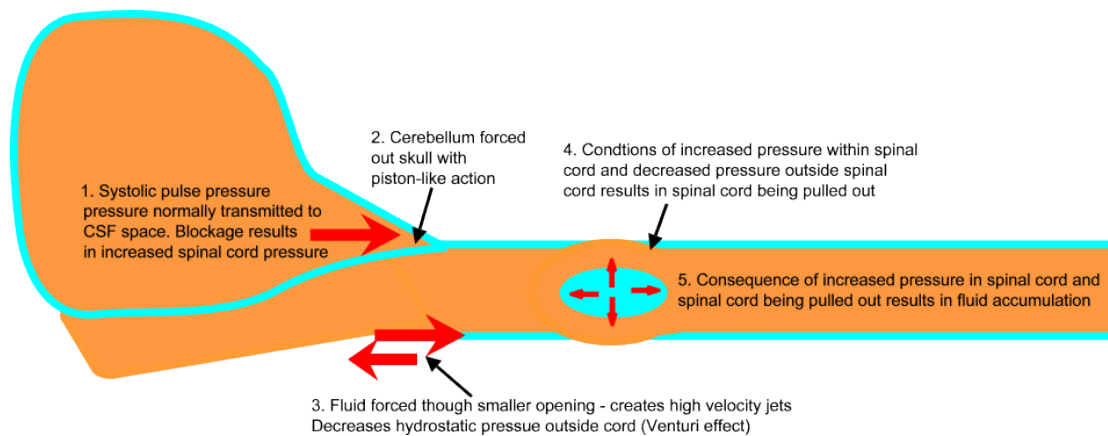


Midsagittal T1 weighted MRI scans and head profiles from 10kg and 16kg CKCS. Both dogs were registered pedigree dogs although the 16kg (left) is considerably bigger than the breed standard. The volume of the brain tissue is similar in both dogs however the volume of the skull, especially the caudal fossa is considerably smaller in the 10kg dog. Consequently there is insufficient capacity for the brain and the cerebellum is herniated into the vertebral canal (arrow) and there is also syringomyelia (asterisks).

One of the enigmas of CM/SM is the difficulty of predicting / explaining which dogs with CM will subsequently develop SM. CM is almost ubiquitous in Cavalier King Charles spaniels (CKCS); Cerda-Gonzalez et al (2009) found that 92% had at least one craniocervical morphologic abnormality detected in MR images. However severity of the CM does not predict the presence of SM (Caruthers et al 2006 Cerda-Gonzalez et al, 2009). There may well be other unidentified anatomical or environmental factors influencing the development of SM.

PATHOGENESIS

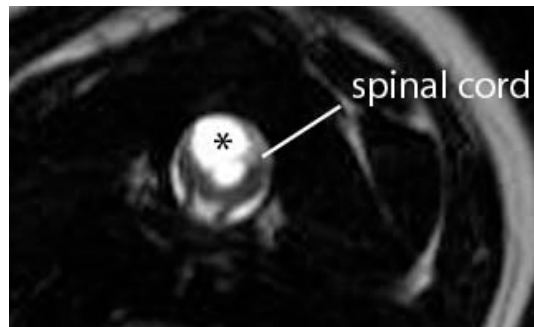
The precise pathogenetic mechanism of development of syringomyelia is much debated (reviewed by Rusbridge et al, 2006; Greiz, 2006). A popular theory is that obstruction of CSF flow results in relative increase in spinal cord pressure and decrease in pressure in the CSF space around the spinal cord, the consequence of which is repeated mechanical distention of the spinal cord. This in turn results in dilatation of the central canal and accumulation of tissue fluid which eventually coalesces into cavities.



INCIDENCE

Both CM and SM have been shown to be inherited in the CKCS (Lewis and others 2010). There is no colour or sex predisposition. As shortened skull is a risk factor, any breed with a degree of brachycephalism and/or miniaturization could potentially be predisposed to CM/SM. To date the condition has been also reported in King Charles spaniels, Griffon Bruxellois, Affenpinschers, Yorkshire terriers, Maltese terriers, Chihuahuas, Miniature dachshunds, Miniature/toy poodles, Bichon Frisé, Pugs, Havanese, Shih Tzus, Papillons, Pomeranians, Staffordshire bull terriers, Boston terriers, French bulldogs, a Pekingese, a miniature Pinscher and a few cats (DSH and Persian).

Not all dogs with SM have clinical signs. The presence of signs is correlated to the transverse diameter of the syrinx and extent of spinal cord dorsal horn damage. Syrinxes can progressively expand and a dog which is asymptomatic in early life may eventually become painful.



T2 weighted transverse image through a wide syrinx (asterisks) demonstrating the asymmetrical involvement of the right spinal cord dorsal horn.

The clinical course may be acute or run an extended course over several months or years. Dogs may be presented at any age although the majority of dogs (approximately 45%) will develop first signs of the disease within the first year of life and approximately 40% of cases have first signs between 1 and 4 years old. As many as 15% develop signs as mature dogs with the oldest reported case first developing signs of disease aged 6.8 years. Due to the vague nature of signs in some cases and lack of awareness about the disease there is often a considerable time period (mean 1.6 years) between the onset of signs and confirmation of a diagnosis.

In clinically affected dogs it is important to image the entire spinal cord to determine the extent of disease. One study demonstrated 76% percent of dogs with a syrinx at C1-C4 also a syrinx in the C5-T1 and T2-L2 regions and 49% had a syrinx in the L3-L7 region. (Loderstedt and others 2009)

CLINICAL SIGNS

The most important and consistent clinical sign of CM/SM is pain however this may be difficult to localise. Owners may describe postural pain; for example, affected dogs may suddenly scream and/or lie with the head on the ground between the paws after jumping up or during excitement. It is also common to sleep with the head in unusual positions, for example elevated. Discomfort often appears worse in the evening and early morning or when excited and can be associated with defaecation or may vary with weather conditions. Pain is positively correlated with syrinx width and symmetry i.e. dogs with a wider asymmetrical syrinx are more likely to experience discomfort, and dogs with a narrow syrinx may be asymptomatic, especially if the syrinx is symmetrical. Dogs with a wide syrinx may also scratch, typically on one side only, while the dog is walking and often without making skin contact, such behaviour is often referred to as an “air guitar” or “phantom” scratching. Dogs with a wide syrinx are also more likely to have scoliosis. In many cases the scoliosis slowly resolves despite persistence of the syrinx.

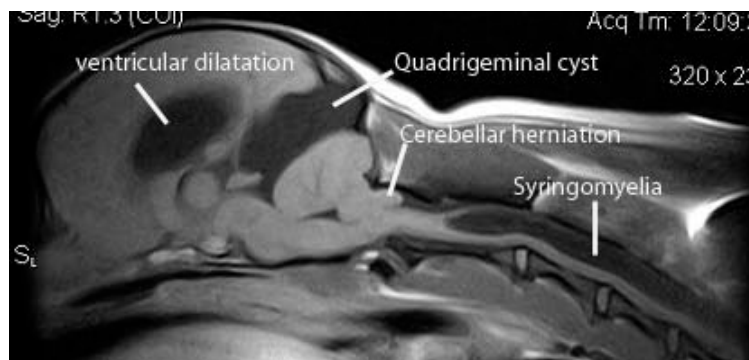
SM may result in other neurological deficits such as thoracic limb weakness and muscle atrophy (due to ventral horn cell damage) and pelvic limb ataxia and weakness (due to white matter damage or involvement of the lumbar spinal cord by the syrinx). Seizures, facial nerve paralysis and deafness may also be seen; however, no direct relationship has been proven and this association may be circumstantial.

CM alone appears to cause facial pain in some dogs with owners describing ear and facial rubbing/scratching. It has been proposed that CM and compression of the brain stem can result a pain syndrome (Thimineur et al, 2002). In this circumstance it can be difficult to be

certain that the CM, as apposed to ear, oral or skin disease, is the cause of the distress especially as CM is a common incidental finding in the CKCS breed.

DIAGNOSIS

Magnetic resonance imaging (MRI) is essential for diagnosis and determining the cause of SM. In the instance of CM/SM the cerebellum and medulla extend into or through the foramen magnum which is occluded with little or no CSF around the neural structures. The size of the cerebellar herniation is not correlated with severity. There is typically ventricular dilatation. SM is indicated by fluid-containing cavities within the spinal cord. The upper cervical and upper thoracic segments are typically most severely affected. Maximum syrinx width is the strongest predictor of pain, scratching behaviour and scoliosis; 95% of CKCS with a maximum syrinx width of 0.64cm or more will have associated clinical signs (Rusbridge et al 2007).

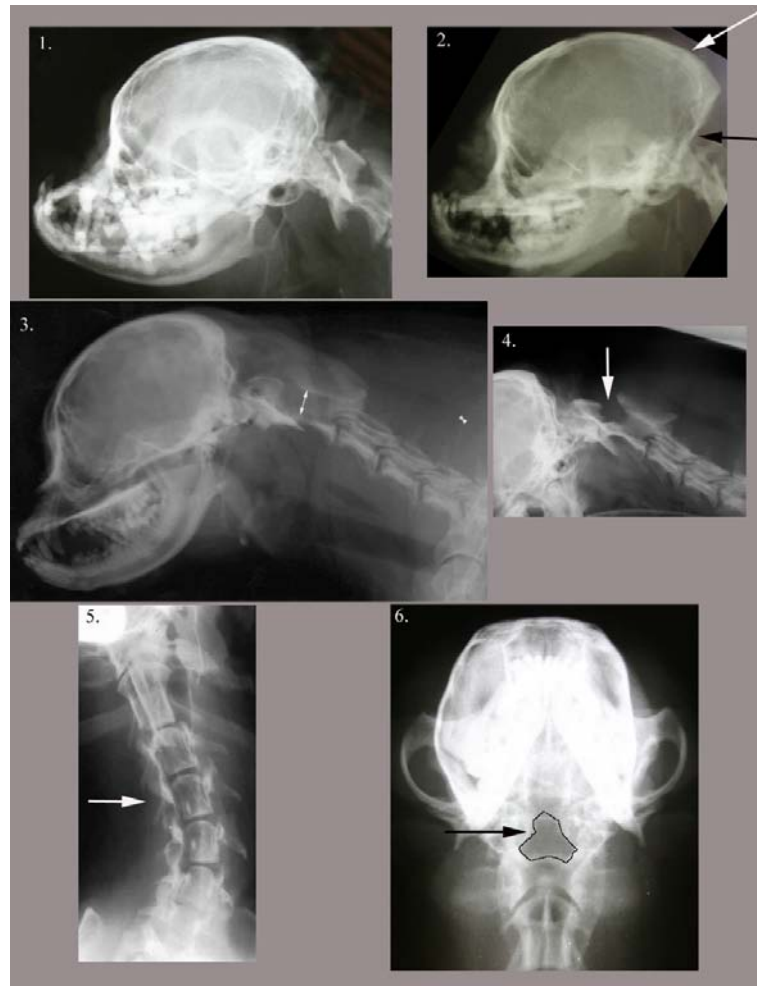


CKCS also have a higher incidence of quadrigeminal cysts. By occupying space within an already crowded caudal fossa this may aggravate the obstruction at the foramen and increase the likelihood of syringomyelia however most quadrigeminal cysts are incidental findings.

CT and radiographs have limited value. CM is appreciable on radiographs and, in the Griffon Bruxellois, a ratio of the height to the length of the caudal skull can be used to predict CM (sensitivity 87%, specificity of 78%). However this is likely to be more of value in predicting the breeding value of a dog rather than as a diagnostic test for SM (Rusbridge et al 2009). In cases with severe syringomyelia cervical images may suggest widening of the vertebral canal especially in the C2 region and/or scoliosis. Radiographs are of greatest value in ruling out other vertebral abnormalities such as atlantoaxial subluxation and for an indication of the likelihood of intervertebral disc disease. Other abnormalities of the craniocervical regions which may be seen in dogs with CM/SM are occipital dysplasia i.e. wide foramen magnum (Rusbridge and Knowler 2006), atlantoaxial subluxation (Stalin and others 2008) and dens abnormalities (Bynevelt and others 2000). Myelography is not recommended for animals suspected to have CM/SM. If CSF analysis is performed then the author recommends a lumbar rather than cisternal puncture.

Ultrasonography through the cisterna magnum may confirm cerebellar vermis herniation however as CM is so common in the CKCS this information has limited value. Likewise a syrinx may be identified if within the cranial/cervical segment; however, failure to detect a syrinx does not eliminate the possibility of one more caudally.

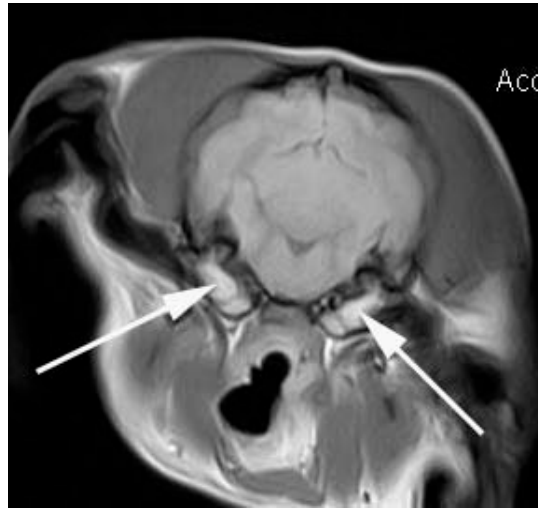
CM/SM does not appear to increase risk of anaesthesia.



Radiographic abnormalities which may be seen with CM/SM. 1. Lateral skull of a normal Griffon Bruxellois. 2. Griffon Bruxellois with CM. The back of the skull has a sloped in appearance (black arrow). By comparison the parietal bone is longer (white arrow) 3. Skull and cervical vertebral column in a CKCS with CM and wide SM. The vertebral canal is wider than normal particularly in the C1-C2 region (arrow). 4. CKCS with atlantoaxial subluxation (this dog did not have syringomyelia) 5. Scoliosis (arrow) in CKCS with wide syringomyelia 6. Occipital dysplasia in a Griffon Bruxellois – there is incomplete ossification of the supraoccipital bone and the foramen magnum is wider with a dorsal keyhole notch (outlined and arrowed).

DIFFERENTIAL DIAGNOSIS

The most important differential diagnoses are other causes of pain and spinal cord dysfunction such as intervertebral disc disease; CNS inflammatory diseases such as granulomatous meningoencephalomyelitis; vertebral abnormalities such as atlantoaxial subluxation; neoplasia; and discospondylitis. When scratching or facial/ear rubbing is the predominant clinical sign, ear and skin disease should be ruled out. The scratching behaviour for SM is classically to one distinct area. It is a common incidental finding for CKCS to have a mucoid material in one or both tympanic bullae and in the majority of cases this is not associated with clinical signs. Some cases with scoliosis appear to have a head tilt which could be confused with vestibular dysfunction. If in doubt cervical radiographs can confirm scoliosis.



Mucoïd material within the middle ears of a Cavalier King Charles spaniel (arrows). This is common in the breed and similar to “glue ear” in children. Typically the material has soft tissue intensity on MRI and there is no evidence of associated inflammation or infection (despite this condition is sometimes confusingly referred to a primary secretory otitis media or PSOMS). The most common explanation is that the material produced normally by the middle ear it is not drained out by the Eustachian tube because of the skull conformation or because of extra soft tissue in the Eustachian tube and pharyngeal area. It is difficult to ascertain how much problem this material causes but reasonable to assume that some dogs have discomfort and/or hearing loss. The material can be removed however if the underlying problem is not resolved e.g. poor eustachian tube drainage then the material will reform. In most cases the problem is minor and is not treated. In some cases using tympanostomy tubes (Corfield and others 2008) or eustachian tube surgery has been suggested.

Fly catching behaviour

There is no evidence that this condition is associated with CM/SM although the two conditions could occur simultaneously. Fly catching is a repetitive behaviour disorder thought to be a compulsive disorder. Classically the dog acts as if watching / catching a fly. Some may also behave as if their ears or feet are irritated and some can also tail chase. Compulsive disorders are compared to obsessive compulsive disorders in humans and are poorly understood; it has been suggested in the Cavalier that there is an underlying neurochemical and/or metabolic imbalance. Diagnosis is typically made on the basis of clinical history and elimination of other behavioural, medical, metabolic, and neurological disorders. Compulsive disorders are managed with a programme of training to interrupt the behaviour sometimes combined with drugs such as selective serotonin re-uptake inhibitors. High protein diets, i.e. high meat content, tend to make compulsive behaviours worse and conversion to a low protein diet can result in improvement of signs although in some dogs this may be only temporary.

Episodic collapse

Episodic collapse or falling is more correctly known as hyperreflexia and characterised by limb cramping (increased limb extensor tone) triggered by excitement and exercise. It is not related to syringomyelia. Affected dogs may show signs from 3 months of age. Many dogs with the condition respond, at least initially, to clonazepam at 0.5mg/kg three times daily (Garosi and others 2002). Some dogs seem to “grow out” of the problem. Clonazepam is thought to be effective because it enhances the GABA-gated chloride channel and presumably compensates for the defective glycine-gated chloride channel in hyperreflexia (Zhou and others 2002).

TREATMENT

The main treatment objective is pain relief. The most common surgical management is cranial/cervical decompression (also described as foramen magnum or suboccipital decompression) establishing a CSF pathway via the removal of part of the supraoccipital bone and dorsal arch of C1. This may be combined with a durotomy (incision of the dura with/without incision of subarachnoid meninges) with or without patching with a suitable graft material. Cranial/cervical decompression surgery is successful in reducing pain and improving neurological deficits in approximately 80% of cases and approximately 45% of cases may still have a satisfactory quality of life 2 years postoperatively (Rusbridge 2007). However surgery may not adequately address the factors leading to SM and the syrinx appears persistent in many cases (Rusbridge 2007). The clinical improvement is probably attributable to improvement in CSF flow through the foramen magnum. In some cases scarring and fibrous tissue adhesions over the foramen magnum seem to result in re-obstruction and 25% to as many as 50% of cases can eventually deteriorate (Dewey et al 2005, Rusbridge 2007). This can be as early as 2 months postoperatively. A cranioplasty procedure used in human cranial/cervical decompression surgery has also been described. The procedure entails placement of a plate constructed of titanium mesh and polymethylmethacrylate (PMMA) on pre-placed titanium screws bordering the occipital bone defect (Dewey et al 2007). An alternative method of managing SM is direct shunting of the cavity. In humans this is not a preferred technique as long term outcome is poor due to shunt obstruction and/or spinal cord tethering.

Due to the persistence of SM and/or spinal cord dorsal horn damage it is likely that the post-operative patient will also require continuing medical management for pain relief and in some patients medical management alone is chosen because of financial reasons or owner preference. There are three main drugs used for treatment of CM/SM: drugs that reduce CSF production; analgesics; and corticosteroids (see treatment algorithm). If the dog's history suggests postural pain or discomfort relating to obstruction of CSF flow then a trial of a drug which reducing CSF pressure, e.g. furosemide, cimetidine or omeprazole, is appropriate. This can also be very useful if it is difficult to determine if the cause of discomfort is CM versus, for example, ear disease. CSF pressure reducing drugs may be sufficient to control signs in some dogs, but additional analgesics are likely to be necessary for an individual with a wide syrinx. In this circumstance it is suggested that non steroidal anti-inflammatory drugs are the medication of first choice partly because there are several licensed products. However, for dogs with signs of neuropathic pain, i.e. allodynia and scratching behaviour (suspected dysesthesia); a drug which is active in the spinal cord dorsal horn is more likely to be effective. Because gabapentin has established use in veterinary medicine we suggest that this is the drug of first choice but amitriptyline or pregabalin may also be suitable. Corticosteroids are an option if pain persists or where available finances prohibit the use of other drugs. Because the mechanisms of development of neuropathic pain are multifactorial, appropriate polypharmacy is likely to be more effective than treatment with single agents. Anecdotally, acupuncture and ultrasonic treatments have been reported to be useful adjunctive therapy in some cases. The dog's activity need not to be restricted but owner should understand that dog may avoid some activities and grooming may not be tolerated. Simple actions, for example raising the food bowl and removing neck collars, can also help.

PROGNOSIS

Prognosis for CM/SM managed medically is guarded especially for dogs with a wide syrinx and/or with first clinical signs before 4 years of age. Study of a small case series (14 CKCS) managed conservatively for neuropathic pain suggested that 36% were eventually

ethanated as a consequence of uncontrolled pain. However 43% of the group survived to be greater than 9 years of age (average life expectancy for a CKCS is 10.7 years). Most dogs retain the ability to walk although some may be significantly tetraparetic and ataxic.

BREEDING RECOMMENDATIONS.

It is recommended that breeders of at risk breeds arrange for MRI screening of their breeding stock. Current CMSM breeding recommendations concentrate on removal of dogs with early onset SM (i.e. within the first 2.5 years of life) from the breeding pool (for details visit www.veterinary-neurologist.co.uk and click on “Syringomyelia” and “SM screening”. In the near future a British Veterinary Association / Kennel Club CM/SM MRI scheme will be available. Owners participating in the CMSM Scheme will receive a grade regarding their dog’s CM and SM status and in addition results from the CMSM Scheme will be used to generate Estimated Breeding Values (EBVs) for SM in the CKCS and in some other breeds. EBVs are a statistical estimate of the genetic risk for a given disease of individual dogs and a measure of the likelihood of their passing on the disease to their offspring. An EBV is the best method of genetic evaluation available for complex traits and can be calculated for most dogs even if they have not undergone an MRI scan, as long as they are related to dogs which have been scanned.

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