

# Chiari-like malformation in the Griffon Bruxellois

**OBJECTIVES:** This study describes Chiari-like malformation and syringomyelia in the Griffon Bruxellois and establishes if skull radiographs are useful for disease prediction.

**METHODS:** Magnetic resonance imaging from 56 Griffon Bruxellois dogs was assessed for Chiari-like malformation and cerebrospinal fluid pathway abnormalities. Skull radiographs were obtained in 33 dogs. Two rostrocaudal and two ventrodorsal measurements were made, and ratios of one length to another were compared.

**RESULTS:** In this selected sample, 60.7 per cent had Chiari-like malformation. Syringomyelia occurred with and without Chiari-like malformation (37.5 and 8.9 per cent study population, respectively). The radiographic study demonstrated that one measurement ratio could be used to predict Chiari-like malformation (sensitivity of 87 per cent and specificity of 78 per cent) and that there were significant interaction factors between sex and syringomyelia for two measurement ratios.

**CLINICAL SIGNIFICANCE:** The study suggests that Chiari-like malformation is characterised by a shortening of the basicranium and supraoccipital bone with a compensatory lengthening of the cranial vault, especially the parietal bone. We described a simple radiographic technique, which may be useful as a screening test until a more definite genetic test for Chiari-like malformation is available.

C. RUSBRIDGE, S. P. KNOWLER, L. PIETERSE\*  
AND A. K. MCFADYEN†

*Journal of Small Animal Practice* (2009)  
**50**, 386–393  
DOI: 10.1111/j.1748-5827.2009.00744.x  
Accepted: 2 January 2009

Stone Lion Veterinary Centre, 41 High Street,  
Wimbledon SW19 5AU

\*<http://www.statuesquedogs.com>

†School of Engineering and Computing,  
Glasgow Caledonian University, Cowcaddens  
Road, Glasgow G4 0BA

## INTRODUCTION

The Griffon Bruxellois (GB) is a brachycephalic toy with terrier characteristics, which has origins from the Smousje (an Affenpinscher-like dog), pug and ruby toy spaniel (Cousens 1969). The toy spaniel is also one of the ancestral dogs for the cavalier King Charles spaniel (CKCS) (Dalziel 1897, Stenning 1980). Both the CKCS and the GB have predisposition for Chiari-like malformation (CM) and syringomyelia (SM), and the conditions are suspected to be inherited in these breeds (Rusbridge 2007). CM is characterised by disparity in size between the brain (too big) and the caudal fossa

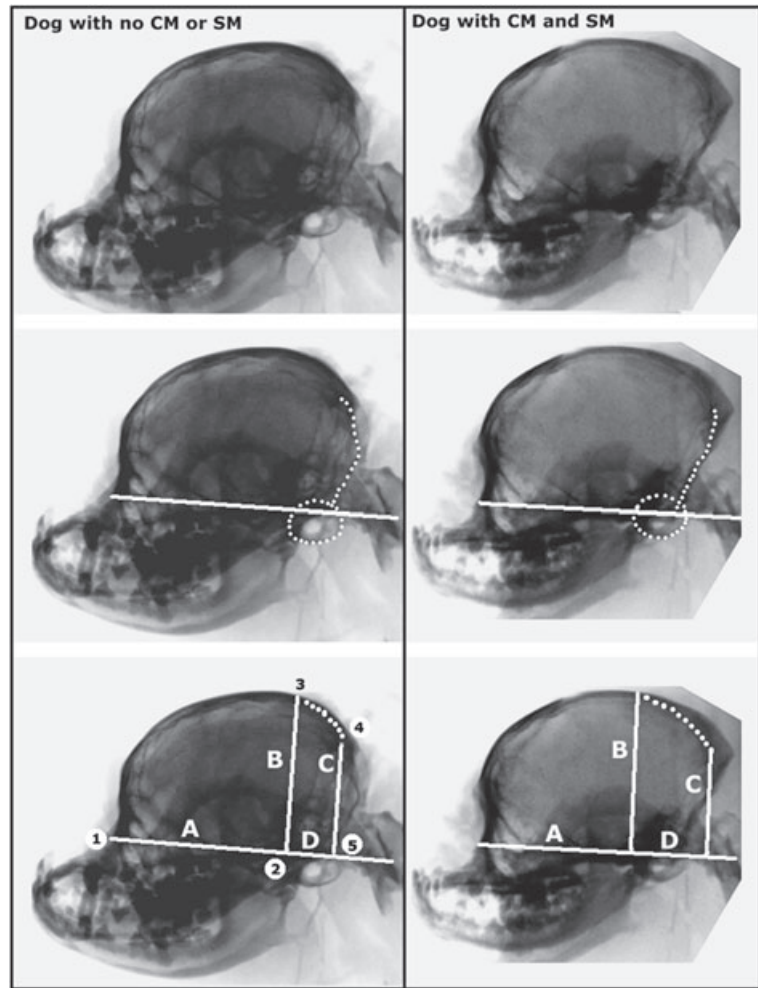
(too small) such that the cerebellum and brainstem are herniated into or through the foramen magnum (Rusbridge and others 2000). There is an association between CM and SM, which is thought to be related, at least in part, to obstruction of cerebrospinal fluid (CSF) through the foramen magnum (Levine 2004, Rusbridge and others 2006). CM/SM can only be confirmed by magnetic resonance imaging (MRI). The prohibitive cost of MRI screening has prompted breeders and veterinarians to investigate cheaper alternatives for early selection of breeding dogs that confer a low risk of CM/SM. The purpose of this study was to characterise the disorder within GB, to identify which GB dogs within an extended family had CM and/or SM, to obtain DNA for subsequent genetic studies and to establish if assessment of skull radiographs could be used to predict CM and/or SM.

## METHODS

A total of 59 GB dogs were originally included in the study – the criteria for inclusion being the availability of appropriate MRI and clinical history. The primary reason for investigation of 44 of the 59 dogs (36 related and eight unrelated, none residing in the UK) was as part of a programme for identifying CM/SM status and collecting DNA for a proposed genome scan. The remaining cases had MRI investigation either as screening for breeding purposes (12 dogs) or as part of a diagnostic investigation (three dogs). All the dogs were owned as pets or for breeding and resided in Australia (37 dogs), Finland (three dogs), USA (six dogs), the Netherlands (eight dogs) and the UK (five dogs). Historical signs of CM/SM were recorded by a questionnaire form before MRI. The details of the questionnaire form have been previously described (Rusbridge and others 2005). Each dog had an MRI scan of the head and neck. Because of varying geographical locations, different machines and protocols were used; however, all images included as a minimum, T1W and T2W sagittal and transverse images of the brain and

cervical spinal cord. All the images were assessed for the presence of CM, SM, spinal cord's central canal dilatation less than 2 mm wide (CCD) and ventricular dilatation (VD). SM was defined as a fluid-containing cavity within the spinal cord parenchyma. For the purposes of statistical analysis, SM is referred to as a syrinx, which has a transverse diameter greater than or equal to 2 mm wide and is coded as 2. Smaller syrinxes and central canal dilatation less than two millimetres wide have been grouped together and coded as 1, and dogs without syrinx or central canal dilatation have been coded as 0. Ventricular dilatation (VD) was graded none (value 0), mild (value 1) (dilatation of rostral and caudal horns of lateral ventricle with less than 2 mm or no dilatation of ventral horn of the lateral ventricle as assessed from transverse T1W MRI images), moderate (value 2) (ventral horn of the lateral ventricle dilated) and severe (value 3) (surrounding temporal lobe cortex thinner than the width of the dilated ventral horn of the lateral ventricle). The assessment of the MRI was made by one of the authors (C. R.) blinded to the results of the questionnaires and radiographs.

Radiographs of lateral skull were obtained for 33 of 59 dogs, 25 related to each other and eight unrelated to this group. Whether skull radiographs were obtained or not depended on owner preference. To attain the radiographs, the dogs were anaesthetised or deeply sedated and the heads were symmetrically positioned so that both tympanic bullae were superimposed on the resulting radiographic image. To improve contrast and aid landmark identification, the digital images of the radiographs were black and white inverted so that the bone had a grey tone. It was then windowed so that areas of greatest bone density were black. Measurements were made (Fig 1) to allow comparison between skull dimensions. The most rostral point of the nasal bone (identified as change in bone density), the tympanic bullae, the basioccipital bone, the occipitoatlantal joints and the area of the lambdoid (occipitoparietal) suture (this was defined as the centre of the area of dense bone rostral to the occipital crest) were identified. A line was drawn from nasal bone (point 1) following the basioccipital bone (that is the caudal fossa



**FIG 1.** Measurements from skull radiographs. Skull radiographs from two Griffon Bruxellois dogs. A normal dog is on the left and a dog with Chiari-like malformation (CM)/syringomyelia (SM) is on the right. Top row, digital images of the radiographs were black and white inverted and windowed so that areas of greatest bone density were black. Middle row, a line was drawn from rostral nasal bone (point 1) following the basioccipital bone and through the dorsal occipitoatlantal joint. An ovoid shape (dotted ovoid) was drawn that was bisected by the line and incorporated the tympanic bullae for its ventral border. A dotted line extends from this, following the outline of the supraoccipital bone, and terminating dorsally at the area of the lambdoid suture. The bisection of tympanic bullae ovoid with solid line was designated point 2, and the area of the lambdoid suture was designated point 4. Bottom row, the following measurements were then made: A, rostral nasal bone (point 1) to bisection of tympanic bullae ovoid with solid line (point 2); B, point 2 to perpendicular point on the dorsal cranium (point 3); C, area of the lambdoid suture (point 4) to perpendicular point on the solid line (point 5) and D, point 2 to 5

skull base) and through the dorsal occipitoatlantal joint. Next, an ovoid shape was drawn that was bisected by the line and incorporated the tympanic bullae for its ventral borders. The rostral point at which this ovoid bisected the line was designated point 2. A perpendicular line from point 2 was drawn and continued to the dorsal cranium (point 3). Finally, a second perpendicular line was drawn from the area of the lambdoid (occipitoparietal) suture (point 4) to bisect the horizontal line at point 5. The following measurements were then

made: point 1 to 2 (A, representing the rostral cranium length), point 2 to 3 (B, representing the height of the cranium), point 4 to 5 (C, representing the height of the cranium to the level of the occipital crest) and point 2 to 5 (D, representing the caudal cranium length). These landmarks and measurements had been decided following several (unpublished) pilot studies that found these to be the most consistent and accurately identified by different viewers using skull radiographs of variable quality and technique and facilitated

investigation of the (null) hypothesis that CM altered the rostrocaudal and ventrodorsal dimensions of the skull. To allow comparison between individual dogs with varying bodyweight (and therefore skull size), ratios of the measurements were compared as follows: A/B, A/C, A/D, B/C, B/D and C/D. The assessment of the radiographs was made by one of the authors (S. P. K.) blinded to the results of the MRI. Summary statistics of each of the six ratio measures were calculated for each category of sex, CM, SM and VD. Four-factor unbalanced general linear analysis of variance (ANOVA) models were then used to analyse each of the six ratio measures. Age was not found to be highly correlated with any of the ratios and hence was not used as a cofactor. A multiple discriminant analysis model was developed in an attempt to ascertain which of the ratios best discriminated between those dogs with and without CM. The level of significance was set at 1 per cent, and single-factor tests were used to ascertain if there was a significant difference in the means of the length ratios between (1) male and female dogs, (2) dog with and without CM, (3) dogs with and without SM and (4) dogs with CM and dogs with CM/SM. All statistical analysis was performed using GenStat v10, SPSS v15 or Microsoft Excel.

## RESULTS

### Study population

MRI studies and questionnaires were available from 59 dogs. Three dogs with CM and without SM but aged less than 2.5 years were subsequently excluded because SM is

an early- to late-onset disease and consequently disease status can change with age. The 2.5 years cut-off is the current accepted guideline for the CKCS breed (Cappello and Rusbridge 2007). Two dogs with CM/SM less than 2.5 years (1.5 and 1.7 years, respectively) were included as their disease status was confirmed. Consequently, a total of 56 GB dogs were analysed (25 entire males, one neutered male, 25 entire females and five neutered females). The oldest dog was 12.6 years, and the mean age was 5.0 years with a median of 4.8 years.

### Clinical and MRI findings

The MRI findings of the 56 dogs are detailed in Table 1. Eleven dogs were clear of CM, SM or CCD (Fig 2a). Nine dogs had CM only (Fig 2b), and 25 dogs had CM in conjunction with SM or CDD, with 21 of 25 having SM equal to or greater than 2 mm (Fig 2c). Seven dogs did not have CM but had SM, two of seven had SM less than 2 mm wide that was dorsal to and appeared unconnected to the central canal in sagittal views (Fig 2d) and five of seven had SM that was equal to or greater than 2 mm (Fig 2e). Four dogs had CDD only (Fig 2f). Four dogs had clinical signs of CM/SM, one additional dog with CM/SM and marked ventricular dilatation also had a large C6/C7 intervertebral disc extrusion, which could have contributed to her signs of neck pain and tetraparesis. Fifty dogs had no clinical signs of pain or neurological deficits recorded by the owner or examining veterinarian.

Ventriculomegaly was common, with only five of 56 dogs (8.9 per cent) having normal-sized ventricles and 42 of 56 dogs (75 per cent) having moderate or severe

dilatation of the lateral or entire ventricular system. If the dog had CCD or SM (36 dogs), then it was highly likely to have a dilated ventricular system with 34 of these 36 (94.4 per cent) having moderate or severe dilatation.

### Familial relationships and CM/SM status

Thirty-two of the dogs were closely related, and their familial connection and CM/SM status are represented in Fig 3. The core of the family tree is made up of three key females; bitch 1 (unaffected) and bitches 3 and 5 (asymptomatic CM/SM) and two "normal" males (dogs 2 and 4). Only one of the 10 MRI-screened offspring from bitches 3 and 5 was clear of disease, and when a first-generation descendant had CM, the bony defect was always in conjunction with SM that was equal to or greater than 2 mm wide. Three of these first-generation descendants with CM/SM had associated clinical signs, and when one was mated to a half-sister, the single male offspring also had clinical signs of CM/SM. Three of the descendants from bitches 3 and 5 were clear of CM; however, all these dogs had a CCD or SM less than 2 mm wide. Two of these dogs (half-siblings) were mated, and two of four offspring had asymptomatic CM. All descendants from a mating between the normal bitch 1 and the dog 2 were free of CM. However, three of the descendants had SM or CCD without the presence of the bony defect. When dog 2 was mated to two bitches of unknown status, all the offspring (two dogs) had asymptomatic CM/SM.

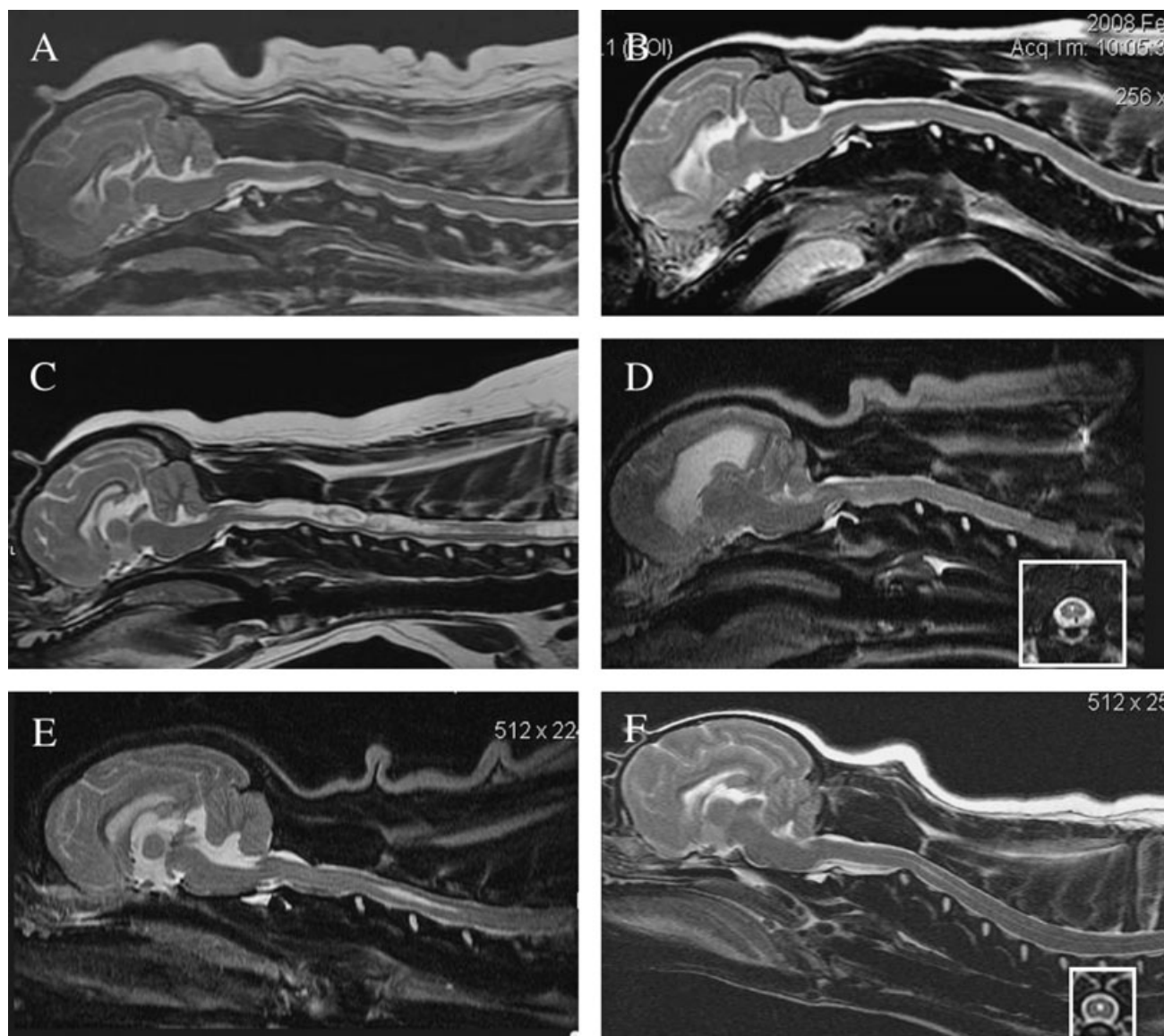
### Radiographic study

Of the 56 dogs included in the study, radiographs were available from only 35. Radiographs from two of 35 dogs were rejected because the images obtained were too rotated, leaving 33 dogs for analysis. The summary results of radiographic measurements for these 33 dogs are indicated in Table 2. The final ANOVA models for the A/B, A/C and B/C ratios yielded no significant factors or interactions. For the A/D ratio, a very significant CM effect was observed ( $P=0.001$ ) but no significant interactions were found. For both the B/D and the C/D ratios, the CM factor was also very significant ( $P<0.001$

**Table 1. Magnetic resonance imaging findings in 56 Griffon Bruxellois dogs**

Dogs	Total	Normal VD	Mild VD	Moderate VD	Severe VD
No CM or CCD or SM	11	4	2	4	1
No CM with CCD/SM<2 mm	6	0	0	5	1
No CM with SM $\geq$ 2 mm	5	0	1	2	2
CM only	9	1	5	2	1
CM with CCD/SM<2 mm	4	0	0	4	0
CM with SM $\geq$ 2 mm	21	0	1	15	5
Total	56	5	9	32	10

VD Ventricular dilatation, CCD Central canal dilatation less than 2 mm wide, SM Syringomyelia, SM<2 mm Syringomyelia is less than 2 mm wide, SM $\geq$ 2 mm Syringomyelia is equal to or greater than 2 mm wide. Thirty-four dogs had Chiari-like malformation (CM), and 22 dogs did not have CM

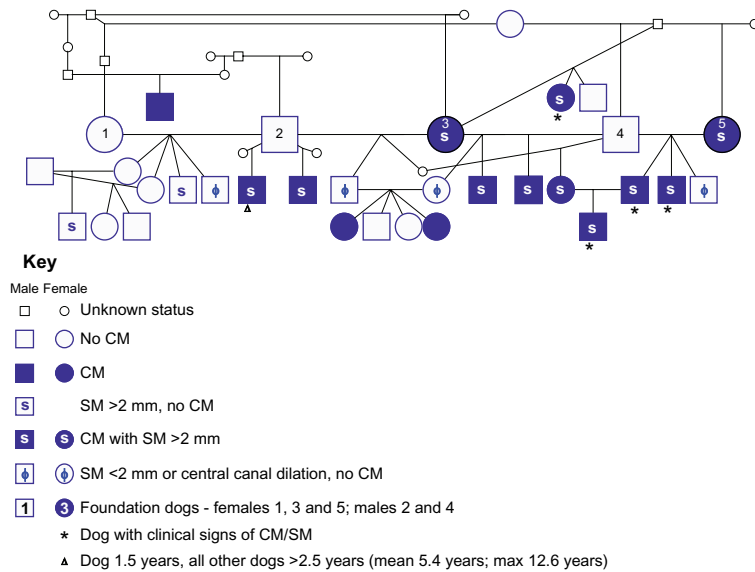


**FIG 2.** Examples of magnetic resonance imaging features of Chiari-like malformation (CM)/syringomyelia (SM) syndrome in Griffon Bruxellois. (a) Normal (sagittal mid-line T2W brain and cervical spinal cord). (b) CM (sagittal mid-line T2W brain and cervical spinal cord). There is coning of the cerebellar vermis into the foramen magnum and moderate ventriculomegaly. (c) CM/SM (sagittal mid-line T2W brain and cervical spinal cord). Note the fluid-filled cavity within the spinal cord. Low signal within high signal fluid is because of fluid movement (fluid flow-void). (d) CM with SM less than 2 mm (sagittal mid-line T2W brain and cervical spinal cord with insert of transverse T2W spinal cord at level of dens). Immediately dorsal to the dens, there is a small area of high signal within the spinal cord. In this dog, there is also severe dilatation of the lateral ventricles. (e) SM and no CM with moderate ventriculomegaly (sagittal mid-line T2W brain and cervical spinal cord). (f) Central canal dilation and no CM (sagittal mid-line T2W brain and cervical spinal cord with insert of transverse T2W spinal cord at level of mid-C2)

for both). These two ratios, however, also yielded very significant interaction factors between sex and SM ( $P=0.002$  for B/D and  $P=0.004$  for C/D). From interaction plots (Fig 4), it was clear that in both ratios for the SM=1 (that is CCD/SM <2 mm category), no difference was present, but for SM=0 (that is no SM), the female mean ratios were slightly higher than those of the males. The more obvious

difference was, however, that for SM=2 (that is SM  $\geq 2$  mm), the female mean ratios were considerably lower than those of the males. Figure 5 plots the values of all the ratios with normal dogs tending towards the left of the x-axis and dogs with CM/SM tending towards the right of the x-axis. This graph illustrates the general trend that the ratios A/D, B/D and C/D tended to decrease when the dogs had CM

and CM/SM. Formally, the discriminant analysis model suggested that the C/D ratio was the only ratio which could predict CM category, and a cross-validation of the model suggested that it was 81.8 per cent successful. Interpretation of the discriminant function estimated that if the C/D ratio for a dog exceeded 1.92, then CM was not present, and conversely, if the C/D ratio was less than 1.92, the dog



**FIG 3.** Family tree of 32 related Griffon Bruxellois dogs. The core of the family tree consists of five foundation animals (numbered 1 to 5) consisting of two normal dogs, one normal bitch and two bitches with asymptomatic Chiari-like malformation (CM)/syringomyelia (SM). The two asymptomatic CM/SM bitches had seven descendants with CM/SM, and four of these had clinical signs. Three first-generation descendants were free of CM, although they did have a CCD or an SM less than 2 mm wide. Two of these dogs (half-siblings) were mated, and two of four offspring had asymptomatic CM. One branch of the family tree was the product of a mating between normal bitch 1 and dog 2, and all animals were free of CM. However, three of the descendants had SM or CCD without the bony defect

was likely to have CM. A sensitivity and specificity analysis of these results suggests a sensitivity of 87 per cent and a specificity of 78 per cent.

**DISCUSSION**

This investigation found a 60.7 per cent incidence (34 of 56) of CM. The study

sample was not random, however, to find such a frequency suggests a predisposition in this breed and that further studies on incidence are warranted. Previous papers have suggested that CM in the dog predisposes to SM, and in some cases, especially when the syrinx is wide, this may be painful and debilitating (Rusbridge and others 2007). The current study found that 61.7 per cent of the CM-affected dogs had SM equal to

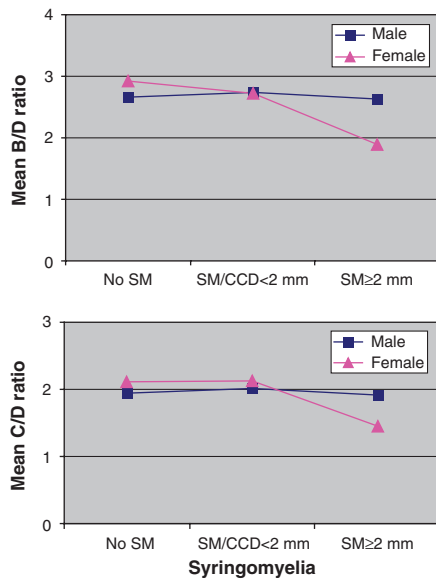
or greater than 2 mm wide (37.5 per cent of the total population). However, 22.7 per cent of the dogs without CM also had SM equal to or greater than 2 mm (five of 22 dogs). A very significant association was found (P=0.004, chi-squared analysis) between dogs having CM or not and dogs having SM greater than or equal to 2 mm or not. These findings suggest that CM is an important risk factor for SM but that other factors may be involved in the pathogenesis. In some instances, dogs with SM but without CM can have dilatation of the entire ventricular system, suggesting that there may be obstruction of the foramen magnum other than CM, for example arachnoiditis (Klekamp and others 2002) and/or an imbalance between CSF production and absorption (Portnoy and others 1994, Levine 2008).

Only four of the 26 dogs with SM equal to or greater than 2 mm had clinical signs of disease, and all these dogs had dams with asymptomatic CM/SM. This highlights a significant problem for breeders, namely that dogs with clinical signs are a minority of the total CM/SM-affected population; however, breeding of asymptomatic dogs can result in offspring with clinical disease. As has been previously described, the syndrome of CM/SM can become more severe in each generation (Rusbridge and Knowler 2004). Breeders are not able to ascertain if their stock is affected without resorting to MRI, which has limited availability and a prohibitive cost.

**Table 2. Summary of skull radiograph ratios**

Ratio		All	Gender		CM		SM		
			Male	Female	No	Yes	No SM	<2 mm/CCD	>2 mm
A/B	n	33	18	15	18	15	16	4	13
	M	1.086	1.073	1.102	1.087	1.085	1.080	1.082	1.094
	se	0.029	0.023	0.058	0.012	0.060	0.020	0.018	0.070
A/C	M	1.472	1.474	1.470	1.477	1.466	1.487	1.456	1.459
	se	0.019	0.029	0.024	0.026	0.029	0.027	0.027	0.036
	M	2.851	2.857	2.844	3.175	2.463	3.051	2.964	2.570
A/D	se	0.093	0.118	0.153	0.106	0.086	0.128	0.230	0.135
	M	1.370	1.376	1.361	1.360	1.381	1.378	1.346	1.367
	se	0.019	0.012	0.041	0.013	0.040	0.012	0.035	0.047
B/C	M	2.647	2.658	2.634	2.922	2.317	2.820	2.737	2.406
	se	0.080	0.082	0.150	0.084	0.089	0.097	0.207	0.134
	M	1.938	1.937	1.939	2.152	1.682	2.050	2.046	1.768
C/D	se	0.060	0.070	0.104	0.068	0.051	0.074	0.190	0.094

CM Chiari-like malformation, SM Syringomyelia, n Sample size, M Mean, se Standard error Ratios A/B, A/C, A/D, B/C, B/D and C/D were compared, and four-factor unbalanced general linear ANOVA models were then used to analyse each of the six ratio measures between (1) male and female dogs, (2) dog with and without CM, (3) dogs with and without SM and (4) dogs with CM and dogs with CM/SM Differences with P<0.01 were considered significant

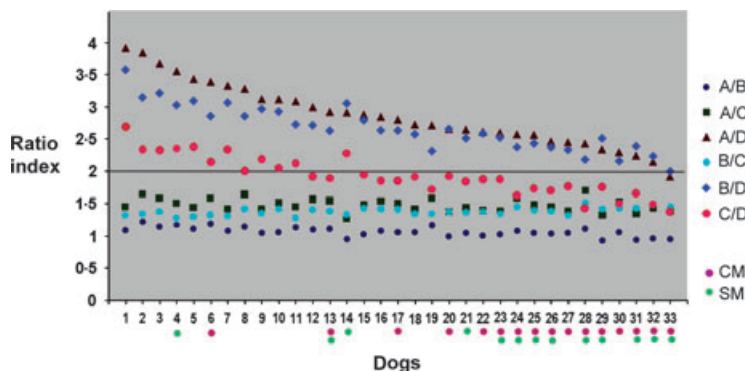


**FIG 4.** Interaction plots between syringomyelia (SM) and sex. For the B/D and C/D ratios, there were very significant interaction factors between sex and SM. When SM=2 (SM≥2 mm), the female mean ratios were considerably lower than those of the males, and when SM=0 (no SM), the female mean ratios were slightly higher than those of the males. When SM=1, that is the SM/CCD category, no difference was observed

Pedigree analysis suggested involvement of genetic factors in the aetiology of both CM and SM; further genetic investigation is ongoing and is the subject of a separate study. The family tree (Fig. 3) illustrated an interesting back-cross of two half-siblings with no CM and CCD/SM less than 2 mm. These dogs shared a common asymptomatic CM/SM-affected dam. Half of the progeny of this mating had CM. This suggests that some sort of carrier state for CM may exist, and dogs with apparently normal skulls can still confer

risk for passing on the bony disorder to their offspring.

This study showed that taking four measurements from skull radiographs and using one of them, D, in a ratio with some of the others may be useful to predict CM. In particular, evidence from this small study would appear suggest that the C/D ratio can, with reasonable accuracy, predict CM. If the C/D ratio for a dog exceeded 1.92, then CM was not present, and conversely, if the C/D ratio was less than 1.92, the dog was likely to have CM

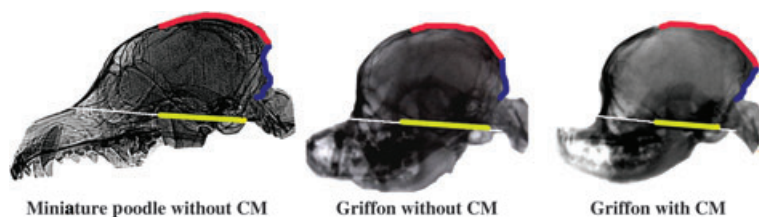


**FIG 5.** Plot of skull radiograph ratios. Skull radiograph ratios (y-axis) for 33 Griffon Bruxellois dogs (x-axis). The dogs are ranked according to descending A/D. Coloured dots (purple for Chiari-like malformation [CM] and green for syringomyelia [SM]) indicate the disease status of individual dogs. A ratio value of 2 is indicated as a horizontal black line. The C/D ratio can be used to predict CM. Dogs with a C/D ratio less than 1.92 were more likely to have CM (a sensitivity of 87 per cent and a specificity of 78 per cent)

(a sensitivity of 87 per cent and a specificity of 78 per cent). It follows therefore that a skull radiographic assessment could be useful and economic for screening for CM in this breed. As there was a significant association between SM and CM, it may also be useful as a prebreeding screening test to reduce the incidence of SM in this breed. A radiographic assessment may also be applicable for puppies, aiding the breeder in his or her initial selection of potential breeding stock. This could be backed up by an MRI assessment when the dog was older. Ideally, however, a genetic test would be more accurate and replace all phenotypic assessment by either radiographs or MRI.

It should also be realised that although this study found a method of predicting CM in the GB, this may not be transferable to other breeds. This may be especially true for the CKCS where CM is almost ubiquitous (Cerdeira-Gonzalez and others 2009). Establishing the normal skull shape could be difficult, and in this breed, it would be most useful to have a test, which reliably predicts which dogs have or carry the tendency for SM. This study did not find a simple way of predicting which dogs had SM. However, there was a significant interaction between sex, SM and ratios B/D and C/D. Females with SM equal to or greater than 2 mm had a lower B/D and C/D; that is compared with males, they had more exaggerated changes in the skull so that D was larger or B and C were smaller or all three of these scenarios.

The normal GB skull was first studied by Charles R. Stockyard whose monograph of his lifetime's work on the genetic and hormonal influences on skeletal development was published in 1941 after his death (Stockyard 1941). Stockyard described the GB as a midget dog, that is of short stature with proportionately short limbs, and distinguished it from the achondroplastic condition of other diminutive dogs such as the dachshund. He described the GB skull as having a disproportionately large spherical cranium with an extremely abbreviated facial skeleton with a very short mandible and maxillae. Stockyard went on to show that brachycephalic dogs such as the GB and the English bulldog have defective growth of the basioccipital and basisphenoid bones,



**FIG 6.** Skull comparisons with and without Chiari-like malformation (CM). Comparison between a dolichocephalic 4.5 kg miniature poodle, a normal brachycephalic 5.7 kg Griffon Bruxellois and a 7.8 kg Griffon Bruxellois with CM/syringomyelia. Red, approximates outline of parietal and interparietal bone. Blue approximates outline of supraoccipital bone. Yellow approximates the basicranium. Note that as a dog becomes more brachycephalic, the basicranium shortens and the skull becomes rounded dorsally and rostrally. In the dog with CM, there is a further shortening of the basicranium, the supraoccipital bone is shorter and straighter and there is an apparent compensatory lengthening of the parietal bone

resulting in shortening of the basicranial axis. The premature fusion of one or more cranial sutures, termed craniosynostosis, alters normal skull growth patterns and results in compensatory changes in the cranial vault (Smit-Vis and Griffioen 1987). Because of the rostral to caudal shortening in the brachycephalic dog, the skull becomes rounded dorsally and rostrally, and the dog has a comparatively broad head. Consequently, the normal GB skull is wider than its length, in comparison to the German shepherd dog, which is often twice as long as it is wide (Stockyard 1941). Our radiographic study has provided further information regarding the bony defect associated with CM. The basicranium (skull base) is formed by three bones – the basioccipital, the basisphenoid and the presphenoid (Evans 1993) – and the caudal fossa is defined by the pyramidal occipital bones – the supraoccipital, basioccipital and paired exoccipitals (Evans 1993, Rusbridge and Knowler 2006). The changes in the skull ratios suggested that with CM, D is longer. D becomes longer if the basicranium shortens and other skull bones of the cranial vault, in particular the parietal bone, lengthen. Of the three D ratios, C/D was the most useful for predicting CM. C represented the height to the occipital crest. A possible explanation is that in addition to a short basicranium and longer parietal bone, dogs with CM have a shorter supraoccipital bone. Figure 6 illustrates these bony changes. It has been proposed that CM is caused by an occipital hypoplasia (Vega and others 1990, Rusbridge and others 2000), and it is suggested that this is because of premature fusion of lambdoid

(occipitoparietal) and cranial base sutures (Cinalli and others 2005, Raybaud and Di Rocco 2007). This study supports this hypothesis providing further evidence that the basioccipital bone is shortened. We are further proposing that the basisphenoid and possibly presphenoid are also shortened, that is shortening of the entire basicranium. We are hypothesising that this additional rostral to caudal shortening in an already brachycephalic dog results in a further compensatory change in the cranial vault, resulting in an apparent lengthening of the parietal bone. Compensatory skull changes with CM, secondary to craniosynostosis, have been previously described in human beings (Pouratian and others 2007). We also suggest that the supraoccipital bone is abnormal. Figures 1 and 6 illustrate how the supraoccipital bone is less rounded, giving the back of the skull a pushed-in appearance. A question which emerges is – if growth of the skull and brain is closely linked and shortening of one area will result in a compensatory increase in another – why is the supraoccipital bone not larger, thereby accommodating the developing cerebellum? One explanation is inadequacy of the supraoccipital bone because of premature closure of lambdoid suture (Cinalli and others 2005, Raybaud and Di Rocco 2007). However, another answer is suggested by study of the development of cerebellum. Examination of normal human fetuses found that growth of the bony caudal fossa parallels the cranial fossa and appears to be in advance and independent of cerebellar growth (Griffiths and others 2004). In other words, as the skull base is shortened, the

enlarging forebrain is accommodated by lengthening of the other bones; however, the cerebellum develops later and grows into an already predestined space formed by the pyramidal occipital bones. If there is a disparity in volume because of inadequate bony growth, then no additional compensation is possible. Further work is necessary to prove this hypothesis, and studies of fetal and neonatal skulls would be invaluable.

Another recent study has suggested abnormal development of supratentorial as well as infratentorial cranium in CM/SM syndrome in the dog. Scrivani and others (2007) described how SM was associated with small frontal sinuses. The volume of the frontal sinus is reduced with brachycephalism (Evans 1993), and it is possible that the compensatory changes required to accommodate the forebrain following CM and skull base shortening forces a further reduction.

Another possible contributory factor to CM/SM, which has not been investigated in this study, is brain size. Studies in the CKCS have suggested that in CM, not only is the caudal fossa small but also the brain is comparatively large, which further compounds the problem (Cross and others 2009).

Ventricular dilatation was a common feature in the GB as it is with other breeds with CM and brachycephalism (Rusbridge and others 2000). Ventricular dilatation can occur secondary to obstruction of the CSF pathway, for example at the foramen magnum (Levine 2004, Rusbridge and Knowler 2004); however, another possible contributory mechanism is intracranial hypertension (Moritani and others 2006). It has been postulated that only a small abnormal gradient of static pressure across the cerebral mantle is sufficient to produce ventricular dilatation (Levine 2008). This has not been investigated in dogs with CM; however, in human beings, it has been demonstrated that venous narrowing at the jugular foramina associated with a small skull base can lead to elevated venous pressure (Cinalli and others 2005). This impairs CSF absorption, resulting in communicating hydrocephalus (Moritani and others 2006). It is also possible that this could be a contributory mechanism to the development of SM in dogs, especially in those GB

dogs that had no evidence of CM. It has also been proposed that in human beings, herniation of the cerebellum and brainstem in craniosynostosis is not only a consequence of the anatomical deformity and small posterior fossa but also because of this intracranial hypertension (Thompson and others 1997). Further work is required to investigate this hypothesis.

In conclusion, we are proposing that CM in the GB dog is characterised by a shortening of the basicranium, a deficiency of the supraoccipital bone and a compensatory lengthening of other bones in the skull, especially the parietal bone. This could be because of insufficiency of the bone and/or craniosynostosis of the lambdoid (occipitoparietal) and cranial base sutures. We described a simple technique for quantifying these bony changes, which may be useful as a low-cost prebreeding screening test until a more definite genetic test for CM is available. SM in the GB occurs with and without CM; it is hypothesised that the bony changes in brachycephalism and/or CM could result in intracranial hypertension, which could be a contributory factor in the pathogenesis of both ventriculomegaly and SM.

## Acknowledgements

The cost of the diagnostic investigation of many of the dogs in this study was paid for by public donations to "Syringomyelia DNA Research" and the "For the Love of Ollie" fund <http://sm.cavalier-talk.com/research/research/donate.html> and by one of the authors (L. P.). We also wish to thank the many veterinarians who obtained the diagnostic images and the breeders who invested their resources into this project. Particular thanks to Ted Humphries, Blair

Kurtz, Dr Anthony Black, Dr Erik Noorman, Dr Nicolas Granger, Dr Sigitas Cizinauskas, Dr Georgina Child, Dr John Field, Dr David Lidbetter and Queensland Veterinary Specialists. The authors also wish to thank Professor Nick Jeffery for reading and commenting on the manuscript.

## References

- CAPPELLO, R. & RUSBRIDGE, C. (2007) Report from the Chiari-Like Malformation and Syringomyelia Working Group round table. *Veterinary Surgery* **36**, 509-512
- CERDA-GONZALEZ, S., OLBY, N. J., MCCULLOUGH, S., PEASE, A. P., BROADSTONE, R. & OSBORNE, J. A. (2009) Morphology of the caudal fossa in Cavalier King Charles Spaniels. *Veterinary Radiology & Ultrasound* **50**, 37-46
- CINALLI, G., SPENNATO, P., SAINTE-ROSE, C., ARNAUD, E., ALIBERTI, F., BRUNELLE, F., CIANCIULLI, E. & RENIER, D. (2005) Chiari malformation in craniosynostosis. *Child's Nervous System* **21**, 889-901
- COUSENS, M. (1969) Origin and History in Griffons Bruxellois. 2nd edn. W & G Foyle Ltd. London, UK. pp 13-16
- CROSS, H.R., CAPPELLO, R. & RUSBRIDGE, C. (2009) Comparison of cerebral cranium volumes between cavalier King Charles spaniels with Chiari-like malformation, small breed dogs and Labradors. *Journal of Small Animal Practice* **50**, 399-405
- DALZIEL, H. (1897) Toy Spaniels. In *British Dogs: Their Varieties, History, Characteristics, Breeding, Management, and Exhibition*. The Bazaar Office, 170, Strand, WC. pp 394-406
- EVANS, H. E. (1993) The skull. In *Miller's Anatomy of the Dog*. 3rd edn. Ed H. E. Evans. W.B. Saunders, Philadelphia, PA, USA. pp 128-166
- GRIFFITHS, P.D., WILKINSON, I. D., VARIEND, S., JONES, A., PALEY, M. N. & WHITBY, E. (2004) Differential growth rates of the cerebellum and posterior fossa assessed by post mortem magnetic resonance imaging of the fetus: implications for the pathogenesis of the chiari 2 deformity. *Acta Radiologica* **45**, 236-242
- KLEKAMP, J., IACONETTA, G., BATZDORF, U. & SAMII, M. J. (2002) Syringomyelia associated with foramen magnum arachnoiditis. *Neurosurgery* **97**, 317-322
- LEVINE, D. N. (2004) The pathogenesis of syringomyelia associated with lesions at the foramen magnum: a critical review of existing theories and proposal of a new hypothesis. *Journal of the Neurological Sciences* **220**, 3-21
- LEVINE, D. N. (2008) Intracranial pressure and ventricular expansion in hydrocephalus: have we been asking the wrong question? *Journal of the Neurological Sciences* **269**, 1-11
- MORITANI, T., AIHARA, T., OGUMA, E., MAKIYAMA, Y., NISHIMOTO, H., SMOKER, W. R. & SATO, Y. (2006) Magnetic resonance venography of achondroplasia: correlation of venous narrowing at the jugular foramen with hydrocephalus. *Clinical Imaging* **30**, 195-200
- PORTNOY, H. D., BRANCH, C. & CASTRO, M. E. (1994) The relationship of intracranial venous pressure to hydrocephalus. *Child's Nervous System* **10**, 29-35
- POURATIAN, N., SANSUR, C. A., NEWMAN, S. A., JANE, J. A. JR & JANE, J. A. SR (2007) Chiari malformations in patients with uncorrected sagittal synostosis. *Surgical Neurology* **67**, 422-427
- RAYBAUD, C. & DI ROCCO, C. (2007) Brain malformation in syndromic craniosynostoses, a primary disorder of white matter: a review. *Child's Nervous System* **23**, 1379-1388
- RUSBRIDGE, C. (2007) Syringomyelia and Chiari-like Malformation in Blackwell's Five Minute Veterinary Consult: Canine and Feline. 4th edn. Eds L. P. Tilley and F. W. K. Smith. Blackwell Publishing Ltd, Ames, Iowa, USA. p 1321
- RUSBRIDGE, C. & KNOWLER, S. P. (2004) Inheritance of occipital bone hypoplasia (Chiari I malformation) in Cavalier King Charles spaniels. *Journal of Veterinary Internal Medicine* **18**, 673-678
- RUSBRIDGE, C. & KNOWLER, S. P. (2006) Co-existence of occipital dysplasia and occipital hypoplasia/syringomyelia in the cavalier King Charles spaniel. *Journal of Small Animal Practice* **47**, 603-606
- RUSBRIDGE, C., MACSWEENEY, J. E., DAVIES, J. V., CHANDLER, K. E., FITZMAURICE, S. N., DENNIS, R., CAPPELLO, R. & WHEELER, S. J. (2000) Syringomyelia in Cavalier King Charles Spaniels. *Journal of the American Animal Hospital Association* **36**, 34-41
- RUSBRIDGE, C., KNOWLER, P., ROULEAU, G. A., MINASSIAN, B. A. & ROTHUIZEN, J. (2005) Inherited occipital hypoplasia/syringomyelia in the Cavalier King Charles spaniel - experiences in setting up a worldwide DNA collection. *Journal of Heredity* **96**, 745-749
- RUSBRIDGE, C., GREITZ, D. & ISKANDAR, B. J. (2006) Syringomyelia: current concepts in pathogenesis, diagnosis and treatment. *Journal of Veterinary Internal Medicine* **20**, 469-479
- RUSBRIDGE, C., CARRUTHERS, H., DUBE, M. -P., HOLMES, M. & JEFFERY, N. D. (2007) Syringomyelia in cavalier King Charles spaniels: the relationship between syrinx dimensions and pain. *Journal of Small Animal Practice* **48**, 432-436
- SCRIVANI, P. V., THOMPSON, M. S., WINEGARDNER, K. R., DEWEY, C. W. & SCARLETT, J. M. (2007) Association between frontal-sinus size and syringohydromyelia in small-breed dogs. *American Journal of Veterinary Research* **68**, 610-613
- SMIT-VIS, J. H. & GRIFFOEN, F. M. (1987) Growth control of neurocranial height of the rat skull. *Anatomischer Anzeiger* **163**, 401-406
- STENNING, E. M. (1980) History of the Breed. 2nd edn. W & G Foyle Ltd, London, UK. pp 9-12
- STOCKYARD, C. R. (1941) The Genetic and Endocrinic Basis for Differences in Form and Behaviour. American Anatomical Memoirs Number 19 Philadelphia Wistar Institute of Anatomy and Biology, Philadelphia, PA USA, pp 40-357
- THOMPSON, D. N., HARKNESS, W., JONES, B. M. & HAYWARD, R. D. (1997) Aetiology of herniation of the hind-brain in craniosynostosis. An investigation incorporating intracranial pressure monitoring and magnetic resonance imaging. *Pediatric Neurosurgery* **26**, 288-295
- VEGA, A., QUINTANA, F. & BERCIANO, J. (1990) Basichondrocranium anomalies in adult Chiari type I malformation: a morphometric study. *Journal of the Neurological Sciences* **99**, 137-145