Section 2

Pathophysiology of syringomyelia

Chapter 2.1

Syringohydromyelia in cavalier King Charles spaniels

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Introduction

Syringohydromyelia is characterized by the development of fluid-filled cavities within the spinal cord. It is an acquired condition often classified into communicating and noncommunicating types.[1] Communicating syringohydromyelia results from disruption of cerebrospinal fluid (CSF) dynamics at the craniocervical junction and is often associated with developmental abnormalities in this area. The fluid is CSF-like in character. [1] Noncommunicating syringomyelia is characterized by cavities containing highly proteinaceous fluid and is found secondary to intramedullary neoplasia, vascular anomalies, arachnoiditis, and trauma.[1] The classical clinical signs of a syringohydromyelia are of a central cord syndrome (i.e., a grey matter lesion).

In veterinary medicine, there have been sporadic reports of syringohydromyelia often concurrent with developmental disorders of the craniocervical junction such as Chiari malformations [2,3] and Dandy-Walker syndrome.[2] It has also been described in association with spinal dysraphism [4] and with a vascular anomaly.[5] Syringohydromyelia with scoliosis secondary to suspected trauma has also been reported.[6] In this paper, syringohydromyelia secondary to deformity and overcrowding of the foramen magnum is described in seven Cavalier King Charles spaniels (CKCS).

Materials and Methods

Medical records of seven CKCS diagnosed with syringohydromyelia were reviewed. All dogs were evaluated by clinical and neurological examinations. The following additional diagnostic tests were performed: serum biochemistry and haematology (n=4), serum Neospora caninum and Toxoplasma gondii titres (n=2), CSF analysis (n=4), spinal radiographs and myelography (n=4), electromyography (n=4), peripheral nerve conduction and amplitude studies (n=3), and technetium-99m bone scintigraphy (n=1). Magnetic resonance imaging (MRI) was performed in all cases (case nos. 1, 2, 4, 5, 7;[a] case no. 3;[b] and case no. 6[c]). The dogs were positioned in sternal recumbency with the head and neck extended and the thoracic limbs drawn caudally. The images were collected using a circularly polarized extremity coil. T1- or T2-weighted sagittal images of the caudal fossa and cervical spine, together with T1- and T2-weighted transverse images of the brain and craniocervical junction, were obtained for each dog. Case no. 3 also had T2-weighted transverse images of the cervical spinal cord and proton density, and T1- and T2-weighted pre- and post-dimeglumine gadopentetate [d] contrast transverse images of the brain.

The extent of the clinical investigation depended on when the dogs were examined and the discretion of the primary clinician. Dogs that were presented first tended to have a more complete investigation. After the clinical syndrome of syringohydromyelia had become recognizable, fewer tests were required to obtain a diagnosis.

Results

Clinical Signs

The clinical signs are detailed in Table 1. Persistent scratching at one side of the shoulder/neck area was the initial reason for seeking veterinary advice. Scratching was most commonly seen by owners when walking their dog on a leash, especially if the collar was tight-fitting. Excitement, exertion, and barking could also elicit the response. In addition, owners commented that their pets resented any touching or grooming of the ear, limb, or neck of the “scratched” side. Occasionally affected dogs would cry as if in pain and often preferred to eat from a height. There were no skin lesions, and the dogs did not make skin contact when scratching. Prior to neurological assessment, all of the dogs had been investigated for possible dermatological or otological causes of their condition. No causes were found. In addition to

the scratching and neck/ear/limb hyperesthesia, variable neurological deficits were found, of which the most common was a lower motor neuron deficit of the thoracic limb ipsilateral to the "scratched" side (n=5). Proprioceptive deficits of this limb were also seen (n=2). Three dogs had ataxia and proprioceptive deficits of the pelvic limbs, and two had facial nerve paralysis. Case no. 6 had torticollis as a result of cervical scoliosis, with the head being twisted toward the "scratched" side. This dog was hyperesthetic in the sternal area. Case no. 3 had a history of generalized clonic seizures that occurred at a frequency of two per year.

Table 1 Clinical Signs of Affected Dogs

Case No	1	2	3	4	5	6	7
Age/Sex*	7 yrs/M	3 yrs/F	6 yrs/F	3 yrs/M	9 yrs/M	11 mos/M	8 yrs/M
Age onset clinical signs	6 mos	2 yrs	2 yrs†	18 mos	‡	8 mos	‡
Scratching shoulder region§	Yes (R)	Yes (L)	Yes (R)	Yes (L)	Yes (L)	Yes (R)	Yes (L, R)
Neck pain	No	Yes	No	Yes	Yes	Yes	Yes
Limb pain/sensitivity	Yes	Yes	Yes	Yes	Yes	No	No
Ear pain/sensitivity	Yes	Yes	Yes	Yes	No	No	No
Lumbar pain	No	Yes	No	No	No	No	No
LMN\ thoracic limb	Yes (R)	Yes (L)	Yes (R)	Yes (L)	Yes (L)	No	No
Thoracic limb CP¶ deficits	Yes (R)	Yes (L)	No	No	No	No	Yes (L)
Pelvic limb ataxia/ CP deficits	No	Yes (L)	Yes	No	No	No	Yes
LMN pelvic limb	No	Yes (L)	No	No	No	No	No
Facial nerve paralysis/ paresis	Yes (L, R)	No	No	No	Yes (L)	No	No
Scoliosis	No	No	No	No	No	Yes	No

* M=male; F=female

† Dog displayed signs since acquired by owners at two years

‡ Dog displayed signs for many years; owners unable to quantify further

§ R=right side only; L=left side only; L, R=bilateral

\ LMN=lower motor neuron neurological signs

¶ CP=conscious proprioception

Diagnostic Tests

Serum biochemistry and haematology tests were done in case nos. 1, 2, 3, and 6 and were unremarkable. Case nos. 1 and 2 were evaluated for possible *Toxoplasma gondii* and *Neospora caninum* infection and had negative titres. Cisternal CSF analysis in case nos. 1 and 6 suggested mild inflammatory change. Case no. 1 had a nucleated cell count of 8 cells/mm^3 (reference range, less than 6 cells/mm^3; lymphocytes, 78%; macrophages, 22%) with a protein level of 29 g/l (reference range, less than 30 g/l). Case no. 6 had a nucleated cell count of 11 cells/ mm3 (lymphocytes, 50%; neutrophils, 50%). The red blood cell count was 183 cells/mm3 (reference range, 0 cells/mm3), and the protein level was 34 g/l. In case no. 2 only a small amount of blood-contaminated CSF was obtained; results were consistent with iatrogenic haemorrhage. Cerebrospinal fluid analysis was normal for case no. 7. The results of electrophysiological investigation in four dogs are detailed in Table 2.

Table 2 Electrophysiological Findings

Case No.	Denervation Changes*†	Ulnar Motor Nerve Conduction Velocity and Amplitude ‡	Radial Sensory Nerve Conduction Velocity and Amplitude ‡§
1	R, L cervical paraspinal muscles	Normal	Normal
	R, L lumbar paraspinal muscles		
	R thoracic limb		
2	None	Normal	NO
6	R, L cervical paraspinal muscles	ND	ND
	R, L lumbar paraspinal muscles		
	L distal thoracic limb		
	R metacarpal interosseous		
	L pelvic limb		
7	R, L extensor carpi radialis and shoulder musculature	Normal	ND

* Presence of fibrillation potentials or positive sharp waves

† R=right side only; L=left side only; R, L=bilateral

‡ ND=not done

§ NO=attempted but could not be obtained

Four dogs had radiographs of the cervical spine. The images were normal for case nos. 1 and 2. Case no. 7 had a narrow fourth to fifth cervical (C4–C5) intervertebral disk space. Cervical radiographs for case no. 6 confirmed scoliosis with the concave side on the right [Figure 1].

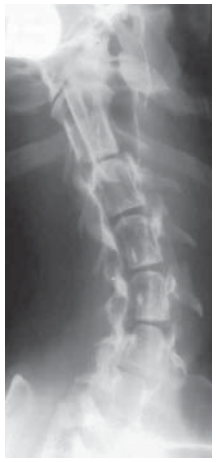


Figure 1 Ventrodorsal radiograph from an 11 month old male cavalier King Charles spaniel (case no 6) with cervical scoliosis

All four dogs also underwent cisternal myelography; the images of the cervical spinal cord were normal for case nos. 1, 2, and 7. In case no. 6, the spinal cord diameter appeared wider than normal. In case no. 2, little CSF was obtained at the cisternal site and there was failure of caudal contrast spread to the lumbar area. A lumbar puncture for intended lumbar myelography was performed. In this instance, the puncture resulted in a fast flow of CSF. This was thought suspicious of a syrinx, so a reduced volume of iohexol contrast media[e] was slowly introduced (50 mg/kg body weight rather than 90 mg/kg body weight). There was no resistance to injection, and the contrast medium delineated a syringohydromyelia extending from the second cervical (C2) vertebra to the cranial border of the fifth lumbar (L5) vertebra [Figure 2]. There were no complications following myelography. Bone scintigraphy in case no. 7 was normal.

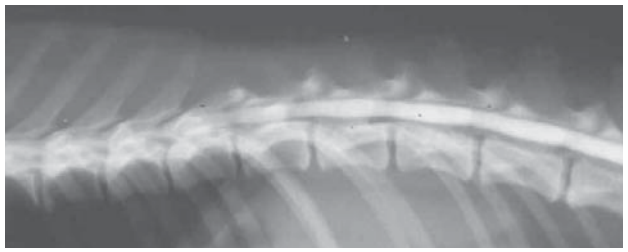


Figure 2 Lateral thoracolumbar radiograph of a Cavalier King Charles spaniel (case no. 2) with evidence of neck pain and neurological deficits of all four limbs. Iohexol contrast is outlining a syringohydromyelia cavity.

Magnetic Resonance Imaging (MRI)

A diagnosis of cervical spinal cord syringohydromyelia was made in each dog. Transverse images revealed lateralization of the syrinx consistent with the clinical signs [Figure 2].

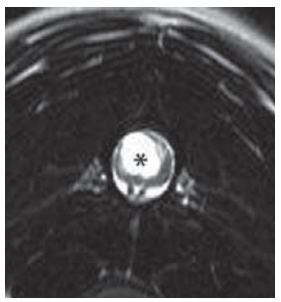


Figure 3 T2-weighted (TR 5090, TE 134) transverse magnetic resonance imaging (MRI) image at the level of the second cervical (C2) vertebra in a cavalier King Charles spaniel (case no. 3), showing a thin rim of spinal cord tissue surrounding a massively dilated syrinx (asterisk) which is lateralized to the right. The dog's main clinical signs were persistent scratching at the right shoulder and lower motor neuron deficits of the right thoracic limb.

The shape of the caudal fossa was disproportionately small resulting in difficulty accommodating the cerebellum and medulla resulting compression and obstruction at the foramen magnum [Figure 4].

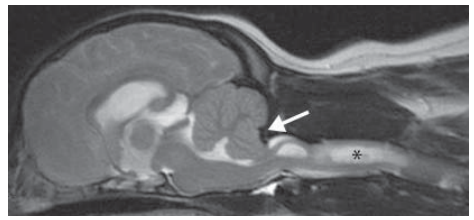


Figure 4 T2-weighted (TR 3800, TE 103) midsagittal MRI image of a cavalier King Charles spaniel (case no. 7), demonstrating cerebellar herniation with syringohydromyelia. The supraoccipital bone is indenting the cerebellum (small arrow). The syrinx (asterisk) is divided into several compartments by septations or haustra.

The abnormal caudal fossa did not accommodate the cerebellum, and there was caudal displacement of the cerebellum to the level of (case nos. 1, 2, 3, 6, and 7) or through (case nos. 4 and 5) the foramen magnum. This resulted in overcrowding within the foramen magnum and apparent compression of the brain stem at the cervicomedullary junction. In all dogs, the tentorium cerebelli osseum was more horizontal than normal, the caudal medulla had a kinked and elongated appearance, and the dorsoventral diameter of the craniocervical vertebral canal was small. The remainder of the skull and brain was normal. Subjectively, case nos. 3, 4, 6, and 7 had slightly larger ventricular systems than would be expected for their breed, suggesting an obstructive hydrocephalus. Ventricular enlargement was more pronounced for case nos. 1 [Figure 5] and 2.

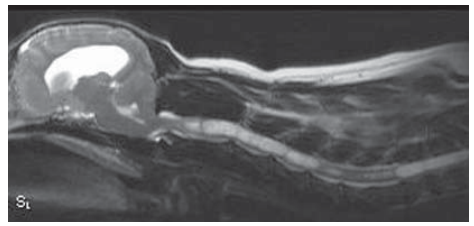


Figure 5 T2-weighted (TR 3400, TE 109) midsagittal MRI image of a cavalier King Charles spaniel (case no.1), demonstrating cerebellar herniation with syringohydromyelia and hydrocephalus. The dog did not have any clinical signs relating to the hydrocephalus.

However, there was no evidence of periventricular transependymal edema, indicating that the hydrocephalus, if truly present, was long-standing. In addition to these findings, MRI revealed a mild C2

to third cervical (C3) disk extrusion in case no. 5. This was suspected to be a contributing factor to neck pain in this dog. The normal MRI appearance of the caudal fossa and craniocervical junction is illustrated in Figure 6.

Figure 6A

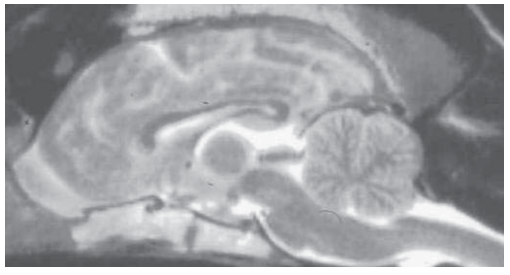
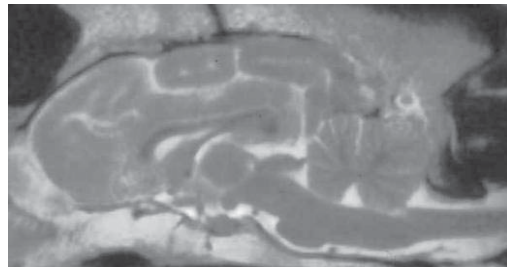


Figure 6B



Figures 6A, 6B midsagittal midline T2-weighted (TR 3500, TE 112) MRI image of the brain of a normal mesencephalic dog, a Staffordshire bull terrier (6A), and the brain of a dolichocephalic dog, a Dalmatian (6B). In comparison to the cavalier King Charles spaniel, the dorsoventral diameters of the foramen magnum and cranial cervical vertebral canal are larger. This is most evident by the amount of cerebrospinal fluid (hyperintense signal) that can be seen in the cisterna magna and around the brain stem and spinal cord. The mesencephalic dog has a small rostral indentation of occipital bone into the caudal fossa, but this is not as pronounced as what is seen in the cavalier King Charles spaniels in Figures 4 and 5.

Treatment and Progression

Surgical management was declined in all patients. The progress of case no. 1 was followed over three years. His discomfort and shoulder scratching did not resolve but were improved when medicated with prednisolone[f] (0.5 mg/kg body weight, per os [PO] on alternate days). Thoracic limb proprioception improved slightly after initiating prednisolone therapy, then it deteriorated to the status at initial presentation. Subsequently he has remained stable. He was also treated with artificial tears[g] (applied to the corneal surface of both eyes, tid) to prevent corneal exposure secondary to facial nerve paralysis. Attempts were made to improve pain control by medication with carbamazepine[h] (100 mg PO bid) and the serotonin uptake inhibitor, amitriptyline[i] (10 mg PO bid). Both these drugs are used as neuralgesics in humans. [7,8] Neither resulted in any clinical improvement; in fact, medication with amitriptyline resulted in a cutaneous drug reaction. Following long-term treatment with glucocorticoids, this dog has had recurrent episodes of pyoderma and has an obesity problem.

For case nos. 2 and 5, the discomfort and scratching were partly alleviated by carprofen.[j] Case no. 2 was initially medicated (2 mg/kg body weight, PO bid) during severe episodes of pain. This appeared to control her discomfort for one year. Subsequently, her neurological status deteriorated. She became more ataxic, there were more severe left-sided proprioceptive deficits, and the discomfort and scratching were worse. Continuous daily medication with carprofen (2 mg/kg body weight, PO, bid 3 months) did not alleviate the signs. The medication was altered to meloxicam [k] (0.1 mg/kg body weight, PO sid), and she appeared less distressed. Case no. 5 was medicated continuously with carprofen (1 mg/kg body weight, PO bid). His clinical signs have remained stable for one year. Case no. 3 (9.8 kg) was also medicated with carprofen (2 mg/kg body weight, PO bid); however, there was inadequate control of pain, and she was subsequently maintained on dexamethasone [l] (0.25 mg PO on alternate days for 2 months; then 0.25 mg PO every 3 days). Her clinical signs were much improved, and her owners reported that they were able to groom and pet her for the first time since she had been acquired. Clinical signs in case nos. 4 and 6 were improved by therapy with dexamethasone at a dose of 0.25 mg PO on alternate days and 0.5 mg PO sid, respectively. Case no. 6 had scoliosis, which also seemed to improve slightly over time. Both dogs were also initially treated with a three-week course of the carbonic anhydrase inhibitor acetazolamide [m] at 31.25 mg PO tid (case no. 4) and 50 mg PO bid (case no. 6). This drug decreases CSF production and was used in an attempt to retard the progression of the syringohydromyelia. After an initial improvement, the clinical status has been stable for both dogs, monitored for a period of 26 months (case no. 4) and four months (case no. 6). Case no. 7 was not treated, and the clinical status has remained stable. At the time of publication, all cases are alive.

Discussion

The clinical signs of cervical paraesthesia progressing to a segmental sensory loss and weakness, with long tract signs, are stereotypic for a cervical central canal syndrome and a gradually expanding syrinx. The abnormalities in these dogs were similar to Chiari type-I malformation in humans. However, in Chiari type-I malformation, the cerebellar tonsil herniation is greater and usually extends well below the level of the foramen magnum. The Chiari type-I occipital bone in affected humans is dysmorphic and the posterior fossa is small, but it does not have the abnormal shape that was typical for the dogs in this series.[1,9] However, in both Chiari type-I and the CKCS malformation, syringohydromyelia occurs secondary to overcrowding of the foramen magnum and obstruction of CSF flow. The first feature of syrinx development is a dilatation of the central canal, termed “hydromyelia.” Initially the cavity is lined by ependyma, but as expansion continues, this lining is split and fluid dissects (usually dorsomedially) into the grey matter, creating a syringohydromyelia [Figure 7].[10]

The term “syringomyelia” refers to a spinal cavity that is not lined by ependyma. The decussating fibres of the spinothalamic tracts, responsible for pain and temperature sensation, are the first to be affected by this syrinx expansion. Damage to these fibres and the interconnections within the dorsal grey column leads to pain and paraesthesia of the corresponding dermatome.[1,11] One hypothesis for the scratching is

that the dogs are attempting to brush off a perceived irritation. Abnormal skin perception is also suggested by the dogs' intolerance of touching and neck collars. Expansion of the syrinx ventrally damages ventral horn cells innervating limb and paraspinal musculature. Muscle atrophy, weakness, and decreased spinal reflexes will be observed clinically (i.e., lower motor neuron signs). If the paraspinal muscle atrophy is severe, the resulting muscular imbalance will result in scoliosis.[1,11] Electrophysiological studies in three of the dogs supported a diagnosis of cervical ventral horn cell damage. Denervation changes were found in the paraspinal and thoracic limb muscles, but motor nerve conduction velocities were normal. These findings suggest axonal loss.[12] The syrinx may extend throughout the length of the spinal cord, resulting in corresponding clinical signs. There was electromyographical evidence of lumbosacral ventral horn cell damage in case no. 6.

Figure 7A

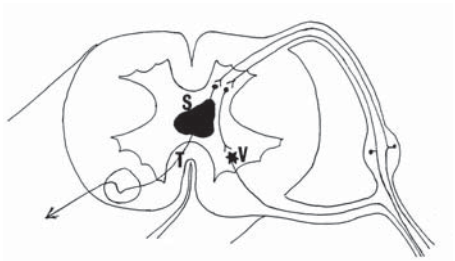


Figure 7B

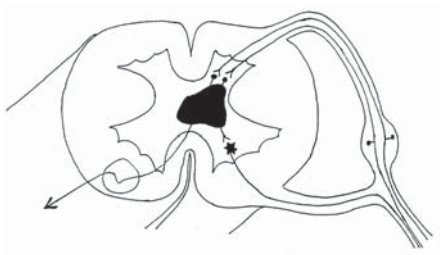
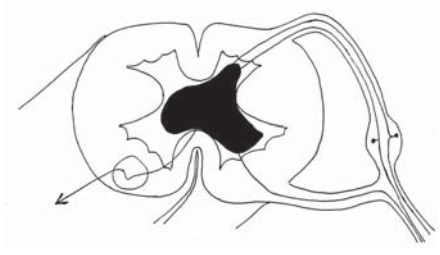


Figure 7C



Figures 7A - C (7A) Transverse section through the spinal cord of a dog with a progressively expanding syringohydromyelia. S=syringohydromyelic cavity; T=decussating spinothalamic tracts; V=ventral horn cell. (7B) The decussating spinothalamic tract and dorsal horn are damaged, resulting in paraesthesia of the corresponding dermatome. (7C)Continued expansion of the syrinx results in ventral horn cell lesions, leading to muscle atrophy and weakness. (*Adapted from Rengachary SS, Wilkins RH, eds. Principles of neurosurgery, 1994. Mosby-Year Book Europe, Ltd. Used by permission of Mosby International, Ltd.*)

Further distension of the syringohydromyelic cavity will lead to compression of the white matter tracts, resulting in pelvic limb ataxia and proprioceptive deficits[11] as seen in two of the dogs. The facial nerve paresis seen in case nos. 1 and 5 is difficult to relate to the underlying malformation. Cranial nerve deficits are common with human Chiari malformation, but they are almost exclusively bulbar (i.e., cranial nerves nine to 12). This is most likely due to traction on the cranial nerves or possibly compression of the caudal medulla within the foramen magnum or an ascending syringomyelia.[13] There was no MRI evidence of facial nerve compression or of ascending syrinx in any of the dogs. Traction of the nerve is possible, but in this instance one would expect other cranial nerves to be affected. Case no. 3 had seizures in addition to her other clinical signs. This was thought to be an unrelated problem; MRI of the forebrain did not suggest any underlying cause of the epilepsy. Humans with syringohydromyelia suffer an exacerbation of clinical signs when intrathoracic or intra-abdominal pressure increases; for example, coughing, sneezing, suddenly rising, or exertion.[13] This also appeared true with these dogs; owners reported increased scratching in their dogs during exertion, barking, or when excited. It is thought that rapid changes in intrathoracic or intra-abdominal pressure are an important factor in the pathogenesis of syringohydromyelia; however, the exact mechanism remains elusive. Several theories have been suggested.[13] The water-hammer effect of pulsatile CSF forced down the central canal from the fourth ventricle as a consequence of increased intrathoracic or abdominal pressure is one such theory.[14] However, a major weakness of this explanation is that it relies on there being a communication between the fourth ventricle and the central canal, which is present in only 10% of human patients. [15,16] The situation in dogs is not known. A second weakness of this theory is that if fluid could not escape through the lateral apertures, then "backing up" would be expected, resulting in hydrocephalus.[16] Hydrocephalus was only seen to a mild extent in the dogs of this study and is present in less than 10% of humans with a Chiari type-I malformation.[1] The suck effect is also a popular theory based on the observation that when intrathoracic or intra-abdominal pressure increases, the pressure in the lumbar sac rises more quickly than the head. Foramen magnum overcrowding may prevent rapid equilibrium of the pressure, resulting in CSF being sucked from the fourth ventricle to the central canal.[17] In addition, when lumbar sac pressure is increased, there is considerable rostral flow of CSF, which may also contribute.[13] This theory also relies on there being a patent connection between the fourth ventricle and the central canal. When syringohydromyelia develops, CSF will move less easily within the narrowed subarachnoid space than within the syrinx. Pressure differences can cause a surge of the fluid within the syrinx, resulting in further fissuring and damage to the spinal cord (i.e., slosh effect).[13] This is thought to be important for the continued development of a syrinx. The cervical vertebral canal stenosis seen in the dogs in this series may be an important contributory factor to this slosh effect. The only theory that does not rely on a fourth ventricle to central canal connection is one that initially seems least plausible. When subarachnoid CSF pressure is increased, fluid could be forced into the substance of the spinal cord. This suggests that the spinal cord is more permeable than it seems; however, since there are no tight junctions and the Virchow-Robin spaces are large, this theory is conceivable.[13,18] Syringohydromyelia may be a common problem within the CKCS breed. In addition to the cases in this

series, a further six dogs with consistent clinical signs have been examined by one of the authors (Rusbridge); however, MRI investigation was not possible. Following a letter reporting this condition,[19 59] anecdotal reports were received from veterinary surgeons and owners in the United Kingdom, Ireland, United States, Australia, Finland, and France describing CKCS with the typical scratching behaviour with or without other neurological signs. With a high incidence of affected dogs within one breed, the possibility of an inherited condition must be considered. Pedigree analysis of the dogs revealed a high frequency of certain names and lines. The same names and lines were commonplace in pedigrees of the anecdotally reported dogs. However, firm conclusions about the possible genetic nature cannot be made at this stage because the number of confirmed cases is small and many of the common names and lines were champion dogs and, therefore, popular for breeding. It has proved difficult to define the normal caudal fossa appearance in the CKCS. It is possible that it is "normal" for a CKCS to have a small caudal fossa, a narrow foramen magnum, and cranial cervical vertebral canal stenosis. The occipital bone abnormality and cerebellar herniation may be exaggerations of this conformational defect. The presence of a small cerebellar herniation in an already crowded foramen magnum may interfere with CSF dynamics, leading to syringohydromyelia. Further studies on CKCS skull morphology are currently in progress. Abnormal development of the occipital bone is the proposed pathogenesis of Chiari type-I malformation in humans.[9] Using computerized tomography (CT) and MRI, Nishikawa, et al., demonstrated a significantly smaller caudal fossa volume in humans with a Chiari type-I malformation (i.e., the hindbrain was literally too large for the skull, resulting in overcrowding).[9] They proposed that this be related to underdevelopment of the occipital somite. Other occipital bone anomalies in toy breeds are recognized.[20] It is possible that breeders of CKCS are unwittingly selecting for an undesirable skull shape much in the same way that in this breed the rostral skull is foreshortened, preventing adequate accommodation of the soft palate and other soft-tissue structures of the head, probably as a result of selection. Most of the dogs in this series were medically managed in a similar way to that described for hydrocephalus, [21] aiming to decrease the CSF volume. Either oral dexamethasone or prednisolone was used. The dogs were maintained on the lowest possible dose to control their clinical signs. Most dogs with neurological deficits made an initial slight improvement and subsequently remained stable or slowly deteriorated. The scratching and discomfort improved but did not resolve. Two dogs initially received the carbonic anhydrase inhibitor acetazolamide. Both glucocorticoids and acetazolamide decrease CSF production.[22] It is possible that glucocorticoids also had an anti-inflammatory effect. Cerebrospinal fluid analysis in two dogs suggested mild inflammation. Meningeal fibrosis and arachnoiditis have been described as associated with cerebellar herniation.[12] These adhesions may further impede CSF flow. Long-term medication with glucocorticoids is undesirable due to concurrent drug effects; case no. 1, which has been monitored for three years, has recurrent bouts of pyoderma and is obese. Attempts to improve pain control with the neuralgesics carbamazepine and amitriptyline were unsuccessful. Owners of case nos. 2, 3, and 5 elected not to medicate with glucocorticoids, because they were concerned regarding the long-term side effects. In these dogs, carprofen was useful in reducing the discomfort; however, it appeared less effective than glucocorticoids. Case no. 2 deteriorated, and medication was altered to meloxicam, which was more effective in this dog. Treatment for case no. 3 was altered to dexamethasone. In humans with a Chiari type-I malformation, early surgical intervention to re-establish CSF flow is recommended for deteriorating patients.[22] The preferred method is to recreate a cisterna magna via a suboccipital craniotomy and first cervical (C1) vertebra laminectomy with dural opening.[1] Dural grafting and cerebellar tonsil resections are performed if necessary.[1] An alternative method is to place a shunt between the syrinx and the subarachnoid space.[23] In theory, similar surgical methods could be used in the dogs in this series. Surgery is performed with a view to preventing further deterioration; existing neurological deficits are often permanent, and pain control can be an ongoing challenge.[1] Surgical management was declined by owners of dogs in this series, because the dogs seemed to cope with their disability, the prognosis for improvement was guarded, and the surgery itself held risks.

Conclusion

Syringohydromyelia results in clinical signs of central cervical spinal cord disease. It should be differentiated from other causes of cervical disease. The CKCS breed is predisposed, and the suggested pathogenesis is abnormal development of the occipital bone leading to a small caudal fossa, cerebellar herniation, and overcrowding of the foramen magnum. Clinical signs can be partially alleviated with glucocorticoid therapy.

A Philips Gyroscan T5-II, 0.5 Tesla, maximum 10 mT/m gradients; Hammersmith, UK
B Siemens Impact Expert, 1 Tesla, 20 mT/m gradients; Bracknell, UK
C 0.5 Tesla Superconducting magnet; SMIS Ltd., Guilford, UK
D Magnevist (469 mg/ml); Schering Health Care Ltd., Burgess Hill, UK
E Omnipaque (240 mg/ml); Nycomed (UK) Ltd., Birmingham, UK
F Prednicare (5 mg); Animalcare Limited, York, UK
G Viscotears Liquid Gel; Ciba Vision Ophthalmics, Southampton, UK
H Tegretol (100 mg); Geigy Pharmaceuticals, Watford, UK
I Tryptizol (10 mg); Thomas Morson Pharmaceuticals, Hoddesdon, UK
J Zenecarp (20 mg); C-Vet Veterinary Products, Leyland, UK
K Metacam oral suspension; Boehringer Ingelheim Limited, Bracknell, UK
L Dexamethasone tablets BP (2 mg); Organon Laboratories, Ltd., Cambridge,UK
M Diamox (250 mg); Lederle Laboratories, Gosport, UK

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Chapter 2.2

Syringomyelia: Current concepts in pathogenesis, diagnosis and treatment

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Introduction

Syringomyelia is a condition in which fluid-filled cavities develop in the spinal cord (Fig 1).
Previously, it was considered a rare condition in veterinary medicine but it is now a relatively common neurological diagnosis. This change is in part due to increased availability of magnetic resonance imaging (MRI) and also due to increased prevalence in certain breeds, most notably the cavalier King Charles spaniel (CKCS)[1].

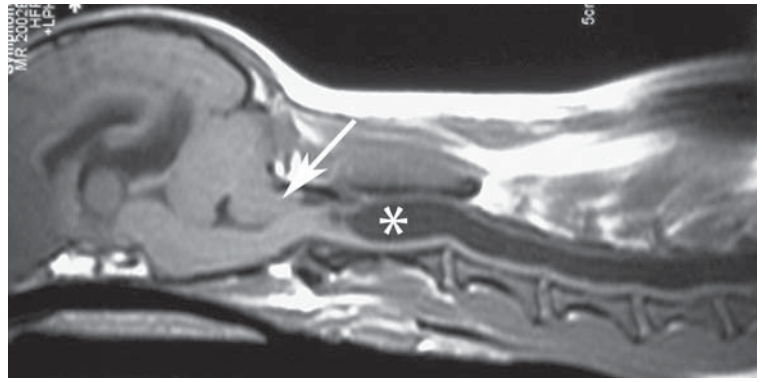

Figure 1 Midsagittal T1-weighted image of the brain and cervical spinal cord of an affected dog. Syringomyelia (asterixis) secondary to occipital hypoplasia in a 21-month female CKCS presented with a 3-month history of yelping and a tendency to scratch at the right shoulder area. Cerebellar herniation through the foramen magnum is present (arrow).

Syringomyelia can be caused by various primary problems, including abnormalities of the caudal fossa (the Chiari malformations), tethered spinal cord, trauma, arachnoiditis, and tumour.[1,2] Here, we review the clinical and pathogenic characteristics of syringomyelia for the purpose of updating veterinarians on current views of pathogenesis, diagnosis and treatment.

History of the classification of syringomyelia and Chiari malformation

Cavitation within the spinal cord was first described by Stephanus in the 16th century.[3] Olivier d'Angers first used the term syringomyelia in 1824 and at that time the cavity was believed to be a dilated central canal that communicated with the fourth ventricle.[4] It was later proposed that dilatation of the central canal be termed hydromyelia and that a distinction be made between this dilatation and syringomyelia on the basis that the former structure was lined by ependyma and the latter by glial cells.[5] It subsequently has been shown that this distinction is somewhat arbitrary in that hydromyelia may extend into the spinal cord substance to form syringohydromyelia partially lined by ependyma[6] and cavities may rupture into the central canal. [7] The term syringomyelia now is generally acceptable for all clinical conditions characterized by spinal cord cavitation containing fluid identical with or closely resembling cerebrospinal fluid (CSF).[7] This classification does not include (protein-containing) cavities associated with tumours.[7]
Syringomyelia traditionally was classified into communicating and non-communicating types in which communicating implies disruption of CSF dynamics at the cranial cervical junction and non-communicating implies a primary spinal cord condition.[8] These terms are confusing however because the communication referred to a connection between the syringomyelic cavity and the fourth ventricle, which actually is present in fewer than 10% of affected human patients. This categorization now tends to be disregarded.[9]

In 1891, Hans von Chiari, a pathologist in Prague, described 4 types of abnormality based on autopsy of infants with hydrocephalus who died shortly after birth. [10,11] The type 1 malformation was described as "elongation of the cerebellar tonsils and the medial part of the inferior cerebellar lobes into cone-like projections, which accompany the medulla into the spinal canal".[12] Arnold's name subsequently was added by two of his loyal students on the basis of the description of a single case consistent with a Chiari type II malformation (i.e., in association with spina bifida). For many years, the spectrum of disorders of cerebello-medullary descent was referred as Arnold-Chiari syndrome.[12] In recent years however the trend has been to simplify the name to Chiari malformation. This name is now convenient shorthand for a wide range of abnormalities not necessarily consistent with Hans von Chiari's original description type I malformation, but all characterized by decreased posterior fossa volume with caudal descent of the cerebellar tonsils, and often the brainstem.[12, 13] It is debatable whether the term Chiari malformation should be applied to the dog. The analogous condition, characterized by decreased volume of the caudal fossa and caudal displacement of the caudal cerebellar vermis into or through the foramen magnum is very similar to the human condition.[14] The condition in the dog however is inconsistent with the historical description, not in the least because dogs do not have cerebellar tonsils. It may be more correct to use an anatomical description (e.g., occipital hypoplasia with syringomyelia[1] or caudal occipital malformation syndrome[15]). Arnold Chiari malformation is an inappropriate descriptive term unless the pathology also includes myelomeningocele in addition to a cerebello-medullary malformation[2].

Pathophysiology of Chiari-associated syringomyelia

The syringomyelia that accompanies caudal fossa abnormalities is thought to be a consequence of abnormal CSF dynamics. In the normal mammal, CSF moves caudally and rostrally between the head and vertebral column. This rapid efflux and influx is due to expansion and contraction of the intracranial arteries during the cardiac cycle.[16] If the subarachnoid space is obstructed (e.g., by cerebellum at the foramen magnum), syringomyelia can develop. In 1950, Gardner proposed the *water-hammer theory* and suggested that when systolic CSF flow through the foramen magnum and outflow from the fourth ventricle were obstructed, ventricular CSF was forced into the central canal with each arterial pulse. This dilated the central canal and eventually resulted in syringomyelia.[17] Although an elegant theory (and one that predated the advent of MRI), it is not supported by clinical evidence because the majority of affected human patients do not have a patent connection between the central canal and the fourth ventricle.[18] Dogs and other small mammals are more likely to have a patent connection (Milhorat, personal communication), but evidence that a syrinx develops from CSF forced into the central canal is lacking (Fig 2).

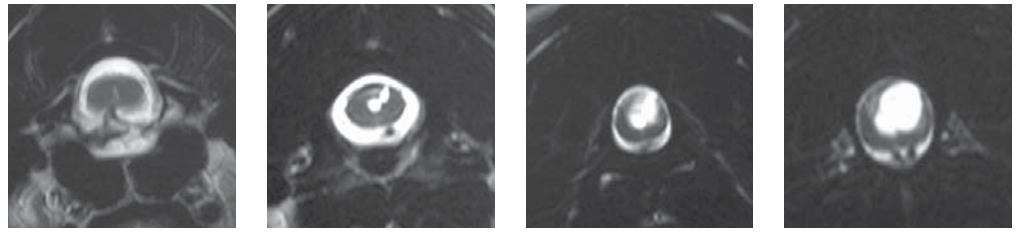

Figure 2 Serial transverse T2-weighted images of the spinal cord (left to right) from the cranial cervical junction to the caudal border of C2 in a 16-month-old male CKCS presented for pain. In the left image (A) a normal central canal is visible as a small white dot in the centre of the spinal cord. In the next image (B) the central canal is dilated but still separate from the developing syrinx within the dorsolateral quadrant of the spinal cord. In the next 2 images (C, D), the 2 cavities are conjoined with what appears to be remnants of the ependymal lining of the central canal traversing the space.

In 1976, Williams described the *suck effect theory*[19] and proposed that when the foramen magnum is obstructed and intraabdominal or intrathoracic pressure is increased (e.g., by coughing), that a pressure difference develops between the head and vertebral column. This pressure difference could result in fluid being sucked from the ventricles into the central canal. This theory however also relies on a connection between the fourth ventricle and central canal, and implies lower pressure in the syrinx when in fact research has shown that pressure in a syrinx is higher than that outside of the spinal cord.[20]

Because it seems unlikely that syrinx fluid comes from the ventricles, it was proposed that spinal CSF is forced into spinal cord parenchyma through the perivascular spaces.[21] Radiographic contrast and horseradish peroxidase studies have shown that CSF can flow into the spinal cord along the outside of veins and arteries.[22] However if syrinx pressure is higher than CSF pressure, this theory also seems implausible and also does not explain why syrinx fluid has significantly lower protein content than CSF.[20]

One of the current popular theories is the *piston theory*,[23, 24] proposed by Oldfield et al, which suggests that the displaced cerebellar tonsils act like a piston and with each systole are forced caudally creating a pressure wave within the entrapped subarachnoid space and syrinx. Movement of fluid and pulsations of the wall of the syrinx cavity can be observed in ultrasound studies performed intraoperatively in human patients, and the pulsations decrease after durotomy.[23] This movement is associated with the cardiac cycle not with respirations. This theory is a reasonable explanation for syrinx progression and is similar to a previously proposed mechanism, the *slosh effect*, which suggests that surging of fluid within the syrinx results in additional fissures and damage to the spinal cord.[25] There are two main arguments against the *piston effect* being the sole mechanism for syrinx formation. Firstly, it also relies on CSF being forced into the spinal cord from the subarachnoid space. Secondly, if the soft spinal cord was exposed to such a force from outside it would seem more likely to be crushed than expand with a syrinx.[26]

New and challenging concepts of syringomyelia

Based on experimental work in laboratory rodents, Greitz and others introduced the *intramedullary pulse pressure theory*[26, 27, 28] which is one of the first general theories to provide an explanation for the pathophysiology of syringomyelia regardless of etiology (e.g., Chiari malformation, post-traumatic syringomyelia, arachnoiditis, syringomyelia secondary to tumours in the caudal fossa or vertebral canal). The main principles of this theory are that 1) syringomyelia is caused by repeated mechanical distension of the spinal cord and 2) the ensuing cavitation arises from extracellular fluid originating from the high-pressure system in the microcirculation of the spinal cord and not CSF from the low-pressure system in the subarachnoid space (Fig 3).

The driving force of syringomyelia is the systolic CSF pulse pressure (i.e. the pressure wave of CSF displaced from the head during arterial pulsations). When the subarachnoid space is obstructed, there is a significant decrease in pressure transmission to distal CSF spaces (Fig. 3, 4a). Consequently, there is increased transmission and reflection of the systolic CSF pulse pressure into spinal cord tissue in close proximity to the obstruction (Fig 4a).

The *intramedullary pulse pressure theory* suggests that this increased pressure in the spinal cord and the decreased pressure in the nearby subarachnoid space distends the spinal cord just below the blockage. In addition, part of the systolic CSF pulse pressure is reflected into the spinal cord at the obstruction also distending the compliant spinal cord just above the blockage[29] (Fig 4b).

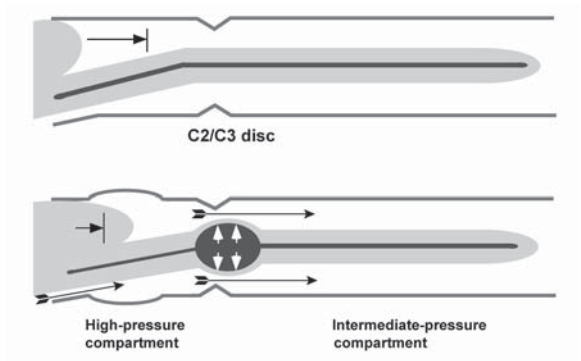

Figure 3 Syringomyelia secondary to Chiari malformation In Chiari malformation, the increased cerebellar motion in the vertebral canal increases the systolic CSF pulse pressure distal to the obstruction at the foramen magnum and a shock-like spinal pressure wave is created. The systolic CSF flow jet ventral in the foramen magnum decreases the hydrostatic CSF pressure, but this pressure difference is rapidly equalized in the cervical high-pressure compartment. At more caudally located physiological impingement of the subarachnoid space, such as C2/C3 intervertebral disc level, the Venturi effect or the suction effect of the systolic CSF flow-jet is unrestricted. Therefore, syringomyelia typically develops at and caudal to the C1 spinal segment.

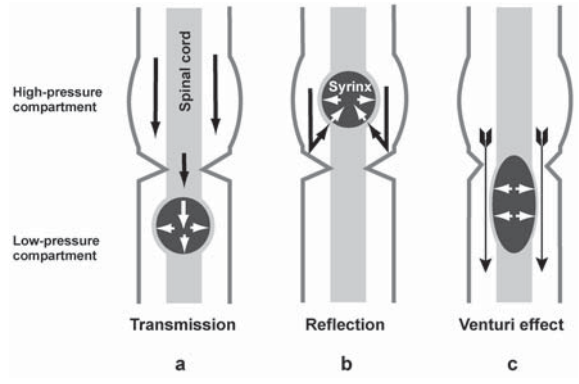

Figure 4 Posttraumatic syringomyelia. Subarachnoid adhesions cause a fixed type of obstruction that decreases the transmission of systolic CSF pulse pressure (i.e. the pressure wave of CSF displaced during systole) distal to the obstruction. a) Systolic CSF pulse pressure (represented by the black arrows) is transmitted through the spinal cord at the obstruction. The increase in spinal cord pressure and decrease in subarachnoid pressure results in distention of the spinal cord just below the obstruction (represented by white arrows). b) Part of the systolic CSF pulse pressure simultaneously is reflected into the spinal cord at the obstruction resulting in an increase in spinal cord pressure and consequently distention of the spinal cord just above the obstruction. c) At partial subarachnoid obstructions, the CSF flow jet (represented by arrows with tails) decreases the hydrostatic pressure in the CSF (Venturi effect) which in turn distends the spinal cord. Syringomyelia develops by collection of extracellular fluid in the distended spinal cord.

This repeated mechanical distention of the cord results in dilatation of the central canal and accumulation of extracellular fluid which eventually coalesces into cavities. Contrary to prevailing theories hypothesizing filling of the syrinx by CSF, this theory is in accord with the second law of thermodynamics indicating that both filling and distension of the syrinx occur along and not against pressure gradients. Thus, filling occurs down the pressure gradient from the spinal cord microcirculation to the syrinx and distension occurs down the pressure gradient from the syrinx to the subarachnoid space. Consequently, development of syringomyelia is independent of the presence of a pathway between subarachnoid space and syrinx. The hypothesis that syringomyelia is due to accumulation of extracellular fluid rather than CSF also provides an explanation for the observation that potentially reversible oedema develops in the spinal cord before syrinx development in some patients.[27,30]

In situations in which partial obstruction of the subarachnoid space occur (e.g., in Chiari malformation), the Venturi effect contributes to decreased subarachnoid pressure (Fig 3, 4c). The Venturi effect (also known as the Bernoulli theorem) states that total mechanical energy of flowing fluid remains constant implying that increased fluid velocity in a narrowed flow channel decreases hydrostatic pressure in the fluid. This type of mechanism lifts the wings of aircraft. When the subarachnoid space is obstructed

(e.g. dorsally within the foramen magnum by displaced cerebellum), CSF displaced by each systole is forced through the narrower opening resulting in high velocity jets of CSF ventrally in the foramen magnum[31] (Fig 5a, b). In accordance with the Venturi effect, this high velocity jet paradoxically decreases the hydrostatic pressure in the subarachnoid space as compared to that in the cord and causes a "suction effect" (i.e. centrifugally directed transmedullary pressure gradients that distend the spinal cord at and immediately below the obstruction). Again, repeated spinal cord distension results in extracellular fluid accumulation and eventually syringomyelia. The Venturi effect also explains why syringomyelia can develop at a distance from the obstruction of systolic CSF flow at the foramen magnum (i.e. in any part of the spinal cord including the medullary conus). The reason for this extended Venturi effect in Chiari malformations is that the piston-like downward motion of the displaced caudal cerebellum increases systolic pressure transmission to the spinal subarachnoid space. In this way, a shock-like CSF pressure wave is created that affects all parts of the vertebral canal.

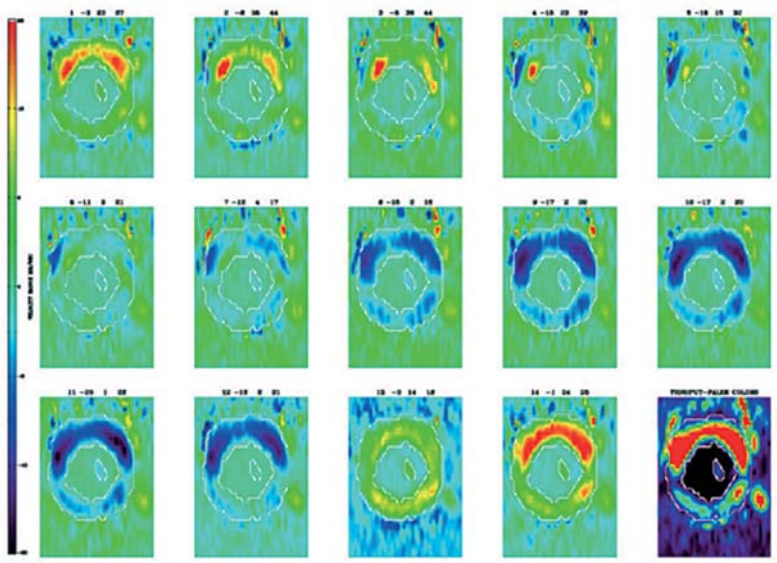

Figure 5a Colour plots of velocities representing the foramen magnum through 14 time points of the cardiac cycle (the last plot is a through-put). Rostral flow velocities are displayed in green, yellow and red with green being the slowest and red the fastest; caudal flow is displayed with light blue, deep blue, violet/black, with light blue being slowest and violet/black faster. In this child with a Chiari I malformation abnormal jets of abnormally high velocities occur in the anterior quadrants of the foramen magnum (note the red colour for velocities nearing 10cm/second in the plots displaying rostral velocities, and the black colour in the plots displaying caudal velocities).

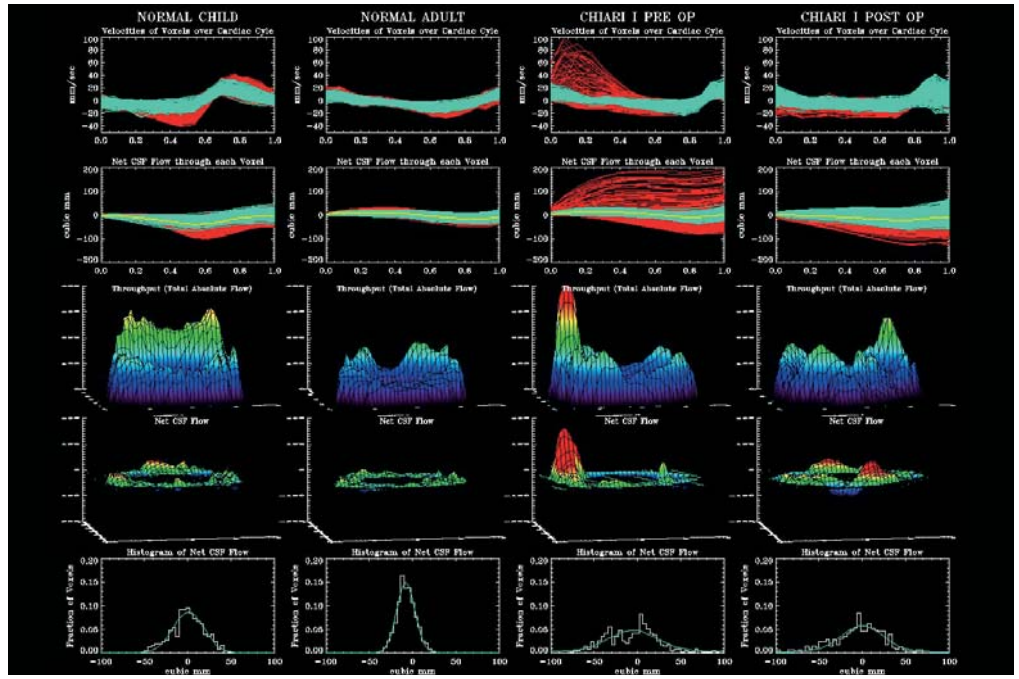

Figure 5b Surface plot images of a normal child, normal adult and child with Chiari I malformation pre- and post-operatively (left to right). In the upper row, each curve represents the velocity in one voxel though the cardiac cycle. The red traces represent the anterior half of the subarachnoid space, and are significantly increased in the preoperative Chiari I child. The green traces represent the posterior half of the subarachnoid space, which tend to be near normal in the Chiari I child. In the second row, cumulative flow volume in each voxel over time (a constant fraction of the cardiac cycle) is displayed in each voxel; anterior voxels are represented in red and posterior voxels are green. Although there are significant abnormalities in selected voxels, the mean CSF cumulative flow in all voxels (yellow trace) is zero. In the third row, the magnitude and spatial distribution of net CSF flow (cumulative CSF flow volume over the entire cardiac cycle) is represented as a surface plot. (Negative net flow volumes are obscured by the plane of the surface). In the normal patients most of the voxels display very little net flow. In the preoperative Chiari I child, a large number of voxels have non-zero net flow at the end of the cardiac cycle. Postoperatively, the net flow in each voxel approaches that of normal. In the fourth row, the figures represent through-put (sum of the absolute value of the velocities in each voxel at different time points in the cardiac cycle). The preoperative Chiari I child had high velocity jets exhibiting a large net rostral flow. This decreased significantly after surgery. The bottom row shows the distribution of the net cumulative flow. Normal subjects show a narrow Gaussian-like distribution, implying that the amount of non-zero cumulative flow volume is determined by random factors. The pre-operative Chiari I child has two distinct distributions: one for the jet and one for the remainder of the non-jet subarachnoid space. The overall distribution is significantly wider than that of the normal subjects. Postoperatively the histogram has a Gaussian-like distribution similar to the normal adult.

The most common location of syringomyelia is in the cranial or middle cervical spinal cord, often with a syrinx-free segment in the most cranial part of the cervical spinal cord (Fig 1). The first cervical spinal cord segment is usually protected from spinal cord cavitation and the suction effect by the increased counter-pressure caused by the moving herniated part of the cerebellum. The cross-sectional area of the vertebral canal varies slightly in dogs with small encroachments at the intervertebral levels. Due to increased CSF velocity at the intervertebral disc level, the Venturi effect is increased and may explain why the syrinx often develops over the first intervertebral disc space in dogs (i.e. within the C2-C4 spinal cord segments) and at the thoracic inlet where there is a narrowing in the diameter and change in angulation of the vertebral canal (Fig 3, 4c, 6). If a slightly bulging disc is present in the lower cervical region in humans, cavitation usually starts immediately below that level.[2] The segmental character with minor intervertebral encroachments of the subarachnoid space contributes to progression of the syrinx.

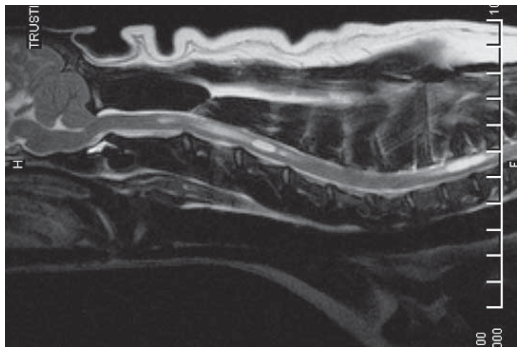

Figure 6 Midsagittal T2-weighted image of the caudal fossa, cervical and cranial thoracic spinal cord of a 20-month-old female CKCS. MRI was being performed as a screening for suitability for use in a breeding program and at the time of the imaging the dog had no clinical signs related to syringomyelia. Syringomyelia is present from C2 to C5 and from T1 toT3. There is noticeable narrowing of the ventral subarachnoid space at the C2/C3 and C7/T1 disc levels implying an increased Venturi effect in these regions. The change in angulation of the vertebral canal at these levels may also contribute to this effect.

Once formed, the syrinx further decreases the cross-sectional area of the subarachnoid space, which in combination with the increased CSF velocity and Venturi effect may cause self-progression of the syrinx. Progression also occurs in accord with the *slosh* and *piston effect* by systolic compression of the upper part and dilatation of the lower part of the syrinx.

Any subarachnoid obstruction decreases craniospinal compliance. Compliance is the "giving property" of a system and craniospinal compliance is decreased by 50% in Chiari malformations.[24] The decreased compliance significantly increases the driving force of syringomyelia (i.e. the CSF pulse pressure). There is an even greater increase in intracranial and spinal systolic pulse amplitude during and immediately after Valsalva manoeuvres such as straining or coughing.[24, 32] The exaggerated systolic pulse pressure explains why patients with Chiari malformations often experience rapid worsening of clinical signs during or immediately after such activities.

In 2004, Levine proposed a *vascular theory*.[20] When the foramen magnum is obstructed, there is a tendency for transiently higher CSF pressure above the obstruction than below it. Consequently, blood vessels tend to dilate below the obstruction and collapse above it. The spatially uneven change in vessel calibre produces mechanical stress on the spinal cord, particularly caudal to the obstruction. The mechanical stress, coupled with venous and capillary dilatation, partially disrupts the blood–spinal cord barrier, allowing ultrafiltration of crystalloids and accumulation of a protein-poor fluid. This theory is basically a variant of the *intramedullary pulse pressure theory* and like that theory offers an explanation for why syrinx pressure is higher than CSF pressure; why extensive gliosis, edema, and vascular wall thickening regularly occur; and, why the composition of syrinx fluid is not identical to that of CSF[20].

At the present time, the exact mechanism of syrinx development and progression still remains unclear. The main debates appear to be: 1) Does the syrinx form because of increased pressure in the subarachnoid space or because of increased pressure within the spinal cord? 2) What is the source of the fluid within the syrinx – CSF or extracellular? As first shown experimentally by Greitz and others[27], most researchers now are concluding that syringomyelia represents a collection of extracellular fluid but the exact mechanism of its accumulation still is under debate[33].

Clinical signs of syringomyelia

By far the most important clinical sign of syringomyelia is pain.[14, 34, 35] Pain is most commonly localized to the cervical region but may be intermittent and difficult to localise. Owners may report that their dog is worse at night, when first getting up, during hot or cold temperature extremes, when excited, or related to posture (e.g. preferring to sleep with its head elevated). Affected dogs may be overly sensitive to touch on one side of the head, neck, shoulder or sternum. In addition, affected dogs often scratch at one area of the shoulder, ear, neck or sternum. Scratching typically occurs on one side only, while the dog is moving and sometimes without making skin contact.[14]

The pain experienced by animals with syringomyelia is likely to be multifactorial and related to obstruction of CSF flow and spinal cord damage. Humans with syringomyelia report headache, suboccipital or neck pain, back pain, trigeminal pain (i.e. facial pain) and radicular pain (e.g. pain that radiates into the lower extremity; pain that has a cape like distribution over the shoulders in syringomyelia).The most disabling pain however is dysesthesia which variously is described as burning pain, hyperaesthesia, "pins and needles" and stretching or pressure of the skin.[35] Dysesthetic pain may be sympathetically mediated and sympatholytic treatment affords relief. [35]

Signs of pain are not well correlated with the size of the syrinx, i.e. human or animal patients with bigger or longer syrinxes are not necessarily in more pain than those with smaller syrinxes.[34, 36] Damage to the dorsal horn is a key feature in the chronic pain of syringomyelia (Fig 2).[35] Human patients with deviated syrinx, especially if deviated into the dorsal horn, were unlikely to have their pain improve even after successful surgery.[34] The duration of pain also was a significant feature (i.e. those who had experienced their symptoms longer were less likely to recover).[34] The dorsal horn of the spinal cord is the most important relay centre for transmission of sensory information to the brain and is subject to a great deal of plasticity, both pharmacological and physiological, in persistent pain states. [37] Expression of substance P in the dorsal horn is altered in syringomyelia and much research now is focused on the changes in neurotransmitters and neuromodulators after injury or development of a syrinx.[38] Clarifying the mechanism of pain will allow development of new avenues of pain management.[38]

Some dogs, more commonly younger patients, develop scoliosis with syringomyelia.[14] It was originally thought that scoliosis was due to unilateral ventral horn cell damage, unequal paraspinal muscle atrophy and muscular imbalance. It appears more likely however that syringomyelia extending into the dorsal grey column over a number of spinal cord segments on one side results in an imbalance of afferent information from the cervical neuromuscular spindles. This unilateral loss of proprioceptive information leads to scoliosis with the neck curving away from the lesion.[39] Humans with Chiari malformation and scoliosis do not necessarily have syringomyelia and the mechanism of scoliosis is not well understood.[40]

Dogs with syringomyelia may have 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).[14] Facial nerve paralysis[14] and deafness[41] have also been associated with the condition in the CKCS. Idiopathic facial paralysis is common in the CKCS as is hearing impairment.[42] Hearing loss and vestibular signs have been documented in human patients with Chiari malformation but these complication typically occur for those with bulbar extension of the syrinx. [43] To the authors' knowledge, none of the documented canine cases [14,41]of syringomyelia with facial paralysis or deafness had bulbar extension of the syrinx and an association has yet to be established. CKCS with syringomyelia and ventricular dilatation secondary to caudal fossa crowding also may be presented with seizures but idiopathic epilepsy also is common in this breed [1] and this association also may be circumstantial.

The first clinical signs of syringomyelia secondary to caudal fossa overcrowding in CKCS typically are recognized between 6 months and 3 years of age. However, dogs of any age may be presented, and dogs with more severe lesions tend to be presented before 2 years of age. [1] Progression of the condition is very variable. Some dogs only have a tendency to scratch with mild pain and other neurological signs such as paresis develop slowly or not at all. Other affected dogs can be severely disabled by pain and neurological deficits within 6 months of the first signs observed. Syringomyelia also may be found as an incidental finding, with no recognized clinical signs, in the investigation of another neurologic disease.[36]

Diagnosis of syringomyelia

MRI is essential for diagnosis of syringomyelia (Fig 1). Syrinx fluid has the T1 and T2 relaxation characteristics of CSF and multiplanar imaging allows assessment of the width, dorsal horn involvement, and longitudinal extent of the cavity. The shape of the cavity may be complex with septations (i.e. haustra) and generally involves a portion of the central canal at some level.[2, 20] Syringomyelia however is merely the effect of an obstruction within the subarachnoid space, and the goal of imaging is to determine the cause of the syringomyelia. In the instance of Chiari-like malformation, the occipital bone is presumed to be small resulting in a reduced caudal fossa volume, the caudal cerebellar vermis and medulla extend into or through the foramen magnum, and there may be ventricular dilatation[14].

The advent of phase contrast MRI which can demonstrate CSF flow (i.e. cine MRI) has greatly improved diagnostic capability in humans. For example, the diagnosis of clinically significant Chiari malformation previously was made on the basis of the size of tonsillar herniation, with greater than 3 to 5mm being significant. [44] However Milhorat et al showed that the size of the herniation was not related to clinical signs and that the most important factor was decreased cerebellomedullary cistern volume, smaller posterior fossa and decreased CSF flow around the tonsils as identified by cine MRI. [44] Another study yielded similar results and also determined that postoperative cine MRI findings correlated with success (i.e. patients with restored CSF flow had improvement in symptoms).[45] Cine MRI is most useful in cases of borderline Chiari malformation, in demonstrating other CSF obstruction; or when the question of whether decompression is needed is not readily answered using traditional MRI.[31] Studies now are focusing on the complex flow patterns at the foramen magnum in human patients with Chiari malformation. Techniques that assume homogenous CSF flow may be too simplistic and measurements of bulk flow or CSF velocity cannot distinguish symptomatic from healthy individuals. [31] Iskandar et al found that children with Chiari I malformation had a marked heterogeneity of flow at the foramen magnum which resolved after successful surgery.[31] The flow abnormalities documented included bi-directional flow with high velocity jets of CSF displaced by each systole forced through a narrower opening, typically anterior in the foramen magnum (Fig 5).[31]

Cine MRI requires additional software and ECG monitoring which is available to veterinarians, and hopefully in the future we will discover whether this diagnostic modality is useful for small animals. A preliminary study in a group of 30 dogs[46] has indicated that non-invasive cine MRI can be performed and that CSF flow is abnormal in dogs with caudal fossa abnormalities.[46]

Treatment of syringomyelia

In humans, a small and asymptomatic syrinx often will not require treatment[2] and the same probably is true for small animals. Thus an argument can be made for monitoring such patients with serial MRI scans. For canine patients, surgical management is indicated when analgesics do not control discomfort or when

neurological deficits are present. Medical management may be chosen for patients with only mild pain, when finances do not allow surgical management, or when surgical management has failed to resolve the signs.

Medical

Long-term studies of medical management of syringomyelia are not yet available. Figure 7 illustrates the treatment algorithm currently used by one of the authors (CR). The drugs used can be divided into 3 types: analgesics, drugs that reduce CSF production, and corticosteroids. Pain in mild cases may be controlled by non steroidal anti-inflammatory drugs (NSAIDs).[14] In more severe cases anticonvulsants (which have a neuromodulatory effect on the hyperexcitable damaged nervous system) may be useful (e.g. gabapentin[a]).[47] Oral opioids (e.g. pethidine[b] or methadone[c]) also are an alternative.

Proton pump inhibitors such as omeprazole[d] can inhibit CSF formation and therefore may be useful in decreasing CSF pulse pressure,[48, 49] but clinical data on their use and effectiveness currently are lacking. They may not be suitable for long-term management and a maximum of 8 weeks of therapy has been recommended because chronic gastric acid suppression results in hypergastrinemia and increased risk of carcinoids in laboratory animals.[50] Carbonic anhydrase inhibitors such as acetazolamide[e] also decrease CSF flow[51,52, 53] and also may be helpful in treating syringomyelia[14] but adverse effects of abdominal pain, lethargy and weakness may limit long-term use (Clare Rusbridge, unpublished findings). Furosemide[f] also decreases intracranial pressure[54, 55] and therefore could be useful in the treatment of syringomyelia. Furosemide's effect however may be due to diuresis and reduction in blood volume and one study found no effect on CSF pressure in nephrectomized dogs.[56]

Corticosteroids are very effective in decreasing both pain and neurologic deficits[14] although the exact mechanism is not known. Corticosteroids may decrease CSF pressure[57] but laboratory evidence of this effect is lacking.[58] Corticosteorids possibly have a direct effect on pain mediators such as substance P.[59] Although corticosteroids may be effective in limiting signs and progression, most dogs require continuous therapy and subsequently develop adverse effects such as immunosuppression, weight gait and skin changes.[14]

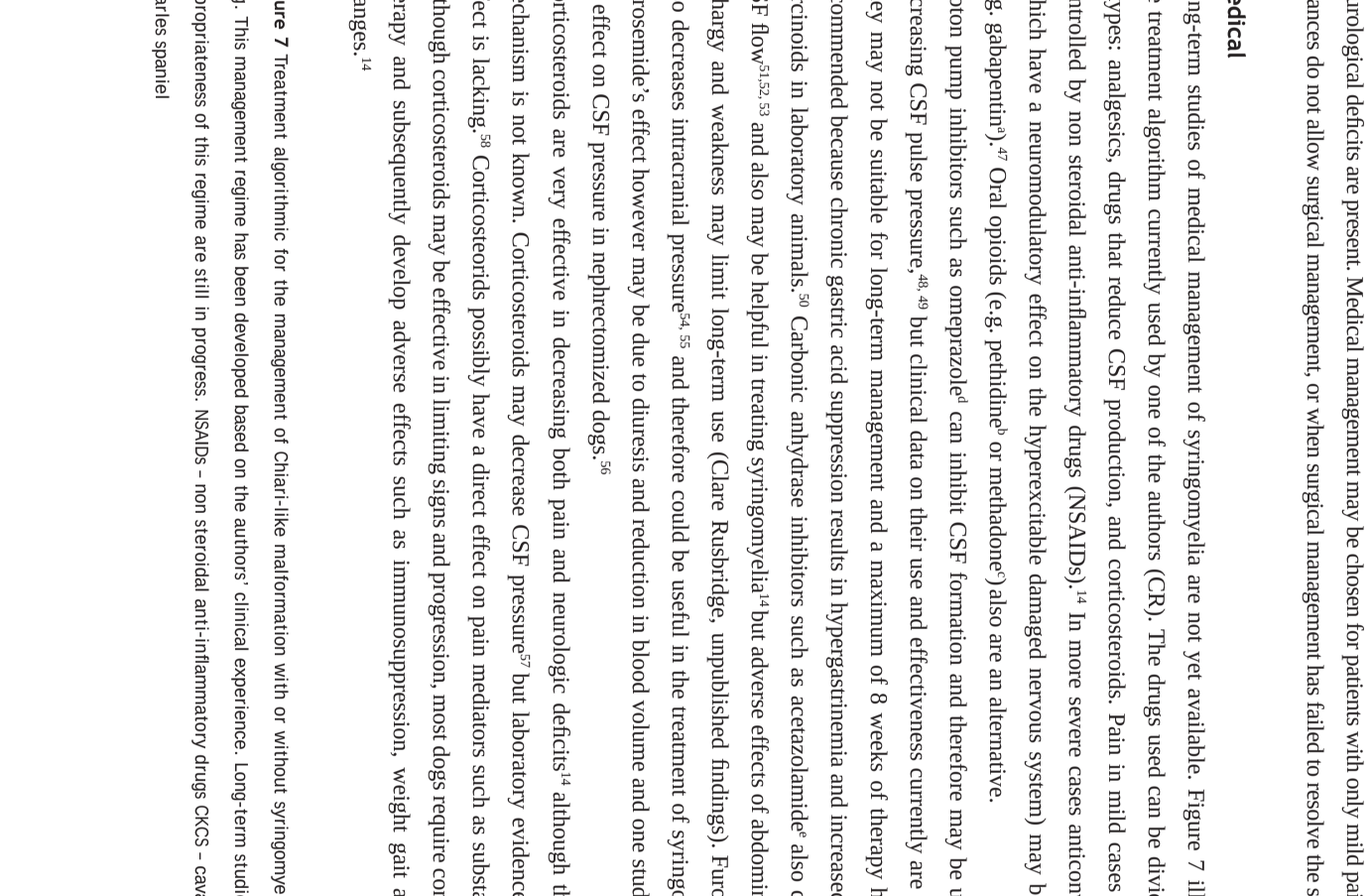

Figure 7 Treatment algorithmic for the management of Chiari-like malformation with or without syringomyelia in the dog. This management regime has been developed based on the authors' clinical experience. Long-term studies on the appropriateness of this regime are still in progress. NSAIDs – non steroidal anti-inflammatory drugs CKCS – cavalier King Charles spaniel

Surgical

Surgical management is indicated for dogs with refractory pain or with worsening neurologic signs. The aim of surgery is to restore CSF dynamics and if this effect can be achieved (e.g. by removing or debulking a tumour) then the syrinx can resolve.[60] The most common procedure for caudal fossa overcrowding is cranial cervical (also referred to as foramen magnum or suboccipital) decompression in which the supraoccipital bone and sometimes the cranial dorsal laminae of the atlas are removed (with or without a durotomy) to decompress the foramen magnum.[15, 61, 62, 63] Success reported in the small number of dogs in these studies varied from no improvement [62] to resolution of clinical signs.[15 63] The largest case series of 16 dogs found that 81.25% of affected dogs had improvement or resolution of clinical signs after surgery, but 25% had a recurrence within the follow-up period. This report also indicated that successful postoperative outcome was more likely if surgery was performed early in the course of the disease.[63] There have been no reports of resolution of syringomyelia after cranial cervical decompression in the dog, but this impression may be in part due to lack of postoperative MRI scans due to financial reasons. Syringo-subarachnoid shunting also has been described. [64]

The general principle for surgical management of humans with syringomyelia is that treatment should be directed at the etiology of the syrinx. [2] Cranial cervical decompression is generally the first procedure of choice for symptomatic humans with Chiari malformation, and it is widely acknowledged that direct draining of the syrinx is not associated with a good long-term outcome because stents or shunts become obstructed and can result in tethering [2]. Shunting to the subarachnoid space or to the pleural cavity is only indicated when the syrinx persists or is progressive after suboccipital decompression.[2, 65] There is great variation in the type of cranial cervical decompression performed. One key argument focuses on whether or not to open the dura. Most surgeons favour routine dural opening at surgery and closure with a pericranial or synthetic patch graft.[2,65] The arguments against dural opening are that this procedure increases the complication rate. Advocates however argue that up to 55% of patients have extensive scarring and other obstructions to CSF flow that can only be identified and removed by durotomy. [66, 67] Some recommend intraoperative ultrasound to tailor surgery to the individual and ensure that optimal CSF flow through the foramen magnum is achieved. [68]

Another crucial issue in surgery for Chiari malformation is the number of patients requiring two or more surgeries. Most large case series in human medicine report a failure rate of at least 10%. [68,69] Researchers have been unable to identify a single reason for surgical failure. [65, 66]. Also of concern is the number of patients with persistent pain post-operatively. Approximately 41% of humans with symptoms of dysesthesia who undergo decompressive surgery for syringomyelia have persistence or intensification of pain post-operatively. Conventional medications such as NSAIDS, opioids and gabapentin provide minimal or no relief and, based on response to sympathetic blockade, pain is thought to be sympathetically mediated. Most human patients gradually improve over several months but in many persistent unpleasant sensations persist.[70] As previously mentioned, damage to dorsal horn and duration of signs are thought to be significant [35,39] and, in a study of persistent post-operative dysesthetic pain, 84% of patients experienced extension of the syrinx into the dorsolateral quadrant of the spinal cord on the same side and level of the pain.[70] In conclusion, our understanding of syringomyelia that results from caudal fossa abnormalities, specifically its pathogenesis and exact relationship to the clinical syndrome still is incomplete. The new theories based on physical principles seem promising and may shed new light on the pathophysiology of syringomyelia. This disorder is an area of active research and it is hoped that the recent description of a naturally-occurring animal model of the condition in the CKCS will encourage the veterinary profession to contribute to the understanding of this debilitating condition.

Foot notes

a. Neurontin 100mg capsules, Pfizer Pharmaceuticals, Ltd. Vega Baja, PR 00694
b. Pethidine hydrochloride 50mg Martindale Pharmaceuticals, Romford, Essex, RM3 8UG
c. Methadone Hydrochloride tablets usp 5 mg, 10 mg, Physeptone, Martindale Pharmaceuticals, Romford, Essex, RM3 8UG
d. Losec capsules 10, 20, and 40 mg; AstraZeneca, Hurdsfield Industrial Estate, Macclesfield, Cheshire, SK10 2NA
e. Diamox 250mg tablets, Lederle Laboratories, Gosport, UK
f. Frusemide tablets 20 and 40mg; Millpledge Pharmaceuticals, Whinleys Estate, Church Lane, Clarborough, Retford, Notts, DN22 9NA
g. Rimadyl Palatable Tablets 20 and 50mg; Pfizer Limited, Ramsgate Road, Sandwich, Kent CT13 9NJ
h. Medrone tablets 2 and 4mg; Pfizer Limited, Ramsgate Road, Sandwich, Kent CT13 9NJ

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