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**CAUDAL CERVICAL  
VERTEBRAL MALFORMATION  
IN THE  
DOBERMANN PINSCHER**

A thesis presented  
in partial fulfilment of the requirements  
for the degree of Doctor of Philosophy  
at Massey University

Hilary Margaret Burbidge  
1999

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## Abstract

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The objective of this research was to further the knowledge and understanding of caudal cervical vertebral malformation, a feature of caudal cervical spondylomyelopathy in the Doberman pinscher.

The first study involved surveying 170 Dobermanns to determine the prevalence of caudal cervical vertebral malformation and neurological signs associated with caudal cervical spondylomyelopathy within this sample population. In addition, the relationship between the presence of cervical vertebral malformation, body conformation and neurological findings was investigated. It was found that 48.8% of adult Dobermanns and 28% of puppies had some feature of caudal cervical vertebral malformation. Dogs with radiological signs of caudal cervical vertebral malformation were 5.56 times more likely to have neurological deficits. In both instances the severity of these changes increased with age. Although the radiological signs of caudal cervical vertebral malformation were present throughout a wide age range (3 to 156 months), the associated neurological signs tended to appear at a later age (six years and over). There was no statistically significant association between body conformation and the radiological signs of caudal cervical vertebral malformation.

The fact that caudal cervical vertebral malformation was found in young Dobermann puppies led to a morphological study of the post-natal ossification of the canine caudal cervical vertebrae. The caudal cervical spines of 51 puppies (aged from 0 to 12 weeks) were examined grossly, histologically and radiographically. This revealed that at birth, three centres of ossification were present: one in the vertebral body and one in the base of the pedicle of each neural arch. By one month of age, secondary centres of ossification were present in the cranial and caudal epiphyses of the vertebral body, and bony fusion of the laminae had occurred at the dorsal aspect of the neural arches. It was deduced that after one month of age and during normal development, the shape of the neural canal could be influenced only by changes within the physes between the vertebral body and the neural arch, or by remodelling of bone formed by intramembranous ossification.

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A prospective study investigating the presence of caudal cervical vertebral malformation in 15 Dobermann puppies (from 0 to 16 weeks of age) found that two of these puppies had radiological signs of the condition by six weeks, and another three by between 12 to 16 weeks of age. The diets of these puppies were either balanced or only transiently deficient or excessive in protein, calcium, phosphorus and/or magnesium. There was no significant association between the growth rate of the puppies, in terms of body weight gain or increase in ulna length, and the presence of caudal cervical vertebral malformation.

The cervical spines from 27 neonatal Dobermanns (Group D) were examined grossly, radiographically and using computerized tomography for the presence of any caudal cervical vertebral malformation changes. The findings were compared to those of six, similarly examined cervical spines from other large breed canine neonates (Group O). A significant difference was found between the two breed groups with the Dobermann spines having evidence of relative stenosis of the cranial neural canal opening ( $p = 0.0001$ ) and some features of vertebral body asymmetry ( $p = 0.04$ ). In addition, the seventh cervical vertebra was found to have the most marked morphological changes when compared to the fifth and sixth. It was concluded that cervical vertebral malformation is a congenital malformation in the Dobermann breed.

In addition to the above studies, the growth characteristics of three breeds of dogs, Dobermanns, Labrador retrievers and Heading Dogs were investigated. It was found that each individual breed grew at a different rate to the other (with the largest breed growing faster than smaller) and that males grew faster than females. It was also realized that both measurement of body weight and increase in bone length was required to characterize canine growth, since there was a poor predictive relationship between these two parameters as the puppies aged.

It was concluded from the studies that caudal cervical vertebral malformation is a congenital malformation and that growth rate, dietary imbalances and body conformation were not significant factors in its initial development. Possible implications of these findings and recommendations for future research are discussed.

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## **Dedication**

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I dedicate this thesis to four men in my life who, in their own way, graciously lifted me upon their shoulders so that I might see new horizons. They are my father, Ralph Burbidge, and my mentors Jim Hardy, Sandy Lyons and Brian Goulden.

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## Publications

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Burbidge H.M., Pfeiffer D.U., Blair H.T. (1994). Canine wobbler syndrome : A study of the Dobermann pinscher in New Zealand. *New Zealand Veterinary Journal* **42**, 221-228.

Burbidge H.M., Thompson K.G., Hodge H. (1995). Post-natal development of canine caudal cervical vertebrae. *Research in Veterinary Science* **59**, 35-40.

Burbidge H.M. (1995). A review of wobbler syndrome in the Dobermann pinscher. *Australian Veterinary Practitioner* **25**, 147-156.

Burbidge H.M. and Pfeiffer D.U. (1998). The accuracy and reliability of linear measurements of the ulna for anthropometrical studies in dogs. *Research in Veterinary Science* **65**, 53-58.

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Burbidge H.M., Pfeiffer D.U., Guilford W.G. A comparison of body weight and skeletal growth in puppies of three different breeds. (Submitted for publication).

Burbidge H.M., Pfeiffer D.U., Jopson N., Broome C. Cervical vertebral malformation in Dobermanns - Are abnormalities present at birth? (Submitted for publication).

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## Introduction

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Disorders of the nervous system have long been recognised in animals. In particular, there is a wealth of information in the literature on the diseases of the vertebrae and spinal cord of small domestic animals. With the steady accumulation of knowledge and understanding of such disorders, has come the constancy of reliable diagnosis and for many conditions, successful treatment. Over the years, remarkable advances have been made such that it is now common practice to safely perform spinal surgery in these species where once techniques such as laminectomies were considered too hazardous to be recommended (Vaughan, 1958).

Cervical spondylomyelopathy (wobbler syndrome) of large breed dogs is one disease which, although commonly recognised, continues to frustrate veterinary surgeons' pursuit of appropriate treatment and consistency of results. The breeds most frequently affected are the Dobermann pinscher and Great Dane. These two breeds account for approximately 80% of reported cases (Seim and Withrow, 1982). In the Dobermann, clinical signs are most commonly seen in middle aged animals. These signs vary from mild ataxia, primarily of the hindlimbs, to acute onset of tetraplegia. In addition, many of the dogs suffer from either acute, intense or chronic, low grade neck pain which necessitates effective treatment. The clinical signs are believed to occur as a result of compression of the cervical spinal cord by a combination of deformed caudal cervical vertebrae, hypertrophied annulus and/or *ligamentum flavum* and/or degenerative disc disease. The exact pathology of the abnormalities vary from dog to dog. A consistent feature of all cases is the presence of some form of vertebral abnormality involving the neural canal, vertebral body, neural arches and/or articular facets (Wright *et al*, 1973; Trotter *et al*, 1976; Seim and Withrow, 1982).

A variety of terms have been used to refer to the syndrome and to avoid confusion the three used in this thesis are defined here. The term "wobbler syndrome" is used to describe the clinical and neurological signs of affected dogs, as described under the sub-section "clinical signs" in Chapter 2. The term "caudal cervical vertebral malformation" is used to refer to the vertebral

deformities/abnormalities/malarticulation, irrespective of cause, that are associated with wobbler syndrome in Dobermanns. The definition for “malformation” is that taken from Dorland’s Illustrated Medical Dictionary (1981), namely: “defective or abnormal formation; deformity; an anatomical aberration, especially one acquired during development”. The term “caudal cervical spondylomyelopathy” is used to denote the combination of clinical signs of wobbler syndrome, the presence of cervical vertebral malformation, and the presence of a confirmed compressive lesion (caused by either disc extrusion, ligamentous structures and/or malformed vertebral bone) on the spinal cord in the caudal cervical region.

The variability and complexity in the nature of the lesions associated with caudal cervical spondylomyelopathy has led to the development of a morass of possible therapies. Both medical and surgical management of affected dogs have been tried with varying results. Surgical techniques which produce consistent, long-term abatement of clinical signs are still being refined. At present, surgical treatment of dogs affected with cervical spondylomyelopathy is less reliable and successful than that of dogs afflicted solely with cervical disc disease. In the latter scenario, success rates of between 80 and 100% have been recorded, with the dog returning to, and maintaining a normal neurological status in the long term (Seim and Prata, 1982; Fry *et al*, 1991). However, for Dobermanns affected with caudal cervical spondylomyelopathy, not only is the immediate effect of treatment more variable and less successful (ranging from approximately 50 to 90%), but clinical signs recur in up to 30% of cases (Bruecker *et al*, 1989a; Bruecker *et al*, 1989b; McKee *et al*, 1989; Rusbridge *et al*, 1998).

The aetiology of cervical spondylomyelopathy remains unknown. Investigations into the relationship between overfeeding and skeletal development in Great Dane puppies led to the hypothesis that the cervical vertebral malformations seen in this syndrome were in part due to excessive energy, protein and calcium intake and consequent rapid growth (Hedhammer *et al*, 1974). More recent investigators (Hazewinkel *et al*, 1985) have proposed that these skeletal changes may be caused by excess dietary calcium. However, the evidence is not conclusive and some doubt remains as to the significance of such dietary over-supplementation in the development of these vertebral abnormalities. The cause of the vertebral malformations that typically occur in Dobermanns affected with caudal cervical spondylomyelopathy has been even

less well investigated; yet the presence of these malformations appear to be one of the fundamental predisposing factors.

The stimulus for the investigations recorded in this thesis was the quest to further our knowledge and understanding of caudal cervical spondylomyelopathy in the Dobermann pinscher. In particular, I wished to establish the possible factors that influence the development of the vertebral abnormalities in this breed.

The work in this thesis is centred on the hypothesis that “*caudal cervical vertebral malformation, a predisposing factor for caudal cervical spondylomyelopathy (wobbler syndrome) in the Dobermann, is a deformity that is present in the very young dog.*”

This work was performed as a sequence of studies, all of which are either already published or in the process of being published. The thesis is therefore presented in the form of discrete papers. References have been combined into a single bibliography.

### **Methodology of research work presented in this thesis**

The studies undertaken in this thesis explore the existence and development of caudal cervical vertebral malformation in the Dobermann pinscher. In addition, since previous experimental work in the Great Dane indicated that nutrition and growth rate could be influencing factors on the development of vertebral abnormalities in this breed, the growth of and food fed to young Dobermann pinscher puppies kept under domestic conditions was examined. The experimental work included:-

1. A review of the literature with emphasis on caudal cervical spondylomyelopathy as it pertains to the Dobermann (Chapter 2).
2. An investigation into the prevalence of caudal cervical vertebral malformation within a sample of the Dobermann population in New Zealand. In addition, the relationship between the presence of these bony changes, the neurological signs of wobbler syndrome and possible risk factors are explored (Chapter 3).

3. A study of the normal development and morphology of the caudal cervical vertebrae in dogs (Chapter 4).
4. An assessment of the accuracy and reliability of performing linear measurements of the ulna as an indicator of ulna length in puppies. Measurement of the increase in length of this bone was used as an estimate of longitudinal skeletal growth in subsequent chapters of this thesis (Chapter 5).
5. An exploration of the growth patterns in three breeds of dog (including Dobermanns) with respect to body weight and increases in bone length under domestic conditions (Chapter 6).
6. An investigation into the relationship between growth, diet and the presence of caudal cervical malformation in Dobermann puppies (Chapter 7).
7. A search for the presence of caudal cervical malformation in neonatal puppies (Chapter 8).
8. A general discussion of the significance of the findings from the studies in this thesis, their relevance to each other and to the literature (Chapter 9).

### A review of the literature

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#### **Abstract**

The known information on caudal cervical spondylomyelopathy (wobbler syndrome) as it affects the Dobermann pinscher is reviewed. The presenting signs usually consist of progressive hindlimb ataxia with upper motor neuron deficits, neck pain, forelimb dysfunction and tetra-or paraplegia. These clinical signs occur as a result of compression of the caudal cervical spinal cord, caused by a combination of malformed cervical vertebrae and/or associated degenerative disc disease. Factors thought to be involved in the aetiology of the syndrome are heritability, body conformation, unbalanced nutrition and altered growth rate, and trauma.

Radiographic studies of the cervical vertebrae and myelography are required to confirm the diagnosis. At present, there is no consistently successful form of treatment. Both medical and a variety of surgical procedures have been used.

#### **Introduction**

The Dobermann breed was developed in the late 1800's by Lewis Dobermann of Apolda, Germany. The basic stock consisted of a cross between the Rottweiler and the Thuringian shepherd dog. Later, the Manchester terrier and the Greyhound were also introduced into the breed, and the term "Pinscher" (meaning terrier) added to the name. Lewis Dobermann's original concept was to produce a breed that had a terrier's agility combined with the strength and aptitude of a guard dog. It is thus ironic, in the present age, that many Dobermanns should suffer from such a debilitating condition as "wobbler syndrome".

The term "wobbler syndrome" refers to the abnormal gait shown by affected dogs which results from malformed vertebra and/or associated soft tissue structures causing compression of the cervical spinal cord.

The syndrome in dogs was first described by Palmer and Wallace (1967) who recorded the

clinical signs and pathology of the condition in a small series of young male Bassett Hounds. The first reported case in the Dobermann breed was by Geary in 1969. Since that time there have been numerous articles published on the syndrome and it is now known to occur in a variety of predominantly large breed dogs. The breeds most commonly affected are the Dobermann pinscher, Great Dane and the Bassett Hound (Lewis, 1989). This paper, unless otherwise indicated, will review the syndrome in the Dobermann pinscher only.

### **Nomenclature**

The term "wobbler syndrome" originated as a graphic description of the inco-ordinated gait of affected animals (Dimock 1939, Selcer and Oliver, 1975), although a variety of different terms has been used over the years to record the condition. Many of these are also descriptive, and are based on the various pathological changes found. Such terms include caudal cervical spondylopathy (spondylo- combining form denoting relationship to a vertebra or spinal column and -pathy meaning "disease of"), cervical vertebral malformation-malarticulation, cervical vertebral deformation, cervical spinal stenosis, progressive cervical spinal cord compression, cervical spondylitic myelopathy and caudal cervical spondylomyelopathy.

Other terms such as cervical subluxation, cervical vertebral instability or dynamic compression of the cervical spinal cord are founded on the supposed existing biomechanical features of the disease. The term cervical spondylolithesis has also been used (de Lahunta, 1971; Gage and Hall, 1972; Gage and Hoerlein, 1973). This name refers to a condition in humans where an articular facet defect at the lumbosacral junction causes attenuation, and usually rupture of the *pars interarticularis*, allowing the last lumbar vertebrae to slip anteriorly. However, since such defects have not been found in "wobbler" dogs, the term has been deemed inappropriate (Wright *et al*, 1973).

### **Species comparison of cervical spondylomyelopathy (wobbler syndrome)**

Cervical spondylomyelopathy has been recognized in a variety of dog breeds, horses and man. In dogs, the breeds predominantly affected are the Great Dane and the Dobermann. In the Great Dane, the vertebral malformation tends to affect any or all of the cervical vertebrae from the third to the seventh. The deformities often include obvious articular facet abnormalities which

encroach on the neural canal of affected dogs. In this breed, most cases present with clinical signs of wobbler syndrome at less than 2 years of age (Lewis, 1989). In the Basset Hound, the vertebral malformations tend to occur at the third and the fourth cervical vertebrae (Palmer and Wallace, 1967; Lewis, 1989). There have been isolated case reports of wobbler syndrome in other canine breeds, including beagles, Borzoi, Boxer, Bull Mastiff, Chow, Dalmatian, German Shepherd, Golden retriever, Irish Setter, Irish Wolfhound, Labrador retriever, Old English Sheepdog, Pyrenean Mountain dog, Rhodesian ridgeback, Rottweiler, Samoyed, Scottish Deerhound, St. Bernard and Weimaraner (Dueland *et al*, 1973; Wright *et al*, 1973; Palmer and Wallace, 1967; Trotter *et al*, 1976; Denny *et al*, 1977; Mason, 1979; Hurov, 1979; Raffe and Knecht, 1980; Seim and Withrow, 1982; Lewis, 1989). In these latter breeds the site of cord compression tended to be at either the second and third or at the third and fourth cervical vertebral articulations.

In horses, the vertebral abnormality can occur anywhere from the first to the seventh cervical vertebrae (Mayhew *et al*, 1978; Reed *et al*, 1981; Mayhew *et al*, 1993). Cervical instability, as characterized by compression of the spinal cord during flexion of the neck, tends to occur at either the articulation between the third and fourth cervical vertebrae or at that of the fourth and fifth. This syndrome is most commonly seen in young thoroughbreds of less than two years of age. Vertebral changes include malformation and stenosis of the neural canal, physal enlargements, extension of the dorsal aspect of the vertebral arch over the cranial aspect of the next vertebral body, intervertebral subluxation and malformed articular processes with osteochondrosis. Cervical static stenosis, where the bony structures impinge on the spinal cord irrespective of neck movements, more often affects the caudal cervical vertebrae (Reed *et al*, 1981). Changes frequently include malformed articular facets with degenerative joint disease, cranial neural canal stenosis, periarticular proliferation with or without epidural cyst formation, and fissure lines and overt fractures of the articular processes (Mayhew *et al*, 1993). Although it is more commonly seen in older horses (five to ten years of age), it has also been reported in younger ones.

The disease in humans that most closely mimics caudal cervical spondylomyelopathy in Dobermanns is cervical spondylotic myelopathy (Sharp *et al*, 1989; Sharp *et al*, 1995). Affected patients present later in life, usually over fifty years of age, with an insidious onset of root

signature signs, and sensory and motor neurological deficits relating to cervical spinal cord damage. Two factors have been shown to be important in the pathogenesis of the disease. The first is the presence of a suspected congenitally narrowed neural canal as evidenced by a reduced sagittal diameter (Crandall and Batzdorf, 1966; Edwards and LaRocca, 1985). The second factor is the occurrence of chronic disc degeneration later on in life which results in compression of the spinal cord and hence the appearance of neurological signs (Montgomery and Bower, 1992).

### **Aetiology**

The aetiology of cervical spondylomyelopathy, and in particular the associated cervical vertebral deformities, has been debated since the early 1970's. Although several causal hypotheses have been proposed, none has been proven. Factors thought to be involved are heritability, body conformation, unbalanced nutrition and growth rate, and trauma.

#### **a) Heritability**

The recorded evidence that heritability plays a role in the aetiology of this syndrome comes mainly from two studies (Palmer and Wallace, 1967; Jaggy *et al*, 1988). The authors of these studies varied in their opinion as to the exact method of inheritance. After examining six closely related affected Bassett Hounds, Palmer and Wallace (1967) proposed that either an X-linked gene or a mode of imperfect penetrance could be involved. Jaggy *et al* (1988) however, concluded from a pedigree analysis on 57 progeny from 17 litters of related Borzoi dogs, that a recessive mode of inheritance existed. To add to the confusion Lewis (1989), after examining the pedigrees of a large number of affected Dobermanns, failed to find any heritable basis for the condition. In a later study (Lewis, 1991) however, he did concede that certain breed lines appeared to be predisposed to the disease. Selcer and Oliver (1975) also considered that the syndrome was transmitted by a simple recessive gene but gave no details as to how they reached this conclusion. Clearly more work is required to establish whether inheritable factors are implicated in the disease, and if they are, exactly what genetic mechanisms are involved.

#### **b) Body conformation**

In 1973, Wright *et al* proposed that the cervical vertebral malformations seen in cervical spondylomyelopathy could develop as a result of abnormal forces influencing the growth of these

bones. The basis for this concept was that the force acting on any one cervical vertebra is a combination of those forces due to the weight of the head and length of the neck, and those due to the action of muscles and ligaments. If the balance of the supporting elements is altered, abnormal forces will be placed on one or more of the vertebrae. The theory proposed was that if this occurred in young growing animals, these abnormal forces could affect the size and shape of the developing vertebrae. It was proposed that breeds with heavy heads, long necks and fast growth rates were predisposed to an imbalance in the forces acting on the cervical spine. A correlation between breed conformation and caudal cervical spondylomyelopathy was also advocated by Lewis (1989) although no objective data was given to support this belief.

### c) **Nutrition and growth rate**

Two nutritional factors, overfeeding and excess dietary calcium, have been considered as aetiological agents in the development of the cervical vertebral malformations.

Evidence that excess energy, protein and calcium intake may be implicated was provided by Hedhammer *et al* (1974) who documented several skeletal deformities including cervical vertebral malformations after overfeeding Great Dane puppies. These authors recorded that in dogs fed *ad libitum*, compared to those whose food intake was restricted, the cervical vertebrae were larger and had asymmetrical cranial neural canal foramina with reduced dorso-ventral diameters. In addition, there was incomplete cartilage coverage and osteochondrosis dissecans lesions on the articular processes of these vertebrae. The authors not only associated these chondro-osseous changes with the development of canine wobbler syndrome, but also recorded myelin degeneration in the spinal cords of all but one dog, irrespective of the diet. Only two of the 12 dogs fed *ad libitum* developed a mild hindlimb ataxia. Since the presence or absence of cervical vertebral malformation and/or wobbler syndrome in the parents of these puppies was unknown and given that some of the puppies were litter-mates, the possible influence of genetic factors on the development of either chondro-osseous changes or neurological abnormalities within these animals remained unanswered.

The role of excess dietary calcium in the aetiology of the syndrome is also unclear. Hazewinkel *et al* (1985) inferred that in puppies a high calcium intake alone caused, or at least

contributed to, the development of various skeletal deformities such as osteochondrosis, retained cartilaginous cores in the ulna, radius curvature syndrome and stunted growth. Such deformities are believed to be brought about by the effect of chronic, dietary calcium excess resulting in hypercalcaemia, hypophosphataemia, increased mineralization of osteoid, and decreased osteoclastic activity with insufficient remodelling of the growing skeleton. *In vivo*, high blood calcium concentrations stimulate release of calcitonin and decrease the concentration of circulating parathyroid hormone (Nunez *et al*, 1974; Goedegebuure and Hazewinkel, 1986). Since one major function of calcitonin is to lower the serum calcium concentration by directly inhibiting bone resorption from the skeleton, hypercalcitonaemia results in decreased osteoclastic activity and therefore reduced bone remodelling. It has been proposed that failure of normal expansion of the cervical neural canal due to this retarded resorption of bone results in stenosis and consequent local compression of the spinal cord (Hedhammer *et al*, 1974; Hazewinkel, 1989).

However, like Hedhammer *et al* (1974), Goedegebuure and Hazewinkel (1986) also found cervical malformations and myelin degeneration in the puppies of both control and calcium over-supplemented groups, thereby casting some doubt that excess calcium in the diet plays a fundamental role in the development of cervical vertebral malformations.

#### **d) Trauma**

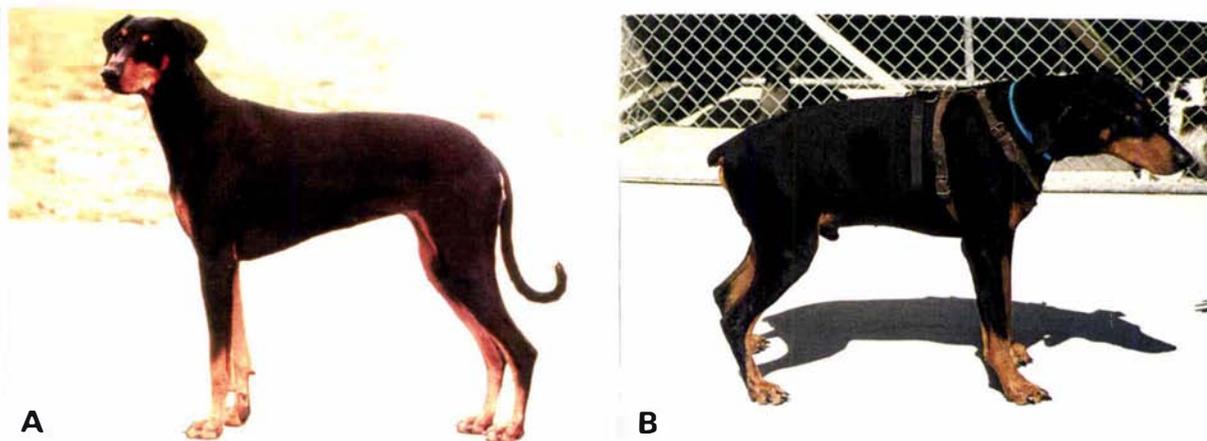
Although few authors consider that trauma plays a major part in the development of the cervical vertebral malformations, Chambers and Betts (1977); and Read *et al*(1983) recorded an association between over-exertion and the sudden onset of tetraplegia in adult dogs.

#### **Clinical Signs**

Although wobbler syndrome can affect Dobermanns at almost any age, the vast majority of reported cases are in middle-aged adults (Trotter *et al*, 1976; Mason, 1977; Denny *et al*, 1977; Chambers and Betts, 1977; Raffe and Knecht, 1980). It is generally accepted that males are more commonly affected than females (Mason, 1977; Denny *et al*, 1977; Seim and Withrow, 1982; Read *et al*, 1983; Lincoln and Pettit, 1985; Lewis, 1989), although some authors quote a more even sex distribution (Selcer and Oliver, 1975; Trotter *et al*, 1976).

Immature Dobermanns suffering from wobbler syndrome typically show a progressive hindlimb ataxia with loss of conscious proprioception. Tetraplegia can occur (Parker *et al*, 1973; Lewis, 1989), but cervical pain does not appear to be a feature of the disease.

Mature dogs often present with a slow progressive ataxia, particularly affecting the hind legs. Neurological examination of an affected animal at this early stage will characteristically reveal hindlimb ataxia, wide base stance, proprioceptive deficits and hyperactive patellar reflexes. The gait is frequently hypermetric. Progressive deterioration over many weeks or months can result in foreleg involvement with atrophy of the scapular muscles, extensor muscle rigidity and incoordination, producing a short-strided gait. Hindlimb dysfunction predominates and some dogs may become paraplegic. Together with these proprioceptive and motor impairments, dogs may have varying degrees of neck pain. These dogs characteristically flex and guard their necks against manipulation, and cry with pain to such manoeuvres (Denny *et al*, 1977; Seim and Withrow, 1982; Read *et al*, 1983; Lewis, 1989)(Figure 2-1).



**Figure 2-1: (A) Healthy Dobermann**

**(B) Dobermann with clinical signs of wobbler disease. Note arched neck and wide based hindlimb stance.**

Dobermanns occasionally present with a sudden onset of clinical signs, varying from neck pain to acute tetraplegia (Denny *et al*, 1977; Mason, 1979; Read *et al*, 1983).

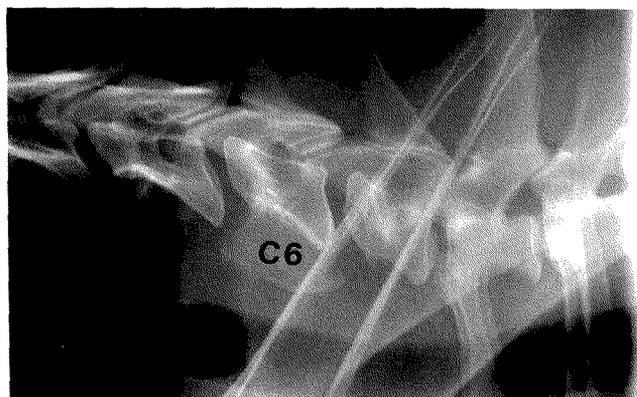
## Diagnosis

A diagnosis of caudal cervical spondylomyelopathy must be suspected from the breed of dog and the characteristic clinical and neurological signs. It is distinguished from other neurological diseases which might cause similar signs by radiographic and myelographic examination of the cervical spine. Abnormal changes are most commonly seen at the level of the fifth, sixth and seventh cervical vertebrae.

### a) Plain radiographic examination

Using a lateral radiographic projection of the caudal cervical vertebrae, various vertebral malformations of one or more of the bones can be detected (Wright *et al*, 1973; Trotter *et al*, 1976; Chambers and Betts, 1977; Raffe and Knecht, 1980; Read *et al*, 1983; Cappello *et al*, 1997). These abnormalities include stenosis of the cranial orifice of the neural canal caused by a combination of vertebral body, neural arch and articular facet deformities. Two authors (Wright, 1977; Lewis, 1991) have quantified the sagittal diameter of the foramen of the neural canal (cranial and caudal) for each cervical vertebra in both affected and unaffected dogs. Lewis (1991) considered a difference of three millimetres or more between the caudal and cranial sagittal diameters of each cervical vertebrae of adult Dobermanns to be abnormal and indicative of stenosis.

Frequently, plain radiographs show tipping of the vertebral body, so that the craniodorsal aspect of this structure tilts dorsally into the neural canal whilst the cranioventral border appears rounded. In severely deformed vertebrae the body may be triangular. In addition, the dorsal spinal processes may be abnormally shaped with new bone forming along their surfaces (Figure 2-2)



**Figure 2-2:**  
**Lateral radiograph of caudal cervical region of a “wobbler” Doberman.**  
**Note the abnormal shape and orientation of the sixth and seventh cervical vertebrae.**

In older Dobermanns, radiological signs of chronic degenerative disc disease may be present (Trotter *et al*, 1976; Chambers and Betts, 1977; Seim and Withrow, 1982; Lewis, 1991). These signs include a narrow wedge-shaped disc space, the presence of calcified disc material either within the disc space or extruded into the neural canal and the development of ventral spondylosis. The most frequently affected disc space lies between the sixth and seventh cervical vertebrae.

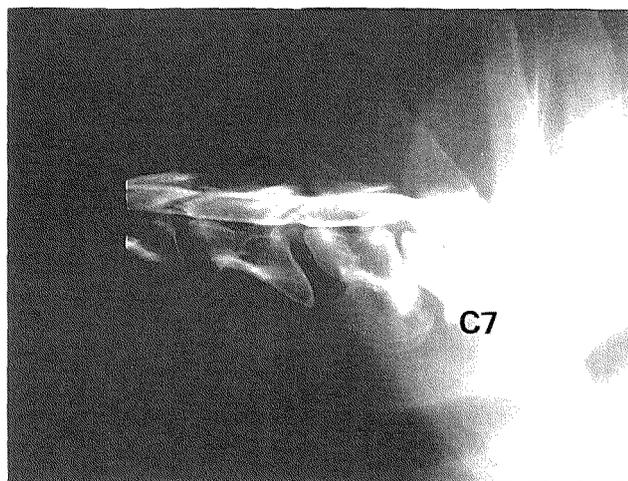
The ventro-dorsal view of the caudal cervical spine may reveal alterations in the articular facets. Although this feature is uncommon in the Doberman, this radiographic view should be included in the examination (Rendano and Smith, 1981; Sharp *et al*, 1992).

#### **b) Myelographic examination**

In 1982, Seim and Withrow recorded that plain radiographs indicated the site of greatest cord compression in only 65% of cases. Similar inconsistencies have also been reported by other authors (Read *et al*, 1983; Lewis, 1991). Therefore a myelogram is essential to confirm, not only the location of the lesion, but also the exact nature and extent of the abnormality.

The most common finding on the lateral radiographic view is the presence of a ventral extradural mass causing narrowing of the subarachnoid space, and in some cases, compression of the cord

as well (Figure 2-3). This mass is believed to consist of the soft tissues of the disc, and may also include herniated *nucleus pulposus* (Seim and Withrow, 1982). Whilst multiple sites of compression can often be detected, there is usually one lesion where the compression is most severe (Sharp *et al*, 1992). The extent of the ventral extradural mass can be sufficient to arrest the flow of contrast agent, whilst asymmetry of the lesion may occasionally cause splitting of the ventral column of contrast agent.

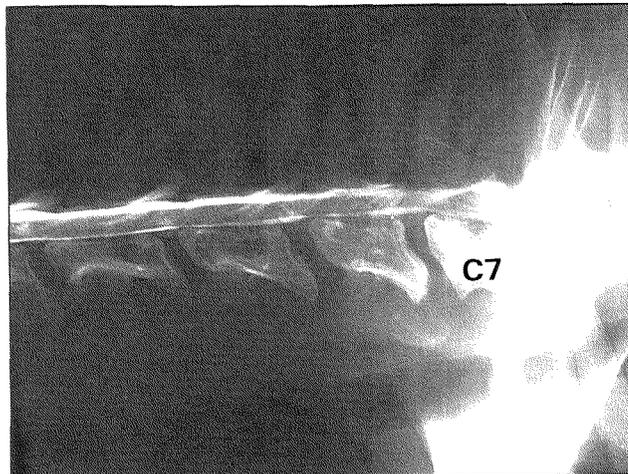


**Figure 2-3:** Radiograph of lateral cervical spine after myelography. The body of the seventh cervical vertebra is deformed and the intervertebral disc space between this and the sixth cervical vertebral body is narrowed. The myelogram shows an extradural ventral mass which is causing spinal cord compression.

Dorsal attenuation of the subarachnoid space is believed to be caused by bulging of the *ligamentum flavum* or changes in the vertebral facets such that these structures encroach into the neural canal (Seim and Withrow, 1982). These abnormalities can be combined with ventral compression at the same intervertebral disc space. Lateral compression of the neural canal may be seen on a ventrodorsal view, and results from malformations of the vertebral arch and facets (Rendano and Smith, 1988).

The use of stress positions during myelography is of great value in the assessment of dogs with cervical cord compression. Extending the neck usually exacerbates both dorsal and ventral compression, whilst flexion may relieve the compression (Sharp *et al*, 1992).

Some authors (Seim and Withrow, 1982) have emphasised the importance of differentiating between "dynamic" and "static" compressions when surgical treatment is to be undertaken. Dynamic compressive lesions are those caused by ligamentous structures whilst static compressions tend to indicate fixed masses such as bone or herniated *nucleus pulposus*. Dynamic lesions can be distinguished from static ones by applying traction to the neck during the radiographic exposure. As the neck is stretched, the compressive mass of a dynamic lesion is diminished, and hence myelographic signs of compression are reduced (Figure 2- 4).



**Figure 2-4: Radiograph of the same section of spine of Figure 2-3 showing how traction on the neck has relieved the compression.**

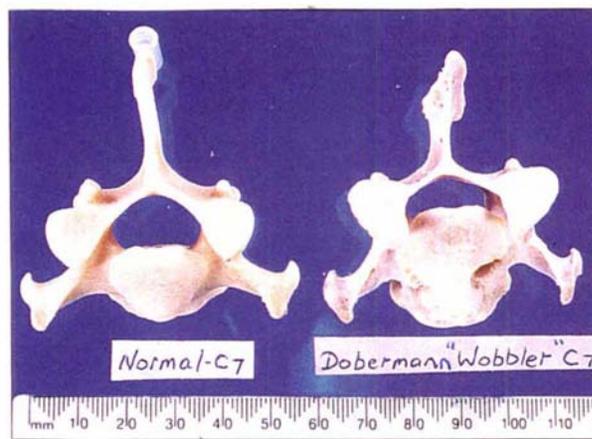
**c) Computed tomographic examination**

Sharp *et al* (1992, 1995) have used computed tomographic (CT) myelography to gain additional information on the location and nature of the lesion. This technique provides a means of detecting spinal cord atrophy which may serve as an important prognostic guide for the clinician.

## Pathology

### i) Cervical vertebral changes

It is surprising that although most authors consider the bony malformation of the cervical vertebrae to be the basis of caudal cervical spondylomyelopathy, there are few detailed descriptions of the pathological changes that occur in these bones. Some papers describe the gross bony changes of the distorted vertebrae, stenosed cranial neural canal, asymmetrical neural canal, and deformed and degenerative articular facets (Trotter *et al*, 1976; Wright, 1977; Shores, 1984) (Figure 2-5).



**Figure 2-5:** The seventh cervical vertebrae from a normal dog (left) and from a Doberman affected with caudal cervical spondylomyelopathy (right). Note the stenotic neural canal and deformed dorsal spinous process in the abnormal vertebra.

Cervical instability has also been described (Read *et al*, 1983) but no details were given of how this change was assessed. One early study in Great Danes (Wright *et al*, 1973) did detail the bony changes in the malformed vertebrae. These were : a loss of marrow at the cranio-ventral aspect of the vertebral body; thickened, unevenly calcified bony trabeculae and distorted lamellar structure. The presence of amorphous hyalinised collagen and pre-collagen fibres indicated that there was continuing breakdown of bone coinciding with osteoid and cartilage formation.

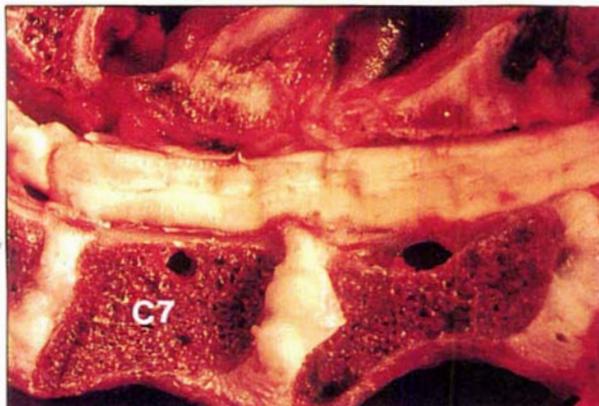
## ii) Intervertebral disc and ligamentous changes

Many authors who have described the pathology of caudal cervical spondylomyelopathy, have concentrated on the intervertebral disc and ligamentous changes which occur at the site of cord compression. The first comprehensive account of the changes that occur was by Seim and Withrow in 1982. Many of the other descriptions ( Read *et al*, 1983; Shores, 1984; Van Gundy, 1989) are similar or merely document minor additional details to this original article.

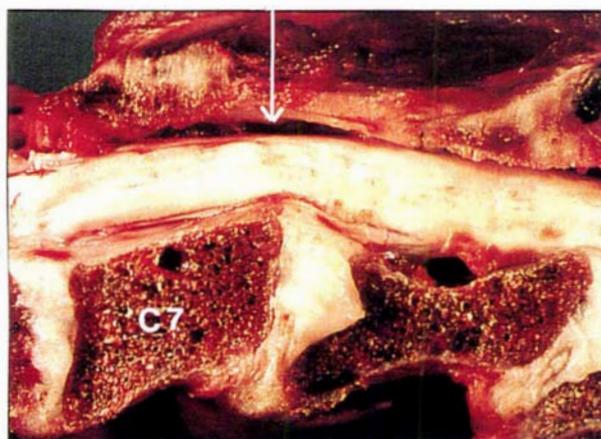
Seim and Withrow (1982) found that in the majority of "wobbler" dogs, the compressive mass was ligamentous and located ventrally in the neural canal. The most commonly involved ligament was the dorsal *annulus fibrosus*, which had either undergone hypertrophy or, secondary to *nucleus pulposus* herniation, had bulged into the neural canal. The dorsal longitudinal ligament contributed little to the bulk of the protruding soft tissue. Dorsal compression was due to hypertrophy or bulging of the *ligamentum flavum*. These authors also described the effect of flexion, extension and traction on sagittally split spinal columns. It was found that full flexion or traction of the neck resulted in relief of the compression, whilst extension increased the degree of compression. Figure 2-6.



Figure 2-6: a) Longitudinal midline section of caudal cervical vertebrae of a "wobbler" dog. The seventh cervical vertebra is tilted and the cranial border of the body impinges on the spinal cord.

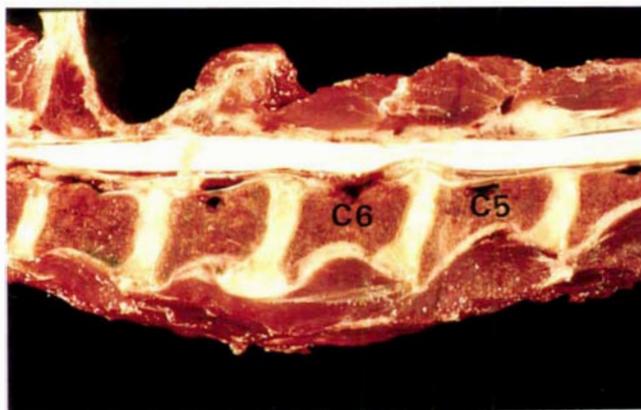


b) The *nucleus pulposus* is within the intervertebral disc space. Extension of the neck increases the compression on the spinal cord both ventrally and dorsally.



c) Flexion of the neck relieves the compression as evidenced by the space dorsally (arrow).

There is some debate regarding the importance of disc degeneration in the pathogenesis of wobbler syndrome. Seim and Withrow (1982) recorded that nucleus herniation contributed to the compressive lesion in only approximately 25% of those cases post-mortemed (Figure 2-7). In addition, they found no cases where nucleus extrusion alone was the cause of the compression.



**Figure 2-7: Intervertebral disc extrusion between the fifth and sixth cervical vertebrae in an 11 year old female Dobermann causing spinal cord compression and haemorrhage.**

Wright *et al* (1973) however, reported gross degenerative changes to the *nucleus pulposus* and *annulus fibrosus* in two of three Basset Hounds, while Mason (1979) recorded similar changes in six of eight affected Dobermanns. In most cases, the *nucleus pulposus* appeared more organised and collagenous, but in some cases it was absent. Rarely is degenerate nuclear material found in the neural canal of affected dogs (Seim and Bruecker, 1993).

### iii) Spinal cord changes

Gross changes to the spinal cord have been noted in dogs with caudal cervical spondylomyelopathy (Wright *et al*, 1973; Trotter *et al*, 1976; Read *et al*, 1983) including narrowing of the cord, or a dorsoventral flattening combined with an increased width at the sites of compression compared to the remainder of the cervical cord. Histologically, most of the *funiculi* of the white matter show focal areas of demyelination, axonal disruption or loss and

astrocytosis. According to Trotter *et al* (1976), white matter degeneration was limited to the ascending tracts in the dorsal and superficial portions of dorsolateral *funiculi* in spinal cord segments cranial to the focal lesion, whilst caudal to the lesion, the degeneration occurred in the descending spinal cord tracts in the ventral and deep lateral *funiculi*. Most of the above authors report varying degrees of malacia of the grey matter with the presence of hypertrophied astrocytes.

**The pathological changes associated with caudal cervical spondylomyelopathy in the adult Dobermann are summarised** as the presence of a narrowed vertebral canal combined with abnormal ligamentous and intervertebral disc changes resulting in compression of the spinal cord.

### **Pathogenesis**

The pathogenesis of wobbler syndrome is still uncertain, but scientific investigation of the condition has increased our understanding and reduced uninformed speculation.

#### **i) Role of cervical vertebrae changes**

The role of malformed or malaligned vertebrae in the pathogenesis of caudal cervical spondylomyelopathy, is thought to depend on whether these structures cause static (ie bony) or dynamic (ie instability/ligamentous) compression of the spinal cord (Seim and Withrow, 1982; Olsson *et al*, 1982). Static compression occurs where constant pressure is exerted on the spinal cord, regardless of the position of the neck (Van Gundy, 1989). This occurs where the malformed vertebrae have such deformed articular facets and narrowed, dorsal to ventral flattened neural canals that all impinge on the cranial neural canal opening to compress the spinal cord. This form of compression appears to be the cause of clinical signs in dogs of less than two years of age (Seim and Withrow, 1982; Seim and Bruecker, 1993). Whilst adults also have malformation of the vertebrae, the spinal cord compression is more frequently caused by intervertebral disc degeneration and herniation. This gives rise to a dynamic compression that is dependant upon movement of the neck, and results in intermittent pressure being exerted on the cord. This form of compression is believed by many authors (Mason, 1979; Seim and Withrow, 1982; Ellison *et al*, 1988; McKee *et al*, 1990) to play a major role in the development of the syndrome in the adult Dobermann. Whether the malformed cervical vertebrae are congenital or post-natal

developmental lesions is not known.

There is still confusion over the effect of cervical vertebral instability. This term is defined as there being sufficient movement of the surrounding bone or ligament to impinge on the spinal cord and/or nerve roots (Vasseur, 1981). The presence of instability is frequently mentioned in relation to wobbler syndrome (Trotter *et al*, 1976; Mason, 1979; Hurov, 1979; Seim and Withrow, 1982; Read *et al*, 1983; Shores, 1984) but has not been confirmed or quantified. Attempts have been made to measure the variation in the alignment of the ventral surface of the neural canal of the cervical vertebrae using flexed, extended and neutral lateral radiographic views (Wright, 1977; Lewis, 1991). However, the presence of a wide variation in angulation between the different views in normal dogs made assessment of these measurements unrewarding. Furthermore, Parker *et al* (1973), specifically looked for cervical vertebral instability at necropsy in three young wobbler dogs and were unable to demonstrate its presence.

Nevertheless, the theory of Trotter *et al* (1976), that cervical vertebral instability is the primary lesion in wobbler syndrome and that disc degeneration, prolapse, osteoarthritis, deformed vertebral bones and associated stenosis are secondary changes, still persists. These authors hypothesised that stenotic neural canals could result from remodelling of the vertebrae due to abnormal stresses placed on the cervical vertebral column.

Whatever their cause, the presence of abnormally shaped vertebrae appears to be a risk factor for the subsequent development of wobbler syndrome.

## ii) **Role of intervertebral disc and ligamentous changes**

In the Dobermann pinscher, fibroid degeneration of the intervertebral disc is considered by some authors to be an important feature in the development of neurological signs in some cases (Mason, 1977; Mason, 1979; Seim and Withrow, 1982; Van Gundy, 1988; Lewis, 1991). This structural change of the nucleus reduces its capacity to act as a shock-absorber, and results in the annulus being subjected to increased loading and therefore mechanical failure with disruption of the annular fibres. Partial rupture of the annular bands allows a Hansen Type II herniation of nuclear material into the neural canal. This event has several effects. The actual presence of disc

material within the canal can cause spinal cord or nerve root compression and pain. Since the dorsal annular region is rich in pain receptors, disruption the dorsal annulus fibres also results in pain (Coventry *et al*, 1945). As a consequence of nuclear herniation, the disc space collapses and the slack dorsal annulus bulges into the neural canal further increasing compression. It is uncertain whether this mass of dorsal annulus simply bulges into the canal or is truly hypertrophied (Seim and Withrow, 1982; Seim and Bruecker, 1993). Since the degree of compression can be altered by neck position, it is classified as dynamic and commonly referred to as "cervical vertebral instability". Similarly, collapse of the disc space or "instability" may also have the effect of allowing the *ligamentum flavum* to bulge into the neural canal, thereby adding to the spinal cord compression.

The combined effects of a constitutionally narrow canal and superimposed degenerative disc changes causing myelopathy also occur in middle aged humans (Yu *et al*, 1986), and some parallels have been drawn between this condition, cervical spondylotic myelopathy and wobbler syndrome (caudal cervical spondylomyelopathy) in Dobermanns (Sharp *et al*, 1989).

### iii) Role of spinal cord changes

How extramedullary compression by the soft tissues of the degenerate disc affects the spinal cord is not completely understood. It has been demonstrated that injury to the spinal cord is dependant on the extent and rate of the compressive force (Tarlov, 1957; Wright *et al*, 1974). The smaller and slower the compression applied, the lesser the resultant neurological damage. The compressive mass is believed to have two effects on the cord ; a direct mechanical effect on the axons, and an indirect injury to the microvasculature causing ischaemia and hypoxia (Wright *et al*, 1974; Bohlman and Emery, 1988). This latter effect is believed to be the predominant damaging factor and can result in intra-medullary oedema which further contributes to compression (Vandeveldel and Wolf, 1993). However, the pathogenesis of cord lesions which result from chronic compression and the role of ischaemia in the formation of neuronal lesions remains conjectural.

What is known is that in a slowly compressive disease, there appears to be considerable compensation in neurological function. Whether this is due to recovery of injured nerves or to

accommodation by spared motor tracts remains speculative (Van Gundy, 1989). The sudden onset of clinical signs in some “wobbler” cases that have apparently long-standing skeletal lesions remains puzzling. It has been proposed that these could be due to repeated small injuries to the cord where the final onset of clinical signs is caused by either a sudden increase of insult to the cord, or by the accumulation of residual cord damage to the point where nerve transmission can no longer occur (Wright *et al*, 1974). Some credence is given to this theory by the finding of spinal cord atrophy at the sites of compression (Sharp *et al*, 1992).

Since the compressing mass deforms the spinal cord along the ventral/ventrolateral border, it is the pyramidal tracts which are mainly affected. These tracts control motor pathways to the skeletal muscle and are responsible for posture as well as more exacting muscular movements (King, 1973a). It is therefore not surprising that ataxia with upper motor neuron deficits is characteristic of the clinical signs of wobbler syndrome. In addition, since the tracts of the hindlimb are positioned more peripherally within the cord, it is these limbs that are primarily affected. In some cases, impairment of foreleg action also occurs as either the brachial plexus nerve roots or the deeper tracts become injured. Any pressure on the dorsal part of the spinal cord, either as a result of the cord being displaced dorsally to impact on the neural arch or secondary to encroachment of the *ligamentum flavum* into the neural canal, may result in compression of the cuneate and gracile tracts. These tracts are afferent in nature, transmitting information of touch, pressure and kinaesthesia. The axons relating to hindlimb motion pass near to the midline, whilst those from the forelimbs are found further laterally (King 1973b). Thus dorsal compression of the spinal cord also has a greater effect on hindlimb locomotion and co-ordination.

## **Treatment**

The objectives of treatment for dogs affected with caudal cervical spondylomyelopathy are to restore neurological function and prevent future insult to the spinal cord. To reduce the effect of the compression on the spinal cord, therapy should be directed at counteracting the biochemical and structural changes that have occurred, relieving the mechanical pressure on the axons and re-establishing perfusion. Both medical and surgical therapy have been used to this end to relieve the clinical signs.

**a) Conservative treatment**

In some early reports (Mason, 1977; Denny *et al*, 1977; Chambers and Betts, 1977), conservative treatment consisting of rest and confinement were tried. However, results were poor with 70% being euthanased due to progression of clinical signs. Most of the remaining dogs failed to improve long- term.

**b) Medical therapy**

Glucocorticosteroids have been the drugs most frequently used to improve the speed and functional recovery of neurons following spinal cord injuries. These drugs are believed to inhibit lipid peroxidation; improve post traumatic spinal cord blood flow, block the release of free fatty acids, eicosinoids and loss of cholesterol, facilitate removal of accumulated intracellular calcium and enhance spinal cord ( $\text{Na}^+$  and  $\text{K}^+$ ) ATPase activity (Braund, 1993). These characteristics are beneficial in suppressing the development of oedema, inhibiting the inflammatory response and stabilising cell membranes thereby limiting the development of harmful free oxygen radicals, and preventing the release of lysosomal enzymes which contribute to myelin and axonal damage.

The use of glucocorticosteroids for treating clinical cases is infrequently reported (Read *et al*, 1983; Hurov, 1979). Remission for several months occurred in five out of the six cases recorded, with two of these dogs being tetraparetic before treatment. Despite the lack of case numbers, textbooks (Meric, 1992; Bruecker and Seim, 1993) recommend the use of these drugs as an initial treatment for dogs presenting with wobbler syndrome. Corticosteroid therapy is advantageous in that it can be effective, is relatively inexpensive, is noninvasive and has low morbidity. Its disadvantage is that since it does not resolve the underlying cause of the spinal cord compression, relapses can occur. In addition, the adverse systemic effects of corticosteroid therapy such as gastro-intestinal haemorrhage and immune suppression should be considered.

Corticosteroids are also frequently used in combination with surgical therapy, particularly when the clinical signs are severe and of sudden onset (Lincoln and Pettit, 1985; Ellison *et al*, 1988; McKee *et al*, 1989; Lyman, 1990).

Since the pathophysiological mechanisms for the myelopathy are still not fully understood, the exact role which glucocorticoids play in alleviating the signs of neurological damage that occur in compressive spinal cord injuries remains unknown. Hall (1990) claimed that recent evidence indicates that prolonged corticosteroid therapy can inhibit early adaptive and regenerative responses of the central nervous system after injury.

Other drugs, such as 21-Aminosteroids, ion-channel blockers and free radicle scavengers are currently being investigated for their neuroprotective properties but are not in current use as their value has not as yet been established (Coughlan, 1993).

### c) **Surgical treatment**

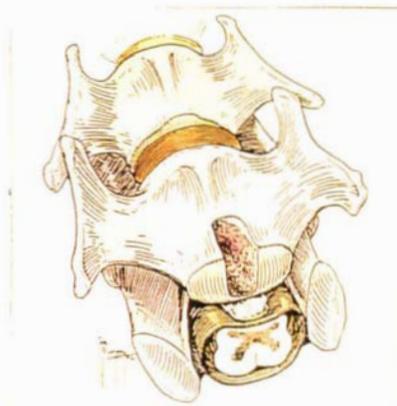
At least 12 surgical procedures have been described to relieve the neurological signs of caudal cervical spondylomyelopathy. These techniques can be grouped into five categories depending upon their mode of action. These categories are fenestration, dorsal laminectomy, ventral slot, fusion and distraction. The term "success" of treatment varies from author to author, but most define it as the dog being mobile and free from pain.

i) **Fenestration.** Fenestration is the removal of the *nucleus pulposus* from within the annulus. Mason (1977) at first experienced encouraging results with this technique but later found only limited success (Mason, 1979). Lincoln and Pettitt (1985) also concluded that disc fenestration alone provided inadequate treatment of caudal cervical degenerative disc disease. This is not surprising since the objective of the fenestration is to eliminate repeated extrusions of *nucleus pulposus*. Fenestration does not remove the compressive mass from the neural canal nor re-establish the disc space width.

ii) **Dorsal laminectomy.** Dorsal laminectomy is the removal of the neural arch in order to gain access to the neural canal and decompress the spinal cord. Following laminectomy it is reasoned that the spinal cord shifts dorsally into the open space (Epstein, 1988). Continuous dorsal laminectomy (from the fourth cervical to the first thoracic vertebra) has been advocated by Lyman (1990) for the treatment of wobbler syndrome where multiple sites of compression were present. Of the 17 "wobbler" Dobermanns reported

in the literature as being treated by dorsal laminectomy (Hurov, 1979; Read *et al*, 1983; Lyman, 1990), 12 were regarded as having a successful long-term outcome. Dorsal laminectomy has also been combined with techniques to fuse the adjacent articular facets in order to achieve stability. Of the five recorded cases in Dobermanns, results were disappointing with only two considered to be successful (Swaim, 1973; Trotter *et al*, 1976; Hurov, 1979).

- ii) **Ventral slot.** A ventral slot procedure involves a ventral approach to the vertebrae, with the removal of a midline segment of bone together with the soft tissues of the affected disc space. Having gained access to the neural canal, removal of the offending mass can be achieved. It has been used for cases of single-site disc-associated wobbler syndrome (Van Gundy, 1988) (Figure 2-8).



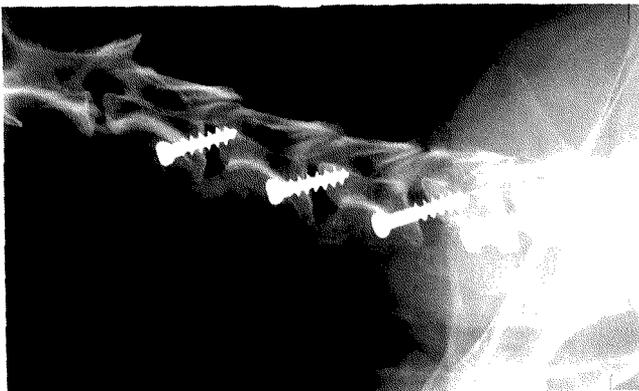
**Figure 2-8: Ventral aspect of cervical vertebrae showing access to the neural canal by ventral slot technique.**

Of the 36 reported cases of this technique in the Dobermann, 27 were reported as being successful (Gilpin, 1976; Chambers *et al*, 1982; 1986; Read *et al*, 1983; Seim, 1985). The causes of failure are not fully understood, but could be due to incomplete removal of the compressive tissue (Chambers *et al*, 1986) and instability from overzealous

removal of bone (Seim and Prata, 1982), ventral ligament and annulus. A more recent study using the ventral slot procedure concluded that although dogs undergoing this procedure had an initial deterioration in neurological status, these cases performed well in the long-term with recurrence occurring in only four out of 14 dogs at a two year follow-up (Rusbridge *et al*, 1998).

Modification to the routine ventral slot procedure have been described (Goring *et al*, 1991), but as yet no clinical evaluation of this technique has been published.

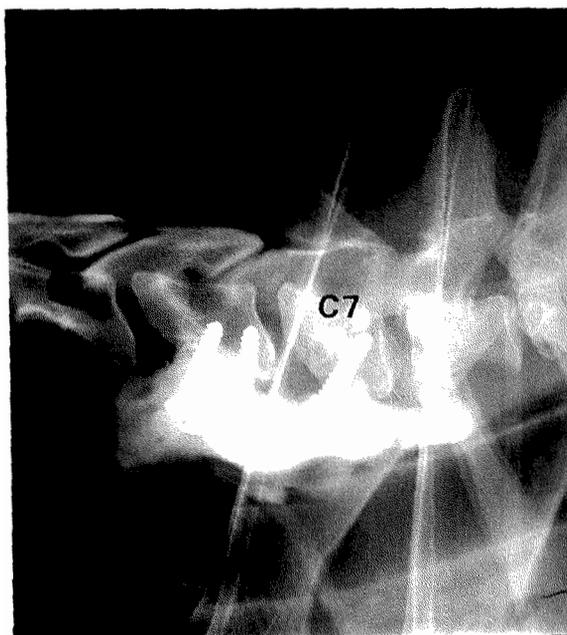
- v) **Fusion.** In the belief that vertebral instability plays an important role in the development of caudal cervical spondylomyelopathy, some surgeons developed a technique of stabilising the cervical vertebrae along their ventral aspect by using vertebral body lag screw fixation (Figure 2-9). This was first recorded in 1973 by Gage and Hoerlein, and additional reports by Chambers and Betts (1977), Denny *et al* (1977), Mason (1977, 1979), and Read *et al* (1983) have also provided further information. In the nine recorded cases in Dobermanns, long-term success was achieved in less than half of these patients.



**Figure 2-9: Post-operative radiograph of ventral body lag screw fixation.**

) **Distraction.** This technique aims to relieve the spinal cord compression caused by the bulging redundant annulus and/or nucleus by stretching these tissues. This is achieved by providing and maintaining cranio-caudal traction on the two adjacent vertebral bodies until fusion occurs.

The original technique involved a ventral slot-like procedure to a depth of three-quarters of the vertebral body. The neural canal was not entered. Distraction of the disc space was provided by either the insertion of allogenic cortical bone graft (stabilised with either a lubra plate or transvertebral screw), use of metallic pins and methyl methacrylate bone cement, or Harrington rods. There have been few studies involving large numbers of cases on any of these techniques, so assessment of success is conjectural and much is based on hearsay. In one case study, 75% of 37 dogs treated with cortical graft and lubra plate stabilisation had improved or acceptable neurological function long-term (Bruecker *et al*, 1989a), whilst another study (Bruecker *et al*, 1989b) reported a 90% success rate in 41 “wobbler” dogs using pins and methyl methacrylate (Figure 2-10).



**Figure 2-10: Post-operative radiograph of distraction-fusion technique at the sixth and seventh intervertebral disc space using screws and methyl methacrylate.**

In both studies, dogs that could not walk or had difficulty in walking on presentation had either prolonged recovery periods or failed to recover. Problems associated with cortical bone graft distraction have been displacement of the graft and its poor incorporation with the adjacent vertebra (Seim, 1985). As with the other implants, loss of distraction has also occurred and complications such as infection and vertebral fracture have been recorded (Walker, 1990).

Another method described for stabilising and maintaining traction of the intervertebral space has been the screw and washer technique (McKee *et al*, 1989). In this procedure a ventral approach to the affected disc space was used, and the ventral annulus and the *nucleus pulposus* removed. A metallic washer was then inserted into the intervertebral disc space, and stability achieved by inserting a screw through the caudo-ventral border of the cranial vertebral body, through the hole in the washer and into the cranial aspect of the caudal vertebral body. In 34 Dobermanns, a long term improvement in neurological status occurred in only 50% of dogs. Failure was considered to be due to loss of distraction, faulty technique and fracture of the vertebral body.

A subsequent technique using a double washer and screw, recorded a successful outcome in 14 of 17 Dobermanns treated (McKee *et al*, 1990). Complications were again due to either fracture of the vertebral body or implant problems.

It would appear that decompression by distraction is the procedure of choice for treating single site lesions and where traction on the affected disc space alleviates the cord compression. However, most of the techniques are surgically demanding and have a number of associated problems such as fracture of the vertebra, infection, inadequate or loss of distraction and improper placement of the implant.

**Conclusion**

Dobermann pinschers affected by caudal cervical spondylomyelopathy are easily recognised by the characteristic clinical signs, neurological deficits and radiological findings. Radiographic and pathological studies of affected dogs by clinicians and researchers have increased our knowledge of this syndrome, but the actual cause and pathogenesis still remain uncertain. Likewise, despite the ingenuity of veterinarians, treatment options have failed to give either consistent and/or long-term relief of clinical signs. Further studies are required to increase our understanding of canine caudal cervical spondylomyelopathy.

### **Caudal cervical vertebral malformation : A survey of the Dobermann pinscher in New Zealand**

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#### **Abstract**

The aim of this survey was to investigate the prevalence of caudal cervical vertebral malformation and neurological signs associated with caudal cervical spondylomyelopathy within a Dobermann pinscher population from three geographical locations in New Zealand. The survey population consisted of 138 adults (aged one to 13 years) and 32 puppies (aged six weeks to 11 months). Data collected for each dog included age, sex, geographic location, if a choker chain was used or not and in adults the following body measurements: dimensions of head length, head circumference, width between shoulders, neck length, height at withers and withers to rump length. In addition, lateral radiographs were taken of the caudal cervical vertebrae of each dog and the radiological vertebral abnormalities associated with caudal cervical spondylomyelopathy scored so that each dog could be assigned to one of three radiological groupings. Based upon a neurological examination of each animal, they were also placed into one of three neurological groupings. The relationship between radiological and neurological groupings and the independent variables was initially compared using a univariate and subsequently a multivariate analysis.

It was found that 48.8% of the dogs investigated had some abnormal radiological sign associated with caudal cervical vertebral malformation, and 32.0% of them showed neurological signs. Dogs with radiological signs of the caudal cervical vertebral malformation were 5.56 times more likely to have neurological signs. Statistical analysis of the data indicated that more severe radiological and neurological abnormalities occurred in the older dogs. In addition, dogs located in the Hawkes Bay region had less chance of having radiological changes than dogs from the other two regions, Hamilton and Wellington.

Twelve of the 32 puppies were examined for radiological and neurological changes over the first year of their life. No abnormalities were detected in puppies under 12 weeks of age, but 28% (n=9) of the 32 puppies over three months of age did have some radiological changes. Only 9%

(n=3) of puppies showed any neurological signs. Although several pedigree lines were investigated, the lineage data was incomplete and therefore no conclusive evidence that caudal cervical vertebral malformation was an inherited trait could be ascertained.

This survey showed that although the radiological signs of caudal cervical vertebral malformation were present throughout a wide age range, the associated neurological changes associated with caudal cervical spondylomyelopathy tended to appear at a later age. In both instances, the severity of these changes increased with age.

## **Introduction**

In the late 1960's, Palmer and Wallace reported a form of progressive hind limb paralysis in Basset Hounds which was caused by a deformity of the cervical vertebrae and resulted in compression of the spinal cord. This syndrome has since been recognised in many breeds of dog, but more commonly in the Dobermann pinscher and Great Dane. The actual site and extent of the cervical vertebral deformity varies from breed to breed and within individuals. This variation has led to a plethora of suggested names for the condition. Terms such as canine wobbler syndrome, cervical spondylopathy, cervical spondylomyelopathy, cervical vertebral instability, cervical malformation/malarticulation syndrome and cervical spondylolisthesis are, but a few, which have been used by various authors (Palmer and Wallace, 1967; Geary, 1969; Selcer and Oliver, 1972; Parker *et al*, 1973; Mason, 1979; Jaggy *et al*, 1980; Seim and Withrow, 1982; Read *et al*, 1983; Shores, 1984; Lewis, 1991).

Numerous articles describing cases have appeared in the literature and there is now a wealth of information on the pathological changes associated with the disorder. In the majority of reported cases, affected Dobermann pinschers are male and middle aged (Raffe and Knecht, 1980; Seim and Withrow, 1982; Read *et al*, 1983; Shores, 1984; Lewis, 1989). Both bony and ligament abnormalities of the caudal cervical vertebral column occur. Seim and Withrow (1982) considered that these changes fitted into five different categories: chronic degenerative disc disease, congenital bony malformation (stenosis of the neural canal and abnormal articulation of the articular facets), vertebral instability or "tipping", hour glass compression by the dorsal and

ventral ligaments and hypertrophy of the *ligamentum flavum*. These changes, either individually or in combination, result in compression of the spinal cord. As a result of this progressive crushing, demyelination and Wallerian degeneration of the ascending and descending tracts occurs in conjunction with focal malacia of the grey matter (Vandeveld, 1981). Consequently in affected dogs, neurological signs vary from bilateral mild hindlimb ataxia and spastic paresis to tetraparesis.

Accompanying the increased recognition of the syndrome has been the development over the years of numerous medical and surgical treatments. Surgeons, in particular, have created a multitude of operations to alleviate the patient's neurological signs. These procedures have met with variable success and no one single therapeutic regime can be recommended since the syndrome has such diverse manifestations.

The suspected aetiology of the syndrome has been frequently debated. Some consider that there is a hereditary predisposition (Selcer and Oliver, 1972; Mason, 1979; Raffé and Knecht, 1980; Jaggy *et al*, 1988; Lewis, 1991). Previous articles (Wright, 1973; Lewis, 1991) have proposed certain conformational features of the dog play an important role in the development of cervical vertebral abnormalities. In particular, authors have suggested that the presence of a long neck and heavy head result in abnormal forces which act on the developing vertebrae and cause them to become deformed (Wright *et al*, 1973; Lewis, 1989; Lewis, 1991). Others suggest gender (Palmer and Wallace, 1967; Jaggy *et al*, 1988), rate of growth and over-nutrition (Hedhammer *et al*, 1974; Lewis, 1989; Lewis, 1991) are important aetiological influences. In addition, trauma has been implicated as a predisposing factor in older animals (Chambers and Betts, 1977; Read *et al*, 1983). Clearly, until the true causes of the syndrome are discovered, our understanding of the condition and its treatment are likely to be limited.

In the late 1970's Chamber and Betts (1977) wrote "Hopefully, a co-operative effort among veterinarians and breeders will lead to a detection/prevention programme in the near future". Sadly their advice was not taken and our efforts have not focussed on this aspect of the disease.

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The aim of this survey was to investigate the prevalence of caudal cervical vertebral malformation and any neurological signs associated with caudal cervical spondylomyelopathy within the Dobermann pinscher population in three geographic regions of New Zealand with a view to identifying possible predisposing factors.

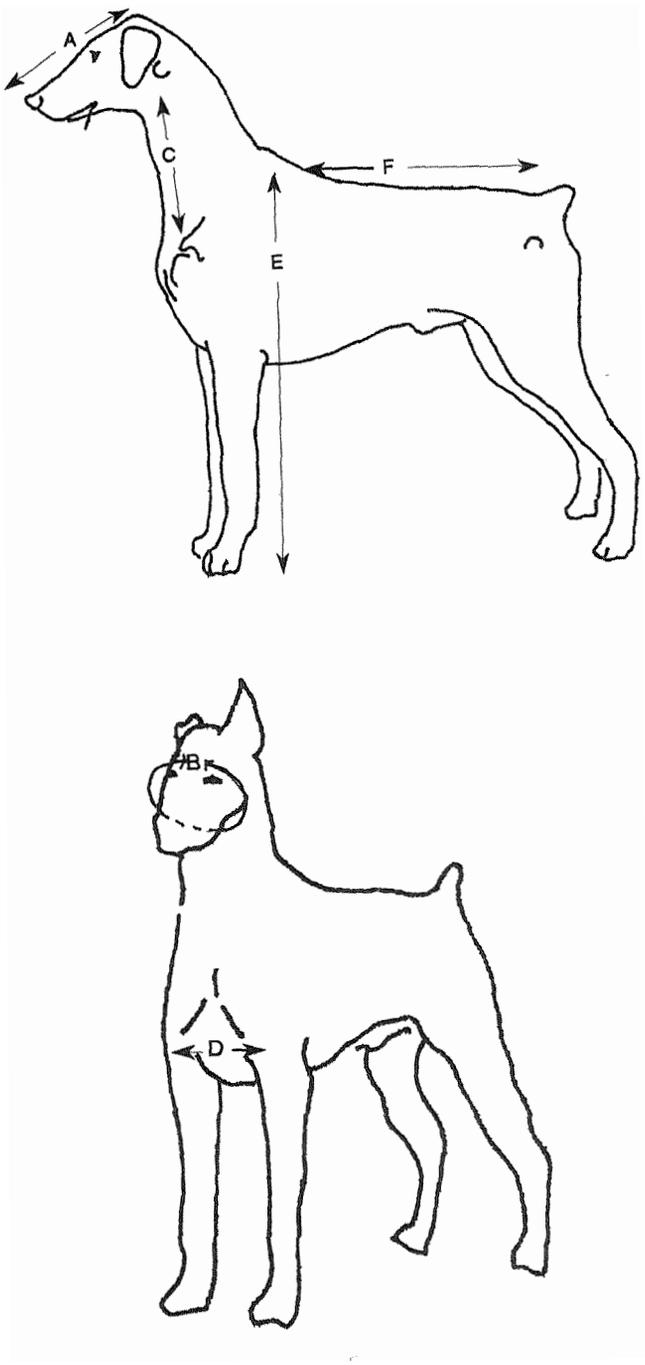
### **Materials and Methods**

The Dobermann dogs used in this study were those volunteered by owners contacted through breed associations, veterinary practices and acquaintances. The final survey population on which all the data could be collected consisted of 138 adults (44 male, 94 female) and 32 puppies (16 male and 16 female). The term "puppy" was used for any dog under one year of age. Dogs were only included into the study once all the required data was collected.

Data collected during the survey consisted of age, sex and location in New Zealand of each animal. Since owners of clinically affected "wobblers" frequently enquire whether the use of a choker chain predisposed their dog to the syndrome, this information was obtained for each dog. In addition, the following body dimensions were measured in dogs aged one year and over (Figure 3-1):

- A. distance from occipital prominence to tip of nose (head length)
- B. circumferential distance of the head at the level of the supraorbital prominences (head circumference)
- C. distance from wing of atlas to greater humeral tubercle (neck length)
- D. width of separation between the greater humeral tubercles (base width)
- E. standing height from the dorso-cranial point of the scapula to the ground (withers height)
- F. distance from the dorso-cranial point of the scapula to level of greater trochanter of the femur measured along the midline of the vertebral column (rump length)

The measurements were made with the dog standing and were taken once on each dog by the same person.



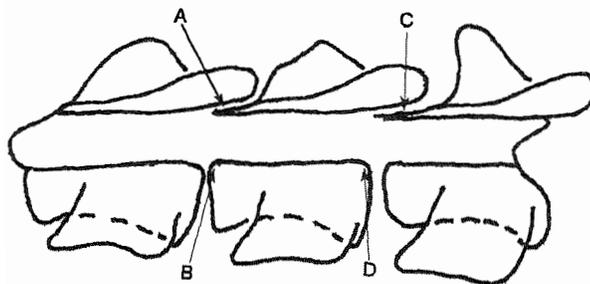
**Figure 3-1:** Topographical diagrams of body measurement points taken in each adult dog. Head length A, head circumference B, neck length C, base width D, wither height E, rump length F.

### ***Radiographic examination***

A radiographic examination, consisting of one lateral view of the caudal cervical vertebrae (fourth cervical to first thoracic) taken under sedation with the neck placed in a neutral position, was then carried out. The developed films were assessed for radiographic quality and correct patient positioning. Where these were deemed to be substandard, the dog was either re-radiographed or eliminated from the survey. In order for the radiological changes to be compared statistically, a scoring system was developed.

### ***Difference in sagittal diameters***

The difference in sagittal diameters was recorded between the caudal and cranial aspects of the neural canal of the fifth (C5), sixth (C6) and seventh (C7) cervical vertebrae. This measurement has been shown to be a reliable indicator of neural canal stenosis (Wright, 1979). The landmarks used were: the cranio-dorsal edge of the vertebral body and the ventro-cranial point of the lamina mid-way between the cranial articular facets (cranial sagittal diameter) and the caudo-dorsal edge of the vertebral body and the ventro-caudal point of the lamina mid-way between the caudal articular facets (Figure 3-2). Normal (Score 0) was taken to be a difference of 3mm or less (Wright, 1979; Lewis, 1989). Those dogs where the difference was 4-6mm scored 1 point, a 7-9mm difference scored 2 points and over 9mm 3 points.



**Figure 3-2:** Diagrammatic representation of a caudal cervical vertebra, showing points for the measurement of sagittal diameters. Cranial sagittal diameter is the distance AB, caudal sagittal diameter is the distance CD and the sagittal diameter difference is (CD) - (AB).

*Vertebral abnormalities*

In any of three caudal vertebrae C5, C6 and C7 the presence of: vertebral tilting, rounding of the cranio-ventral border of the vertebral body, alteration of the intervertebral disc space and ventral spondylosis was recorded. The presence of an abnormality in any vertebra (C5, C6 or C7) was scored as one point.

From the arithmetic sum of these radiological scores, the dogs were assigned to one of three categories: I (score 0 or 1, regarded as normal), II (score 2-4) and III (score over 4).

*Neurological examination*

The neurological examination consisted of recording each dog's response to the segmental reflex arcs of flexor, extensor and patellar reflexes. Postural and attitudinal reactions of placement, proprioception, hemi-walk, hemi-stand, extensor postural thrust and tonic neck response were also recorded. The dogs were divided into three neurological groups. Dogs where no neurological deficit was detected were placed in Group A. Animals which were judged to have proprioceptive deficits and exaggerated patellar reflexes were assigned to Group B. Those with marked proprioceptive deficits and/or additional neurological signs of scuffed toes, forelimb extensor rigidity and neck pain were placed in Group C.

*Investigation of puppies*

Twenty of the 32 puppies were examined once. The remaining 12 of these puppies were examined neurologically and radiographically at different times during their first year of life (Figure 3-3). The puppies were included into the radiological and neurological group statistics based upon the result of their last examination.

*Genetic study*

Dam and sire names were collected where the pedigree was known. These were then collated in an attempt to identify any simple mechanism of inheritance of the disease.

Puppy	Age (months)								
	1.5	2	3	4	5	6	7	8	12
1					I				I
2				III					III
3				I		I			
4				I		I			
5				I		I			
6	I		I			I			
7	I		I			I			I
8	I		II			II			II
9				III	III				
10		I		I					
11		I		I					
12		I		I					

**Figure 3-3: The relationship between age of examination for 12 puppies which were examined repeatedly (the number indicates the radiological group at the time of examination for an individual puppy).**

### *Statistical analysis*

The statistical analysis consisted of two steps 1) a univariate analysis to individually examine the independent variables and 2) a multivariate analysis which tested the independent variables in conjunction with each other. Separate analyses were conducted for each of the dependent variables, radiological score and neurological score. In the *univariate analysis* the statistical association between the independent variables (body dimensions, age, gender, location, use of choker chain) and each dependent variable (radiological and neurological score) was tested using

Chi-squared tests for heterogeneity and analysis of variance (Snedecor and Cochran, 1989). Multiple comparisons of means were done using Bonferroni's method (Anon,1991). In the second step, independent variables which were statistically significantly associated with the dependent variable were included in a *multivariate analysis*. Stepwise logistic regression for a binary and an ordered categorical response were used to identify the most important variables. A p-value of less than 0.10 was used as the significance level for entry of the independent variables into and staying within the models. For the ordered response a parallel lines regression model was fitted to the data based on cumulative distribution probabilities of the response categories. The parallel lines assumption was tested using a chi-squared score statistic (Anon, 1991). If this assumption was violated the response variable was aggregated from three into two categories (healthy and affected), so that it could be modelled as a binary response variable. The Wald chi square statistic was used to test if individual regression coefficients were different from zero. The score statistic for Goodness of Model Fit, tests the joint effect of the explanatory variables in the model (Hosmer and Lemeshow, 1989). The regression procedures were implemented in SAS version 6.08 using PROC LOGISTIC (Anon, 1991). Variables included in the final regression models were tested for the presence of interaction terms. Coefficients in the regression model were converted into odds ratios for binary response variables and into cumulative odds ratios for ordered categorical response variables (Milliken and Johnson, 1984; Agresti, 1989).

## **Results**

### ***Characteristics of the study population***

The study population comprised of 170 animals (60 male, 110 female) with a mean age of 43

months (range 4-156 months, mean 43.1, median 36). The adult dogs lived in three regional localities in New Zealand. These were: Hamilton (32 animals), Wellington/Palmerston North (68 animals) and Hawkes Bay (38 animals). Table 3-1 lists the descriptive statistics for the body dimensions measured in this study.

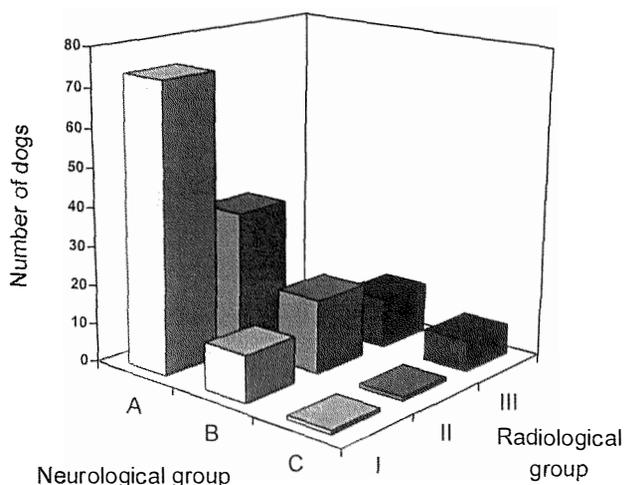
Variable	Number	Mean	Standard Deviation	Median
Base length (cm)	138	16.0	2.7	16
Head length (cm)	138	26.4	1.4	26
Head width (cm)	138	38.8	2.6	39
Neck length (cm)	138	22.4	2.8	22
Rump length (cm)	138	43.5	4.0	43
Withers height (cm)	138	67.5	3.7	67

**Table 3-1: Descriptive statistics of body dimensions for the adults dogs in the study population.**

Of the adult dogs and puppies examined, 48.9% (n=83) (including nine puppies) showed some radiological sign of caudal cervical malformation. Thirty three percent (n=56) of the dogs were grouped into category II and 15.9% (n=27) into category III. Neurological examination of the 170 animals showed that 68% (n=116) were normal (Group A), 26% (n=44) had some proprioceptive deficits with or without exaggerated patellar reflexes (Group B) and 6% (n=10) were regarded as having more marked neurological signs typical of clinical wobbler syndrome (Group C).

**Univariate Analysis**

Dogs with radiological signs of the disease (categories II and III) were 5.56 times more likely to have neurological deficits (at least group B) than dogs which did not show radiological signs ( $\chi^2=23.26$ ,  $p=0.001$ ; figure 3- 4).



**Figure 3-4: The relationship between neurological signs and radiological findings.**

**Radiological Score**

There was no statistically significant association between radiological score and gender ( $\chi^2=1.43$ ,  $p=0.49$ ) or the use of choker chains ( $\chi^2=4.08$ , 2df,  $p=0.13$ ). When the relationship between radiological category and location was examined it was found that dogs residing in the Hawkes Bay region were less likely to have cervical vertebral abnormalities than dogs from Hamilton and Wellington ( $\chi^2=9.88$ ,  $p=0.04$ ). Table 3-2 shows the results of the statistical comparison of the distribution of continuous independent variables (age and body dimensions) between the three different radiological groups using analysis of variance.

Variable	Group I			Group II			Group III			F-test			Bonferroni's pairwise Comparison <sup>a</sup>
	Mean	SD	n	Mean	SD	n	Mean	SD	n	F	df	p-value	
Age (months)	35.7	31.1	87	45.0	31.2	56	63.0	36.8	27	9.52	2167	0.0002	I-III
Base length (cm)	16.4	3.1	64	15.7	2.1	49	15.7	2.6	25	1.17	2135	0.3128	
Head length (cm)	26.5	1.5	64	26.6	1.4	49	25.9	1.2	25	2.54	2135	0.0804	
Head width (cm)	38.7	2.7	64	39.2	2.6	49	38.4	2.2	25	0.95	2135	0.3920	
Neck length (cm)	22.5	2.5	64	22.9	3.0	49	21.5	3.1	25	2.37	2135	0.0948	
Rump length (cm)	43.2	4.3	64	43.5	4.2	49	44.3	2.73	25	0.77	2135	0.4687	
Withers length(cm)	67.6	3.8	64	68.1	4.1	49	66.3	2.13	25	2.09	2135	0.1249	

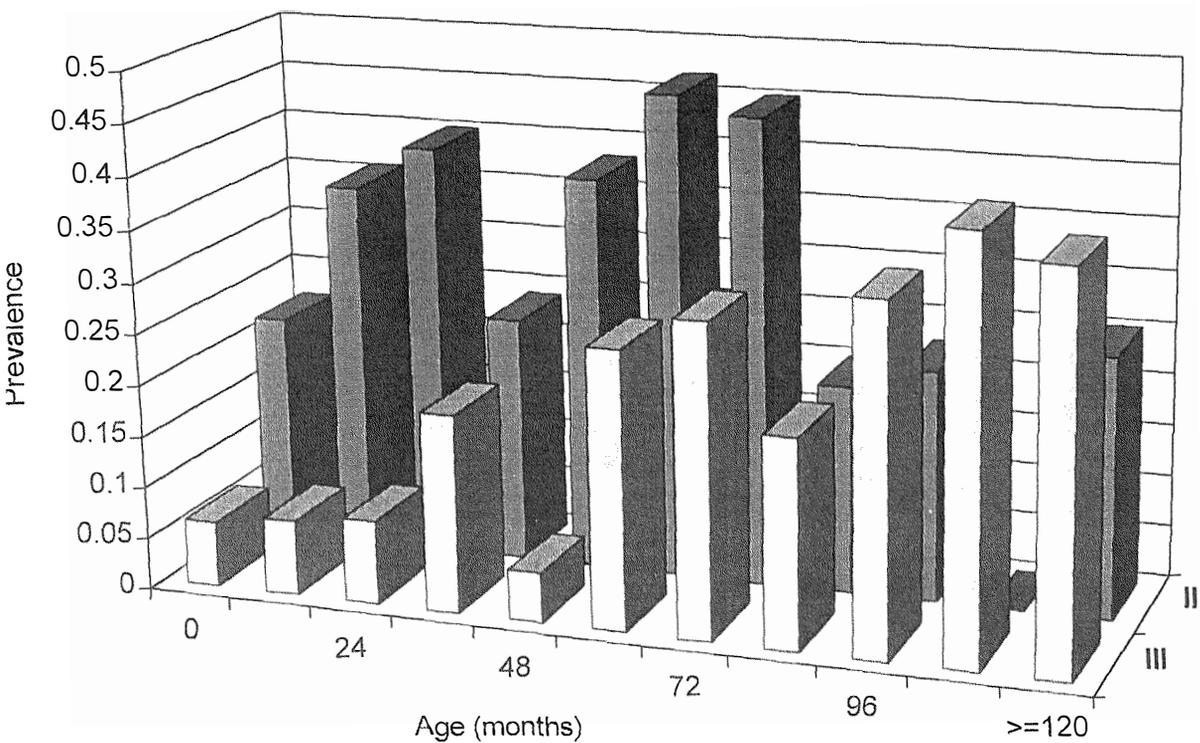
a = Indicates groups which were statistically significantly different in a multiple comparison of means ( $p < 0.05$ ).

SD = Standard deviation

n = Number

**Table 3-2: The distribution of age and body dimensions between different radiological groups, I, II and III.**

There was a statistically significant difference between the distribution of ages of dogs in group I compared with the distribution of ages of dogs in group III. However, this was not so between dogs in group I and II or II and III. Dogs in group I were on average younger than dogs in group III. Figure 3-5 shows the prevalence of radiological changes for different age intervals. There was no statistically significant association between body dimensions and radiological score.



**Figure 3-5:** Prevalence of dogs with radiological changes by age II = prevalence of dogs with radiological Group II findings in the sample (Group II / Group (I + II + III)); III = prevalence of dogs with radiological group III findings in the sample (Group III / Group (I + II + III)).

*Neurological Score*

There were no statistically significant associations between the variables, location, gender and use of choker chain and the dependent variable neurological grouping (location  $\chi^2=4.43$ ,  $p=0.35$ ; gender  $\chi^2=2.37$ ,  $p=0.30$ ; choker chain  $\chi^2=2.17$ , 2df  $p=0.34$ ). The results of a statistical comparison of the distribution of age and body dimensions between the three different neurological groups using analysis of variance are presented in Table 3-3.

Variable	Group A			Group B			Group C			F-test			Bonferroni's pairwise Comparison <sup>a</sup>
	Mean	SD	n	Mean	SD	n	Mean	SD	n	F	df	p-value	
Age (months)	36.7	31.9	116	49.6	26.0	44	89.2	38.7	10	35.7	2167	0.0000	A-C, B-C
Base length (cm)	15.6	2.5	87	16.4	3.1	42	17.4	1.5	9	5.21	2135	0.0067	
Head length (cm)	26.3	1.3	87	26.6	1.7	42	26.1	1.4	9	0.87	2135	0.4237	A-C, B-C
Head width (cm)	38.7	2.3	87	39.2	3.0	42	38.9	2.3	9	1.72	2135	0.1805	
Neck length (cm)	22.7	2.7	87	22.4	2.7	42	19.7	3.3	9	11.5	2135	0.0000	
Rump length (cm)	43.0	3.7	87	44.2	4.6	42	45.2	3.1	9	3.84	2135	0.0234	
Withers length (cm)	67.6	3.8	87	67.6	3.8	42	66.1	2.3	9	1.56	2135	0.2122	

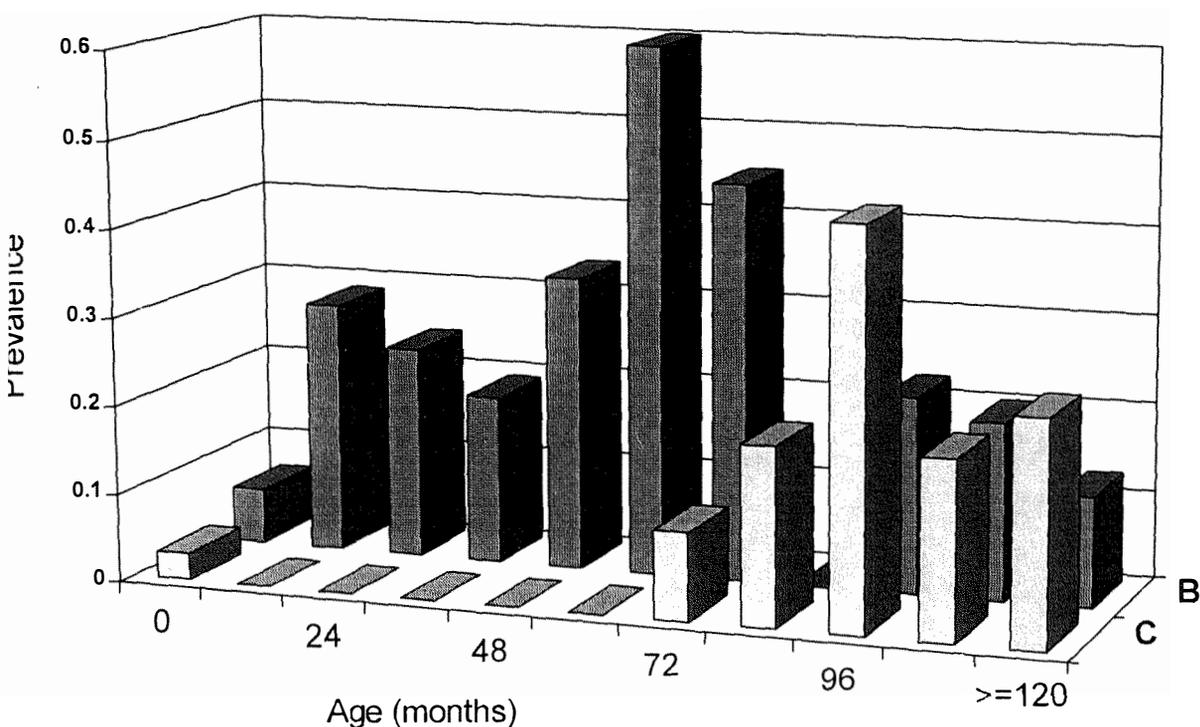
a = Indicates groups which were statistically significantly different in a multiple comparison of means ( $p < 0.05$ ).

SD = Standard deviation

n = Number

**Table 3-3: The distribution of age and body dimensions between different neurological groupings, A, B and C.**

There was a statistically significant difference between the mean ages of dogs in neurological groups A and B compared with group C. Dogs in neurological group C were on average older than dogs in group A and B. Figure 3-6 shows the prevalence of neurological signs for the different age intervals. Furthermore dogs with a neurological score of group C had on average shorter necks than dogs in groups A and B.



**Figure 3-6:** Prevalence of dogs with neurological signs by age (B = prevalence of dogs with neurological Group B signs in the sample (Group B / (Group A + B + C)); C = prevalence of dogs with neurological Group C signs in the sample (Group C / Group (A + B + C))).

The result of analysis of variance suggested that the mean values for average base length and rump length were different between the neurological groupings. However, the Bonferroni's method which was used for pairwise comparisons of means indicated that there was no statistical difference between neurological groups.

**Multivariate Analysis***Radiological Score*

The final ordinal regression model for radiological scores indicated a relationship between these scores and both age and location. There was no statistically significant interaction between these two factors. The regression coefficient suggests that the risk of having a higher radiological score increased with age and decreased if the dog lived in the Hawke's Bay area (Table 3-4).

Variable	$\beta$ - coefficients	SE	Odds ratio	Wald $\chi^2$	p-value
Intercept 1	-2.0956	0.3904	0.123	28.81	0.0001
Intercept 2	-0.2543	0.3367	0.775	0.5706	0.4500
Age (months)	0.0158	0.0055	1.016	8.0768	0.0045
Hawke's Bay location	-1.3509	0.4013	0.259	11.3291	0.0008

Score Test for Goodness of Model Fit:  $\chi^2 = 18.245$  (two df),  $p = 0.0001$ .

Score Test for Proportional Odds Assumption:  $\chi^2 = 2.7661$  (two df),  $p = 0.2496$ .

SE Standard error

df Degrees of freedom

**Table 3-4: Final ordinal regression model for radiological findings.**

*Neurological Score*

The final ordinal regression model for neurological score did not fulfill the proportional odds assumption ( $\chi^2=19.26$  (5df),  $p=0.002$ ). The dependent variable was aggregated to two categories, 0 for a neurological grouping A and 1 for a neurological grouping B or C. The final logistic regression model showed the risk factors age and rump length were the most important predictors of neurological score. The risk of neurological signs increased with age and rump length. There was no statistically significant interaction between these two independent variables. Table 3-5 provides detailed information on the final regression model.

Variable	$\beta$ - coefficients	SE	Odds ratio	Wald $\chi^2$	p-value
Intercept 1	-5.2175	2.1097	0.005	6.1159	0.0134
Age (months)	0.0139	0.0061	1.014	5.2802	0.0216
Rump length (cm)	0.0902	0.0468	1.094	3.7095	0.0541

Score Test for Goodness of Model Fit:  $\chi^2 = 9.046$  (two df),  $p = 0.0109$ .

SE Standard error

df Degrees of freedom

**Table 3-5: Final logistic regression model for neurological signs.**

### *Serial Survey of Puppies*

No radiological abnormalities were detected in puppies radiographed before three months of age. However radiological abnormalities of vertebral tilting and increased caudal and cranial sagittal diameter differences (>3mm) were detected in 28% of puppies (n=9) over three months of age. One of these puppies had been radiographed at six weeks of age. After three months of age, the radiological category did not change in any puppy. Figure 3-3 shows the radiological scores for each of the puppies that were radiographed on more than occasion. Only 9% of puppies (n=3) showed any neurological deficits. One of these had sufficient radiological abnormalities to be placed in Category II and had slight proprioceptive deficits. The other two had marked radiological changes (Category III) and were euthanased due to the severity of their neurological signs. The remaining six puppies with radiological signs showed no neurological deficits.

### *Genetic Study*

Whilst several pedigree lines were traced, the data was incomplete with regard to ancestral and other littermate status. Therefore no conclusive evidence supporting a genetic basis to the defect was found.

**Discussion**

The finding that nearly 50% of the dogs in this survey had radiographic changes of cervical vertebral malformation that are associated with caudal cervical spondylomyelopathy confirmed the findings of the only other published survey of clinically normal Dobermanns (Lewis, 1991). In this latter publication nearly 25% of the 115 dogs studied possessed obvious radiological abnormalities with a further 61 dogs having minor changes only. These minor radiological findings were changes in the shape of the cranio-ventral border of the vertebrae, slight stenosis of the neural canal and ventral narrowing of the disc spaces.

The vertebral abnormalities associated with the caudal cervical spondylomyelopathy appear to be present from an early age and throughout adult life since they were detected radiographically throughout the whole age range in this study. The finding that proportionally more of the older dogs were graded in radiological group III probably indicates that they had increased secondary changes such as intervertebral disc space narrowing or ventral spondylosis and therefore received a higher score.

In contrast to several clinical papers on caudal cervical spondylomyelopathy (wobbler syndrome) (Palmer and Wallace, 1967; Read *et al*, 1983; Raffe and Knecht, 1980; Lewis, 1989), the presence of radiological changes in this study population did not reveal any gender predilection. Clinical disease is reported to be more common in males (Raffe and Knecht, 1980; Seim and Withrow, 1982; Read *et al*, 1983; Shores, 1984; Lewis, 1989), but perhaps this is because they may be more active and consequently prone to neck injury.

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The discovery that geographic locality of the dog had an influence on radiological category was interesting. The reason for this difference could be due to environmental factors peculiar to each locality but since in New Zealand these animals tend to be bred within regions this result could reflect the existence of a familial trait.

In this survey there was no confirmation of the hypothesis that the cervical vertebral deformity seen in caudal cervical spondylomyelopathy arises secondary to affected dogs having a longer neck and heavier head (Wright *et al*, 1973). Indeed the radiological changes were independent of any of the body dimensions measured including neck length and head size (both length and circumference).

Neurological assessment of a population of apparently healthy Dobermanns has not been reported previously. In this study, 54 of the 170 dogs examined did show some neurological signs. However, for the vast majority of those affected (Group B) the signs were so slight that the owners were unaware of them. The strong association between neurological grouping and the radiological grouping was expected because wobbler syndrome (caudal cervical spondylomyelopathy) is the most commonly reported cause of cervical spinal cord disease in Dobermanns.

One other important factor which influenced the extent of neurological signs was age. Marked neurological signs of wobbler syndrome occurred more often in older dogs (over six years of age). This finding is in agreement with reports of clinical cases of caudal cervical spondylomyelopathy where the average recorded age of presentation is seven years of age (Seim and Withrow, 1982; Lewis, 1989) and is probably indicative of the progressive degeneration of

the cervical spinal cord which results from the continued or increased compression of the cord by the vertebral column deformity and associated soft tissue changes.

In this survey, the only other statistically significant factor associated with neurological grouping was rump length. The association of longer rump length with increased risk of neurological disease is difficult to explain. It may be that this is a true risk factor for the development of neurological signs of wobbler syndrome.

The survey of puppies provided new information on the disease. Firstly, although it was known that wobbler syndrome occurs in puppies ( Raffe and Knecht, 1980; Read *et al*, 1983; Lewis, 1989) it has not been shown that the radiological signs of cervical vertebral malformation can be detected from approximately three months of age. As in the adult, radiological changes did not necessarily indicate the presence of neurological signs, but each puppy with neurological signs did have marked radiological abnormalities. Interestingly the cervical vertebrae of one of the puppies which was radiographed at six weeks of age appeared normal but when subsequently radiographed at three months of age, showed signs of vertebral tilting. Possible reasons for this are that at the earlier age there was insufficient ossification present to detect a deformed cartilaginous template radiologically or that the vertebral deformity occurs between the ages of six to 12 weeks.

Possible main factors for influencing vertebral shape and growth at less than three months of age are hereditary factors and nutrition. Both have been implicated by several authors (Selcer and Oliver, 1972; Palmer and Wallace, 1973; Hedhammer *et al*, 1974; Jaggy *et al*, 1988; Lewis, 1989).

Three studies (Palmer and Wallace, 1967; Selcer and Oliver, 1972; Jaggy *et al*, 1988) have indicated that cervical spondylomyelopathy in dogs has an hereditary basis, with two of them (Selcer and Oliver, 1972; Jaggy *et al*, 1988) stating that the mode of inheritance is recessive. However, neither of these studies provided conclusive evidence for this assumption and, to the author's knowledge, a properly designed test-mating study has not been performed. One survey in Dobermanns (Lewis, 1991) failed to find any clear-cut genetic basis. Unfortunately, insufficient lineage data was available in the study presented here to indicate any hereditary trait.

It was concluded from this survey that in the population of Dobermanns studied, radiological changes of cervical vertebral malformation characteristic of caudal cervical spondylomyelopathy were present throughout a wide age range. However the associated neurological signs tended to appear in dogs aged six years and over.

### Post-natal development of canine caudal cervical vertebrae

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#### Abstract

This study describes the morphology and post-natal ossification of the fifth, sixth and seventh cervical vertebrae. Its objective was to provide information on the normal development of the caudal cervical vertebrae in breeds of dog not usually affected by cervical vertebral malformation. The caudal cervical spines from 51 crossbred puppies (age range birth to 12 weeks) were examined grossly, histologically and radiographically. At birth, three centres of ossification exist, one in the vertebral body and one in the base of each pedicle of the neural arch. By one month of age secondary centres of ossification were present in the cranial and caudal epiphyses of the vertebral body. By two months of age these epiphyseal centres began to show signs of closure. Endochondral ossification of the neural arch occurred from a single ossification centre within each pedicle with bony fusion of the laminae occurring by one month of age. In addition the neural canal dimensions were recorded. The measured difference between caudal and cranial sagittal diameters was 1 mm or less for each vertebra. It was concluded that, after one month of age and during normal development, the shape of the neural canal can be influenced only by changes within the physes between the vertebral body and neural arch, or by remodelling of bone formed by intramembranous ossification.

#### Introduction

There have been few studies published, based on a Vet CD (1973-1991) and CAB abstract on CD-ROM (1984-1993) literature search<sup>1</sup>, on the post-natal development of canine cervical vertebrae (Hare, 1961; Watson *et al*, 1986; Watson and Stewart, 1990). Only one study (Hare, 1961), covering the radiographic anatomy of the developing vertebrae, gives any information on the sequence of ossification in the caudal cervical vertebrae. This lack of information is surprising in light of the conformational abnormalities that are known to affect this region of the vertebral column. One disease, in particular, that affects the developing caudal cervical vertebrae is caudal cervical spondylomyelopathy or wobbler syndrome. This disease has long been

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<sup>1</sup> Silver Platter International, Boston

recognised and reported in dogs, particularly within the Dobermann pinscher and Great Dane breeds (Wright *et al*, 1973; Chambers and Betts, 1977; Denny *et al*, 1977; Seim and Withrow, 1982). The aetiology is unknown but genetic and nutritional factors which influence skeletal development have been implicated (Hedhammer *et al*, 1974).

The embryological development of the vertebrae has been described in mammals (Noden and de Lahunta, 1985; Uthoft, 1990). During early embryonic life the paraxial mesodermal tissues coalesce to form aggregations of cells called somites. The vertebrae form from the ventro-medial (sclerotome) portions of these somites. The development of the sclerotomes proceeds in a craniocaudal sequence as does chondrification of the vertebrae. However ossification of the vertebrae is less ordered (Lindsay, 1972; Bagnall *et al*, 1977). In the dog, vertebral ossification begins in the sixth week of gestation with primary ossification centres appearing laterally in the base of each pedicle of the neural arch and in the middle of each centrum (Noden and de Lahunta, 1985).

The aim of this study was to describe the morphology and post-natal ossification of the fifth, sixth and seventh cervical vertebrae in breeds of dogs not usually affected by cervical vertebral malformation or caudal cervical spondylomyelopathy, thus providing a basis for interpreting abnormalities in dogs predisposed to this abnormality.

### **Materials and Methods**

The cervical vertebral columns from 51 cross-bred puppies were obtained from unwanted litters that had been humanely killed. In each case the cervical vertebral columns were dissected from the cadavers within 24 hours of death. The age of the puppies ranged from newborn through to approximately 12 weeks (Table 4-1). The exact age of some of the older puppies was unknown, but was estimated from the radiographic appearance of the ossification centres in each of the forelimbs (Schebitz and Wilkens, 1986). This comparison required the radiographic examination of forelimbs of all the dogs. The puppies were then divided into five age groups (i) newborn, (ii) one week, (iii) three to four weeks, (iv) seven to eight weeks and (v) 10 - 12 weeks.

Number of puppies	Approximate Age	Number of specimens used for techniques			
		Radiography	Bacterial maceration	Cleaning by dermestid larvae	Histology
12	0-1 day	12	2	2	8
2	1 week	2		1	1
19	3-4 weeks	19		9	10
12	7-8 weeks	12		6	6
6	10-12 weeks	6		2	4

**Table 4-1 :** Details of processing techniques used on 51 puppies for studying post-natal ossification of the caudal cervical vertebrae.

The caudal cervical vertebrae from the fourth cervical to the first thoracic were examined *en bloc* in three ways, radiographically, grossly and histologically. Firstly, all cervical vertebral columns were examined radiographically using non screen film<sup>o</sup> and a cabinet x-ray with a fluoroscopic inspection system\*\* (0.5 mm focal spot). By examination of lateral and ventro-dorsal radiographic views the presence and the developmental sequence of the ossification centres of each vertebra were recorded.

Two of the caudal cervical vertebral columns from newborn puppies were then subjected to bacterial maceration. This had the effect of removing the soft tissue, but leaving the cartilage and bone intact. These specimens were then placed in 10% formalin and examined. In addition, two other dissected cervical columns from newborn puppies and 18 from older puppies were placed in a colony of *Dermestes maculatus* larvae. The larvae removed all the soft tissue, leaving dry cleaned vertebral bones. These were also examined grossly.

The remaining 29 caudal cervical vertebral columns were dissected from much of the surrounding musculature and fixed in 10% formalin. Demineralisation was performed by

<sup>o</sup> Fuji Medical x-ray film. Super HR-G. Fuji Photo Film Co Ltd. Japan

\*\* Torrex 150 Torr x-ray Corporation Harbour City, California.

immersion in 8N formic acid and 1N sodium formate (1:1) and the process monitored radiographically. Once complete demineralisation had occurred histological sections of the caudal cervical vertebral column were prepared. This consisted of cutting 0.5 cm slices taken in one or more of the following planes i) a median longitudinal plane through the fifth, sixth and seventh vertebrae, ii) a longitudinal plane through the articular facets of these vertebra and iii) a series of transverse sections through each the caudal cervical vertebra. After routine processing the histological sections were cut at three  $\mu\text{m}$  thickness and stained with either haematoxylin and eosin or by the PAS/alcian blue method.

The information gained from these four techniques was used to compile a description of the developmental anatomy of the caudal cervical vertebrae from birth to 12 weeks of age.

In addition, the cranial and caudal sagittal diameters of the neural canal of the fifth, sixth and seventh vertebrae were recorded in the dermestid-cleaned bones from puppies aged three-four weeks and older. The sagittal diameter was measured with calipers from the mid cranial and caudal points at the base of the dorsal spinous process to the corresponding midpoint of the dorsal surface of the vertebral body. The difference between cranial and caudal sagittal diameters was calculated for each vertebra.

## **Results**

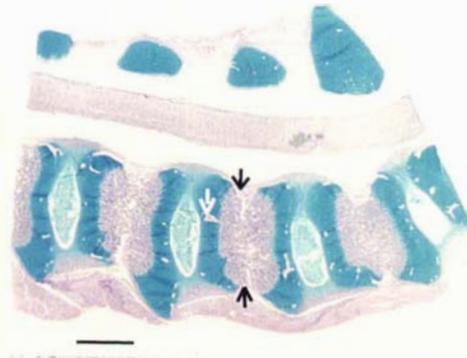
### ***Ossification centres***

In the newborn puppies, three separate ossification centres were identified in each of the caudal cervical vertebrae, one in the middle of the body and one at the base of each pedicle of the neural arch. The development of these centres from newborn to 12 weeks of age will be described separately.

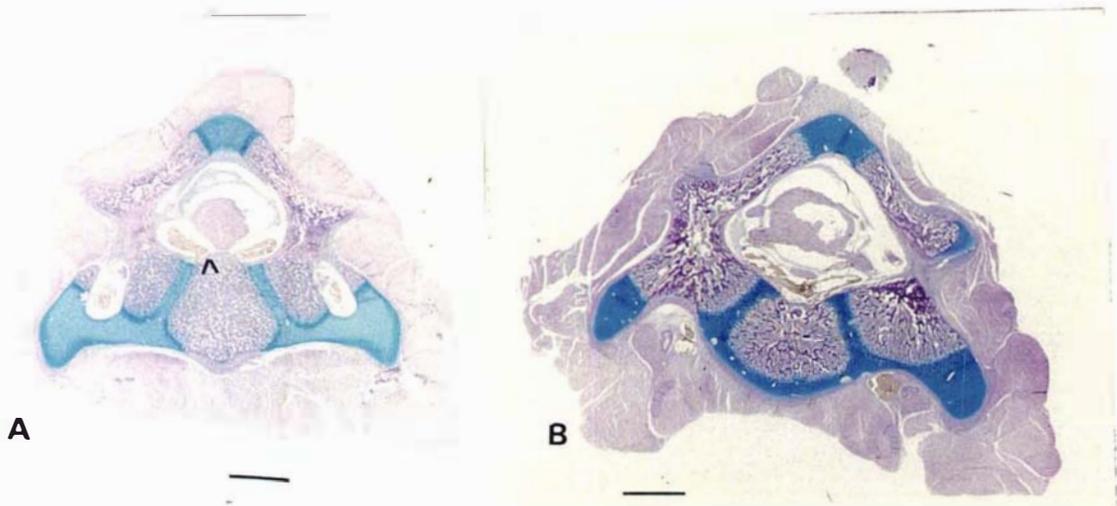
#### ***1) Vertebral body***

In the newborn puppies the primary centre of ossification of the vertebral body was surrounded by hyaline cartilage except at the median point dorsally and ventrally. At these points, a cuff of bone was present through which vessels penetrated to enter the centre of the vertebral body. Furthermore, at these sites, bone formation was occurring by intramembranous ossification beneath the periosteum (Figure 4-1 and 4-2). Within the primary ossification centre, haemopoietic tissue filled the spaces between bone trabeculae. At this stage of development

most bony trabeculae still contained fragments of mineralised cartilage.



**Figure 4-1 :** Longitudinal midline section through the caudal cervical vertebrae of a newborn puppy. Stained by PAS/Alcian blue method. Bar = 0.22 cm. Note the bony cuff dorsally and ventrally (black arrows) and the cartilage canals (white arrow).



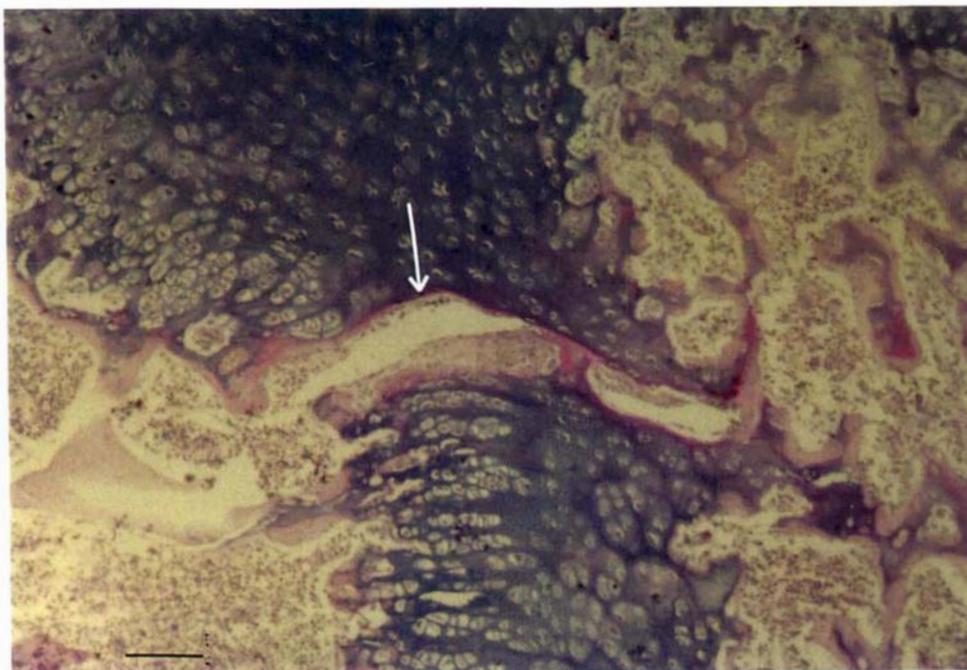
**Figure 4-2 :** Transverse section of A) sixth and B) seventh cervical vertebra of a newborn puppy. Note the sites of endochondral ossification of the neural arches and vertebral body. The arrow indicate the vessel of drainage into longitudinal ventral vertebral sinuses. Stained by the PAS/Alcian blue method. Bar = 0.15 cm.

At the chondro-osseous interfaces, active endochondral ossification was taking place. Several canals containing blood vessels were present within the cranial and caudal hyaline cartilage. Since there was no degeneration or bone formation around these vessels, they were considered to be nutrient vessels to the cartilage within cartilage canals (Figure 4-1). At the vertebral body/disc interface, the lamellae of the *annulus fibrosus* merged with the cartilaginous end plate and surrounding perichondrium and periosteum.

Dorso-laterally, at the junction of each neural arch with the vertebral body, there was a large vascular foramen containing a thin walled vein which joined the ipsilateral longitudinal ventral vertebral sinus (Figure 4-2).

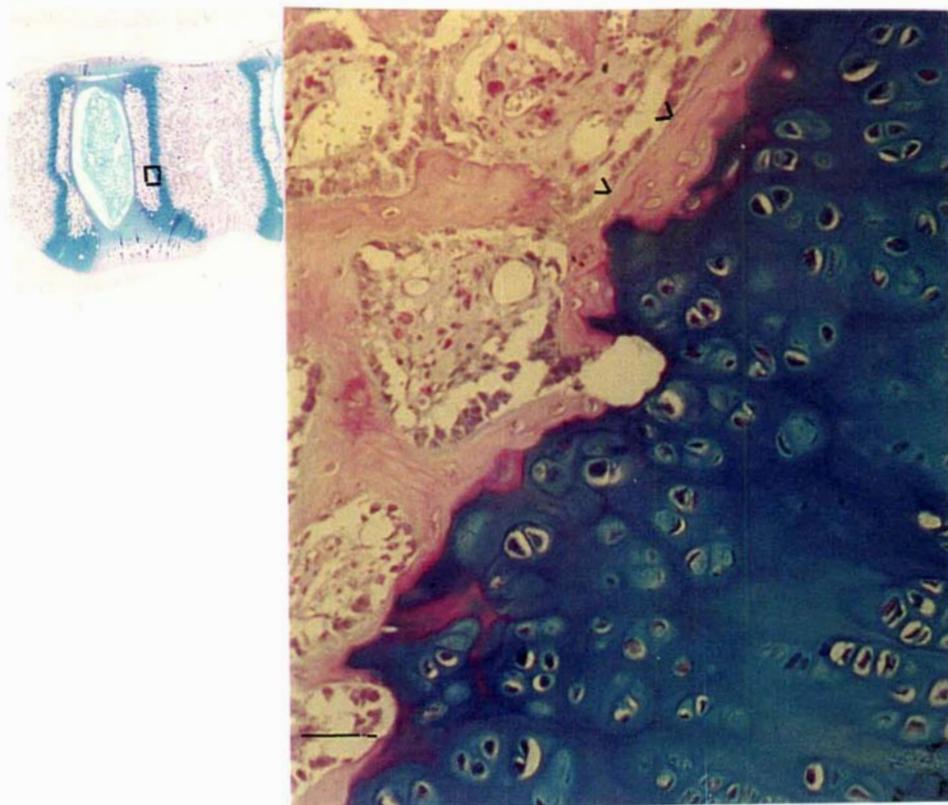
No differences in the anatomy of the vertebral body were detected between the puppies examined at birth and at approximately one week of age.

By three to four weeks of age, secondary centres of ossification had developed within the cranial and caudal epiphyses. Cartilage canals were present in the remaining thick zones of cartilage dorsal and ventral to the newly ossified tissue. Some blood vessels entered or crossed the growth plate between the epiphyseal and metaphyseal sinusoids (Figure 4-3). These transphyseal vessels were usually associated with a cartilage cone projecting into the sinusoidal area. Within the epiphyses, spicules of recently formed bone contained cords of mineralised cartilage. However, the amount of mineralised cartilage in the primary ossification centres had markedly diminished. Endochondral ossification was occurring at all chondro-osseous junctions.



**Figure 4-3 :** Longitudinal section of cervical vertebral body of a three to four week old puppy showing the growth plate between primary centre of ossification and the caudal secondary centre. The arrow shows a transphyseal vessel. Stained by the PAS/Alcian blue method. Bar = 0.006 cm.

By seven to eight weeks post -partum, the secondary centres of ossification had expanded to occupy most of the epiphyseal regions. Some bony trabeculae, on either side of the epiphyseal growth zones, were now parallel in orientation indicating impending closure (Figure 4-4). In addition there was loss of hypertrophied chondrocytes at these growth sites. The dorsal vascular foraminae at this age were surrounded by bone.



**Figure 4-4 :** Longitudinal section of cervical vertebral body in a seven to eight week old puppy showing parallel orientation of the bony trabeculae on the epiphyseal side of the growth plate (arrows). Stained by the PAS/Alcian blue method. Bar = 0.006 cm.

At 10 - 12 weeks of age endochondral ossification was still occurring in vertebral bodies at the cranial and caudal poles of the primary ossification centre and at the junction of the neural arches and vertebral body.

Overall there was little evidence of mineralised cartilage within the bony spicules in any of the ossification centres, indicating that remodelling of the primary spongiosa had occurred.

## 2) Neural arches

The ossified portion of each ventral pedicle of the arch in the newborn puppies had a thickened base from which four processes extended, one cranially, one caudally, one dorsally and one ventrally (Figure 4-2). The cranial and caudal processes were recognised as the developing articular facets. Each of these facets was capped by hyaline cartilage with active endochondral ossification occurring at the chondro-osseous junctions.

The process extending dorsally formed the lamina of the neural arch (Figure 4-5a,e). This structure was joined (dorsal to the neural canal) to the lamina from the opposite side by cartilage. The cartilage extended dorsally to form the rudimentary dorsal spinous process. Active endochondral ossification was occurring at the chondro-osseous junction.

The ventral process was also capped by hyaline cartilage and represented the rudimentary transverse process. In the fifth and sixth cervical vertebrae, cartilage surrounded the blood vessels which pass through the transverse foramen. In the seventh vertebra, these vessels were seen to pass ventro-medially to the developing transverse processes. In the sixth vertebra, the cartilaginous precursor of this process protruded ventrally to form the wings. The cartilage of these processes in all three vertebrae was confluent with the cartilage between the ossification centres of the neural arch and the vertebral body. Again, active endochondral ossification was present at all chondro-osseous junctions.

By three to four weeks of age bony fusion of the neural arches was present (Figure 4-5b,f). This fusion appeared to be more complete in the seventh than in the fifth. A progressive increase in height of the cartilaginous dorsal spinous process between the fifth to the seventh was evident and active endochondral ossification was occurring at the bone-cartilage interface. The cranial and caudal articular facets were now easily recognised. Their articular surfaces were covered by cartilage and endochondral ossification was occurring at the chondro-osseous junctions. The growth plates of the ventral process and neural arch/vertebral body were also still open.

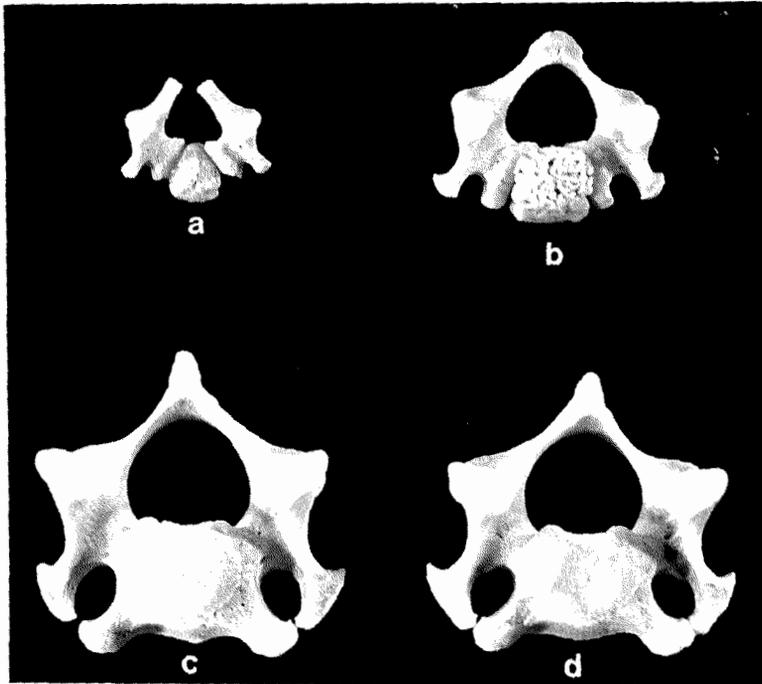
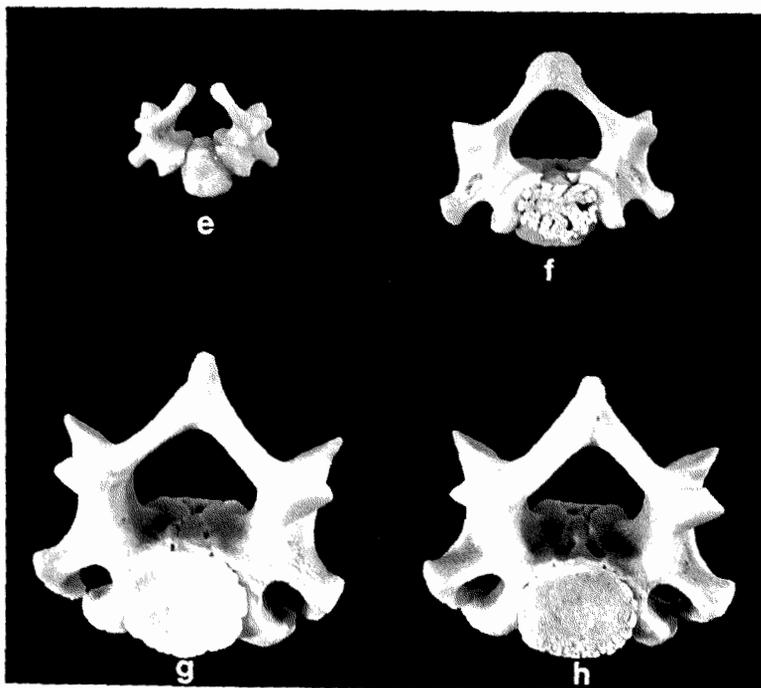


Figure 4-5 : A. Gross specimens of the sixth cervical vertebrae a) newborn, b) three to four weeks, c) seven to eight weeks and d) 10 to 12 weeks of age. Viewed cranial to caudal. Bar = 0.5 cm.



B. Viewed caudal to cranial.

By seven to eight weeks of age the bone content of the dorsal spinous processes, articular facets and transverse process had increased. The transverse foramen in the fifth cervical vertebra was completely surrounded by bone, but in the sixth a band of cartilage still existed ventrally (Figure 5c,g). Active endochondral ossification was still in progress at all chondro-osseous junctions at 10-12 weeks of age. Furthermore, in the sixth vertebra, commencement of ossification of the wings was now detected radiographically. Gross examination of this vertebrae revealed that bony fusion was occurring ventral to the transverse foramen (Figure 4-5d,h).

### *Intervertebral Discs*

The intervertebral discs showed few morphological changes over the age range studied. In newborn puppies the *annulus fibrosus* was seen to be thicker ventrally than dorsally. It consisted of fibrocartilaginous lamellae with many fibroblasts interspersed between them. These cells were more numerous at the inner margins of the annulus. The directional arrangement of the fibrous bundles alternated in sequential lamellae. Collagen fibres from the *annulus fibrosus* merged directly with the surrounding perichondrium, periosteum and cartilaginous end plates (Figure 4-6).



**Figure 4-6:** An intervertebral disc from a newborn puppy. Stained by the PAS/Alcian blue method. Bar = 0.013 cm

The *nucleus pulposus* consisted mainly of ground substance which was deeply basophilic and stained positively for proteoglycans. Within the centre of this homogenous material there were multiple large empty vacuoles. Dispersed between these vacuoles were single or clusters of small cells which were frequently joined by fine interlacing fibrils. Surrounding this central area was a fibrillar matrix merging with the cartilaginous end plate. At the nucleus-cartilaginous end plate junction the connective tissue cells appeared thin and elongated.

By 12 weeks of age the structure of the *annulus fibrosus* was maturing. The fibres were thicker, and fewer cells were present, particularly towards the periphery.

### ***Sagittal diameters of the neural canal***

The difference between the cranial and caudal sagittal diameters of the neural canal for each of the fifth, sixth and seventh cervical vertebrae was 1.0 mm or less (Table 4-2).

	vertebrae					
	C5 cranial	C5 caudal	C6 cranial	C6 caudal	C7 cranial	C7 caudal
	Puppies aged 3 - 4 weeks					
sagittal diameter (mm)	6	6	6	7	7	7
	6	6	7	7	7	6
	5	6	6	7	6	6
	7	7	7	8	7	7
	6	6	6	6	6	7
	6	7	7	7	7	7
	6	6	6	7	6	6
	6	6	6	7	7	7
	5	6	6	7	6	7
mean	5.8	6.2	6.3	7	6.5	6.6
	7 - 8 weeks					
sagittal diameter (mm)	9	10	10	11	11	10
	8	9	9	10	9	9
	7	8	8	9	8	8
	8	9	9	10	10	10
	8	10	9	10	9	9
	8	9	9	10	9	9
	8	9	9	10	9	9
mean	8	9.1	9	10	9.3	9.2
	10 - 12 weeks					
Sagittal diameter (mm)	8	9	9	10	9	9
	9	10	10	11	10	10
mean	8.5	9.5	9.5	10.5	9.5	9.5

**Table 4-2: Measurements of the cranial and caudal sagittal diameters of the fifth (C5), sixth (C6) and seventh (C7) cervical vertebrae.**

## Discussion

The traditional methods for studying ossification of skeletons have included gross examination of the cleaned bones, radiography and serial histology (Meyer and O'Rahilly, 1958; Watson *et al.*, 1986). The suitability of some of these techniques for studying skeletal ossification has been reviewed by several authors (Meyer and O'Rahilly, 1958; Watson *et al.*, 1986). They concluded that histological sectioning was the most sensitive technique for detecting fusion of the bony elements and for assessing the internal architecture of the bone. In addition, the tissues immediately surrounding the vertebrae such as the intervertebral discs, spinal cord and ligaments could also be examined. Gross examination was useful for examining the bones in their entirety and, in particular, their external surface. Detection of ossification centres by radiography is the least sensitive method.

The presence of the primary centre of ossification in newborn puppies and the development of the cranial and caudal epiphyseal centres by three to four weeks of age agrees with the radiographic findings of Hare (1961). Although by two to three months of age, active endochondral ossification was still occurring at the metaphyseal sites of the vertebral body and along the lateral walls at the junction of body and neural arch, the epiphyseal centres did show signs of impending closure. This difference in growth between epiphyseal and metaphyseal zones has been recorded in other bones and exactly how these epiphyseal areas continue to increase in size is unknown. The occurrence of transphyseal vessels in some of the histological sections was an interesting observation. The penetration of vessels across growth plates has been the subject of much debate (Firth and Poulos, 1982) and has only once been described in dogs (Haines, 1933).

The finding that primary ossification centres occurred in the base of each ventral pedicle of the neural arch in this study agrees with descriptions in other mammals (Hare, 1961; Lindsay, 1972; Uthoft, 1990). Unlike the vertebral body, each pedicle and lamina develop from enlargement of this single ossific centre. The cartilaginous precursors of the dorsal spinous process, articular facets and transverse processes undergo endochondral ossification at the adjacent parts of the neural arches. Since bony union of the neural arches occurs dorsally at three - four weeks, the shape of the neural canal can, under normal development, be influenced only by changes within the physes between the vertebral body and each neural arch or by remodelling of bone formed by intramembranous ossification.

Post-natal development of the intervertebral disc has been studied in man (Peacock, 1952) and rabbits (Scott *et al*, 1980). The structure of the *annulus fibrosus* and cartilaginous end plate in the present study was similar to that described in these species. The constituents of the *nucleus pulposus* were also similar. However, in this study identification of the cell type was not possible. A variety of cell types have been described in the *nucleus pulposus* (Trout *et al*, 1982; Johnson *et al*, 1986). These include chondrocytes, fibroblasts, notochordal cells, intermediate type cells and secretory cells. Since these cells have often been seen to share a common cell nest, it has been proposed that the different cells of the *nucleus pulposus* represent different degrees of maturity of a single cell type and have a common ancestry (Hansen, 1952; Johnson *et al*, 1986).

The sagittal diameter of the neural canal of cervical vertebrae has been commented on in several studies (Wright, 1977; Wright, 1979; Lewis, 1991). Comparison of cranial and caudal sagittal diameters has been shown to be a reliable indicator of cervical spine disease, in particular cervical stenosis (Wright, 1979; Lewis, 1991). Normal ranges of sagittal diameters and the differences between caudal and cranial measurements have been recorded for several breeds (Wright, 1979). In the majority of dogs that exhibited clinical signs of cervical spondylomyelopathy, these neural canal measurements fell outside the normal ranges. In this study, the difference between cranial and caudal sagittal diameters was small, agreeing with findings of other investigators.

Knowledge of the normal morphology and ossification of the caudal cervical vertebrae in puppies facilitates recognition of abnormal development. This is of particular relevance to the cervical spondylomyelopathy (wobbler syndrome). This syndrome is believed to be a multifactorial condition where primary vertebral developmental abnormalities and secondary degenerative changes lead to vertebral canal stenosis and spinal cord compression (Rusbridge *et al*, 1998). Suggested causes for the vertebral changes are over-nutrition, genetic defects and abnormal biomechanical forces acting on the growing vertebrae. Over-nutrition in Great Dane puppies has been associated with abnormal neural canal configuration, dorso-ventral compression of the spinal cord and cartilage deformities of the articular facets (de Lahunta *et al*, 1974). Others hypothesise that the malformation is due to osteochondrosis within the vertebral body (Lewis, 1992) or to hypercalcaitonism (Hazewinkel, 1989). It is unlikely that the cause of this syndrome will be understood until a thorough morphological study of developing cervical

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vertebrae in high risk breeds or families is conducted. The present study, using puppies from normally unaffected breeds, provides a basis for comparison for such a study.

### The accuracy and reliability of linear measurements of the ulna for anthropometrical studies in dogs

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#### Abstract

This study investigated the accuracy and reliability of measuring the distance between two surface landmarks (the point of the *tuber olecrani* and the proximal aspect of the stopper pad) as an indication of ulna length in the live dog. It was found that the chosen landmarks did correlate well with the length of the ulna bone. The reliability of such measurements was high when all were performed by one person, however the repeatability fell to unacceptable levels when more than one person made the measurements.

It was concluded that if this technique was to be used in studies to serially record the bone length in live growing dogs, then such measurements should be taken by a single person.

#### Introduction

The term “growth” has no single definition, but it is used to describe a quantitative process such as: to increase in size, to advance towards maturity, to extend, to become greater in any way. Anthropometry is the technique used to express body configuration quantitatively and serial recordings can be used to assess somatic growth. The number of measurements which can be applied are numerous and the selection of such measurements must be dictated by the purposes of the study.

Body weight has been used extensively in animals and man as a measure of growth, probably because of its ease of execution and for animals, importance in terms of carcass and market value. However, body weight is considered a poor index of skeletal growth due to the other contributing components of the body. Studies on the growth of long bones provide information on skeletal development, both for the individual and between individuals, thus enabling comparison between the differing growth patterns in diseased and non-diseased states. In order to study growth at the metaphyses of endochondrally formed bones in live animals, serial linear measurement studies are required. Few of these anthropometric studies are available in animals

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(Hintz *et al*, 1979; Watts, 1985; Thompson, 1995).

One factor common to all anthropometrical studies is the requirement to maintain accuracy of measurement despite numerous potential sources of variation such as subject, measurer, and instrumentation. Despite this, there are few definitive works on the reliability of such measurements (Tanner and Weiner, 1949; Kemper and Pieters, 1974; Jordon *et al*, 1975; Martorell *et al*, 1975).

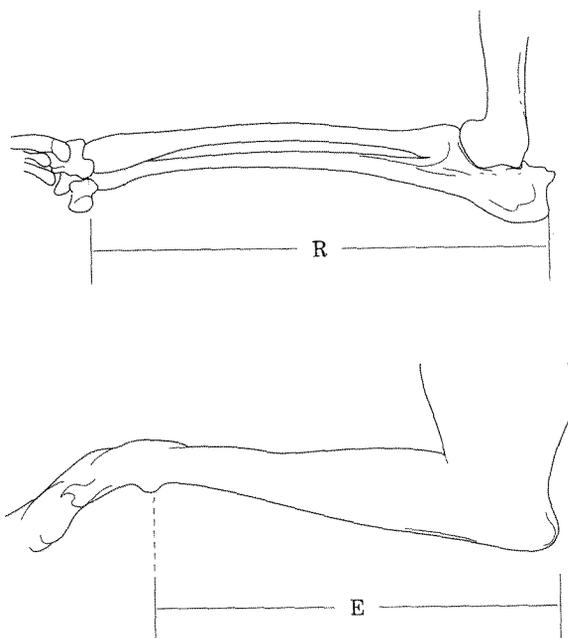
This paper describes the accuracy of measurement of the distance between chosen surface landmarks as an estimate of ulna lengths and the reliability (both “within observer” and “between observer”) of measuring this distance for use as an anthropometrical measurement for studying linear bone growth in dogs.

### **Materials and Methods**

To test the reliability and validity of measurement of the ulna bone for use in skeletal growth studies, three investigations were conducted. The methods and notation for the different intraclass correlation coefficients follow Shrout and Fleiss (1979). The statistical significance of the intraclass correlation was assessed using the row effects F statistic as described in McGraw and Wong (1996). The “within subjects coefficient of variation” was also calculated to give a percentage value of measurement error in relation to the absolute value (Bland, 1995).

#### ***Study 1      Assessment of the accuracy of the chosen surface land marks as an estimate of ulna length.***

Twenty-five adult dogs from large non-chondrodystrophoid breeds were used in this study. With each foreleg held in a flexed position, one person measured the distance along the caudal aspect of the antebrachium, between the palpable point of the *tuber olecrani* and the junction of the proximal aspect of the stopper pad with the hairy skin (Figure 5-1). The leg was held with the elbow joint flexed at a 90° angle to the humerus. This measurement was repeated twice on each foreleg and the average of the three recorded.



**Figure 5-1** Diagrammatic representation of the external (E) and radiographic (R) measurement of the distance between the *tuber olecrani* and the tip of the styloid process.

Radiographs of both antebrachii were then taken using a lateral view with the elbow flexed at 90 degrees. The length of the ulna bone was measured from the point of the *tuber olecrani* to the distal tip of the styloid process as seen on the radiographic image (Figure 5-1).

For each leg, the distance measured between the two surface landmarks (E) was compared with the length of the ulna bone as measured on the radiograph (R). The relationship between the two methods of measurement was explored by generating a scatter diagram of the two variables. It was quantified by conducting a two way analysis of variance using measurement method and dog leg as random effects and calculating the intra-class correlation coefficient for model ICC(2,1) following the notation by Shrout and Fleiss (1979). In addition, using the technique described by Bland (1995), a scatter plot was produced of the

difference of the two measurements, E and R, against their average. Pearson's product moment correlation coefficient was calculated to assess if there was a relationship between this difference in measurements and actual (average) length measured. The average difference between both methods of measurement was used to provide an estimate of the bias and the mean and standard deviation of the differences used to estimate the limits within which 95% of the differences lay

**Study 2**      ***Reliability of repeated measurements by a single person (intra-observer error).***

Ten crossbred puppies from two different age groups (6 weeks and 10 weeks) were used in this study. In all puppies the direct distance between the point of the *tuber olecrani* and the junction of the proximal border of the stopper pad with the hairy skin was measured along the caudal aspect of the antebrachium. This measurement was taken and recorded three times for both the right and left forelegs at one hourly intervals by the same person.

A scatter diagram was created of the average ulna length measured against the maximum difference between the three repeated measurements. A Pearson's product moment correlation coefficient was calculated to quantify this relationship. A two-way analysis of variance was conducted to quantify the relationship between ulna length measurement and the random effects; time of measurement, dog and leg. The intra-class correlation coefficient for model ICC(2,1) was used to quantify the reliability of the repeated measurements. The measurement error was calculated as a percentage using the within subjects coefficient of variation (i.e. standard deviation divided by the mean and multiplied by 100).

**Study 3**      ***Study to estimate the reliability of measurements by more than one person (inter-observer error)***

Seven people of differing occupations were chosen to measure the direct distance

between the point of the *tuber olecrani* and the junction of the proximal border of the stopper pad with the hairy skin in the right and left forelegs of 14 Dobermann puppies. The puppies were aged less than 10 weeks. The measurements made by each of the seven participants were recorded for each dog.

A scatter diagram was generated of the maximum difference between measurements on a dog's leg against the average of these measurements. A Pearson's product moment correlation coefficient was calculated. A two-way analysis of variance was performed to explore the relationship between ulna length measurements and the random effects, observer, dog and leg. An intra-class correlation coefficient for model ICC(2,1) was calculated to quantify the importance of inter-observer variation. In addition, an interrater reliability analysis was performed using Cronbach's coefficient Alpha to identify any inconsistent individual measurer as described in MacLennan (1993).

Statistical analyses were performed using the computer software packages SAS for Windows Version 6.11 (SAS Institute, Cary, North Carolina, U.S.A.) using the SAS macro INTRACC available in the SAS macro sample library.

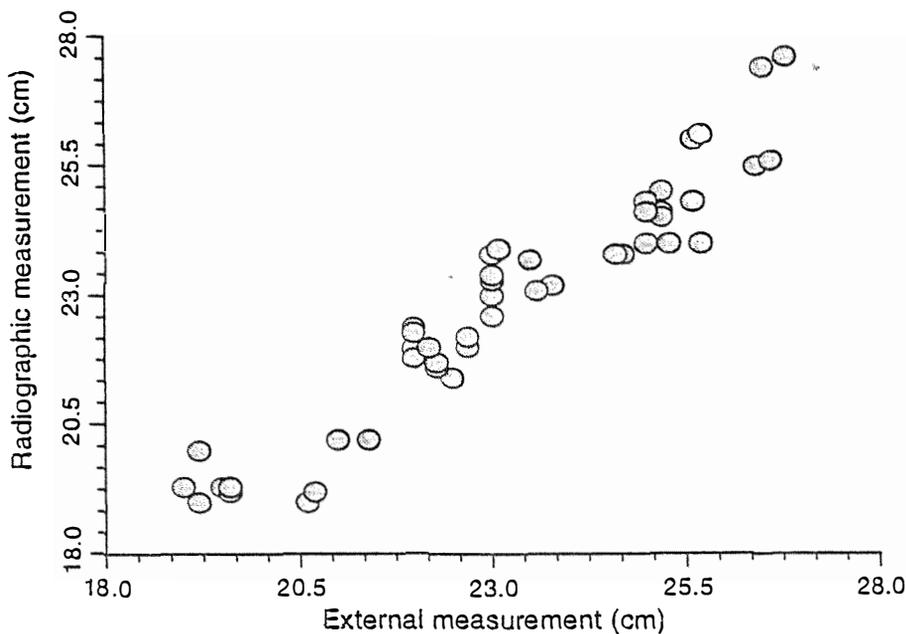
## Results

### *Study 1 Assessment of the accuracy of the distance between the chosen surface land marks as an estimate of ulna length.*

A total of 50 measurements from 25 adult dogs was used in this data analysis. The mean of the ulna measurements (E) was 23.3 cm (s.d.<sup>1</sup> 2.2) and that of the radiographic ulna measurement (R), 23 cm (s.d. 2.3). The scatter diagram (Figure 5-2) shows the relationship between the external (E) and the radiographic (R) measurements of ulna length.

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<sup>1</sup> (s.d. = standard deviation)



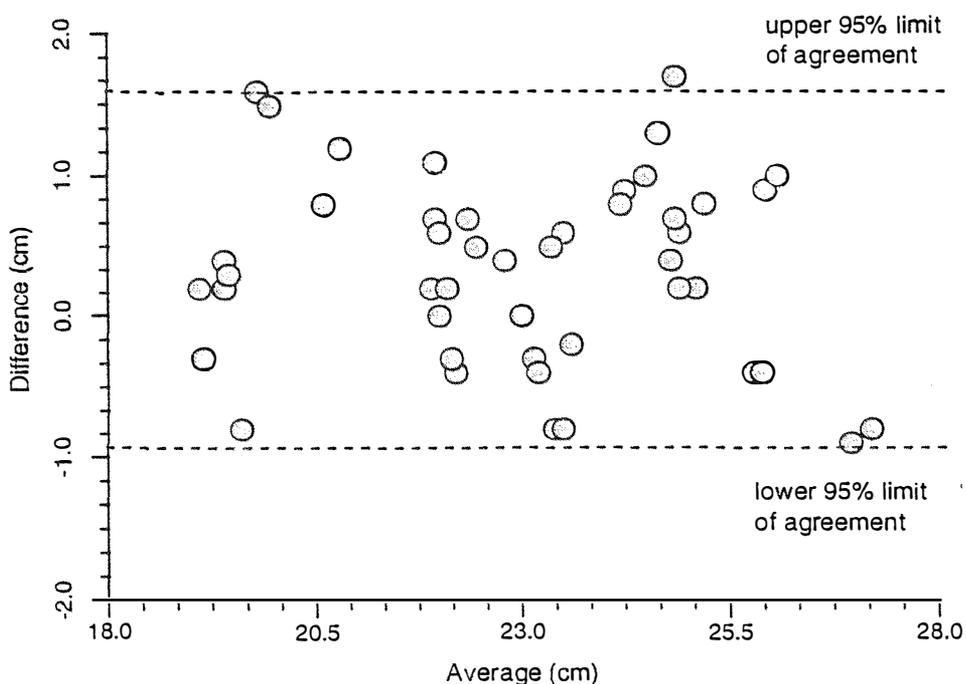
**Figure 5-2** Scatter diagram of external and radiographic measurements of ulna length.

The results of a two-way analysis of variance of the relationship between ulna length estimates and the main effects, dog and measurement method are presented Table 5-1.

Source Term	DF	Sum of Squares	Mean Square	F-Ratio	P-Value
Dog	49	485.63	9.91	44.22	0.000
Method	1	3.063	3.06	13.66	0.001
Error	49	10.98	0.22		
Total	99	499.68			

**Table 5-1 :** Results of two-way analysis of variance analysing the effect of dog and measurement method on ulna length in the study assessing the validity of external compared with radiographic measurement.

Both main effects were statistically significantly associated with ulna length. The intra-class correlation coefficient was 0.95 (95% CI 0.89-0.98;  $F_{24/24} = 39.1$ ,  $p=0.0001$ ). This indicates that 95% of the variance in the measurements was due to 'true' variation among dogs and not from differences between the two methods of measurement. Figure 5-3 presents a scatter diagram of the relationship of the difference between the two measurements against the average of the two measurements, which was quantified with a Pearson's product moment correlation coefficient ( $r=0.039$ ,  $p=0.79$ ,  $N=50$ ).

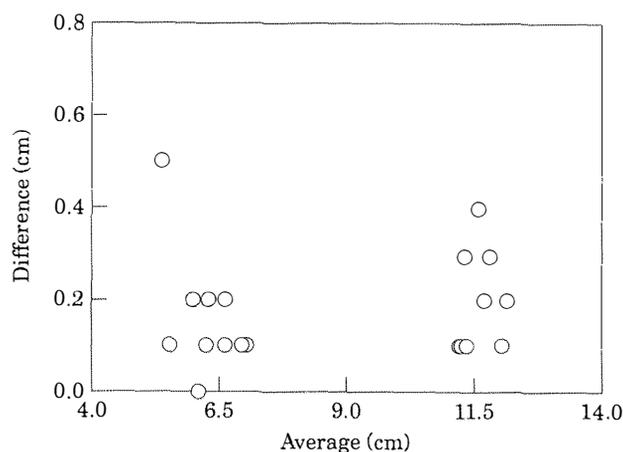


**Figure 5-3 :** Scatter diagram of the average of the two ulna length measurements (external and radiographic) against the difference between the two measurements including 95% limits of agreement.

This indicates that the difference between the two methods of measurement does not depend on the average of both measurements, thus ascertaining that the following estimates would be the same whatever the value of the measurement. In order to assess if the two measurement methods were interchangeable the average of the differences was used as an estimate of the bias. This amounted to 0.35cm (95% CI 0.16-0.54). This measurement error, using the within subjects coefficient of variation method, represents a coefficient of variation of 2%. Given that there was no statistically significant correlation between the difference and the average of the measurements and that the difference was normally distributed it was estimated that for 95% of the observations, the difference lay within -0.99 and 1.69 cm.

#### **Study 2** *Reliability of repeated measurements by a single person (intra-observer error).*

A total of 60 measurements was made resulting in a bimodal distribution representing the two age groups of dogs included in this study. Figure 5-4 presents a scatter diagram of the average ulna length against the maximum difference between the three repeated estimates.



**Figure 5-4 :** Scatter diagram of average ulna length measurements against maximum difference between repeated measurements taken by the same person.

The graph shows two clusters of length measurements representing the two age groups of dogs. The mean difference between repeated measurements was 0.18 cm  $\pm$  0.12 (N=20). The Pearson's product moment correlation coefficient of 0.12 ( $p=0.16$ ) suggested that there was no association between the ulna length and the mean difference between measurements. A two-way analysis of variance showed that the main effect variables, leg and time of measurement were not statistically significant (Table 5-2).

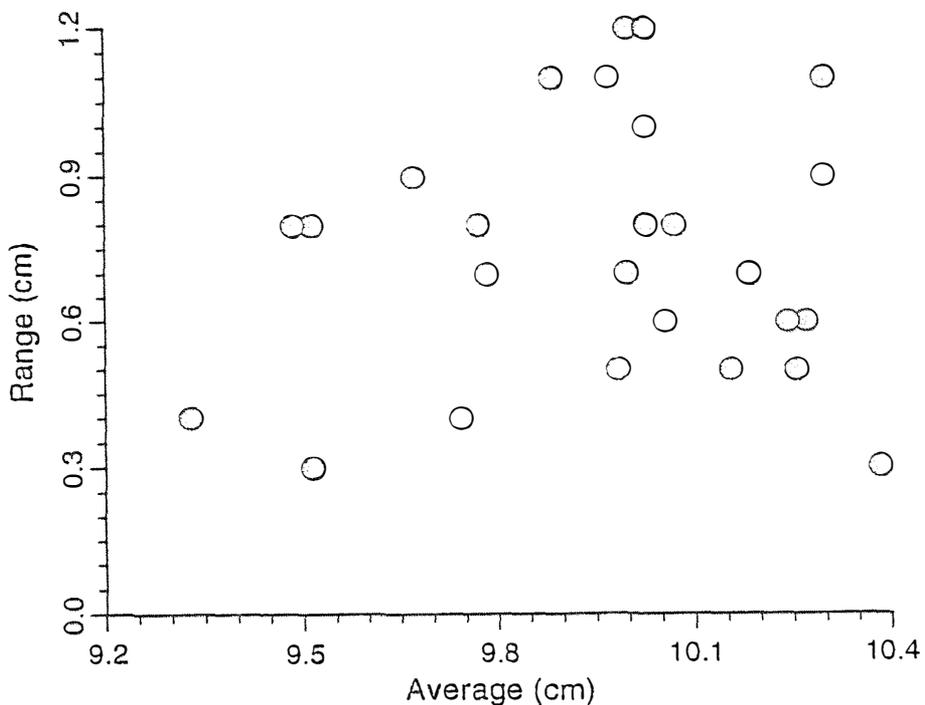
Source Term	DF	Sum of Squares	Mean Square	F-Ratio	P-Value
Dog	19	435.02	22.89	1552.43	0.00
Measure	2	0.001	0.001	0.03	0.97
Leg	1	0	0	0.00	1.00
Error	37	0.55	0.005		
Total	59	435.5			

**Table 5-2 :** Results of two-way analysis of variance analysing the effect of dog, leg and repeat measurement on ulna length in the study assessing the reliability of repeat measurements by the same observer.

An intra-class correlation coefficient of 0.998 (95% CI 0.996-0.999;  $F_{19/38}=1594.39$ ,  $p=0.000$ ) was estimated for the intra-observer variation, indicating that 99% of the variance in measurements was caused by variation between dogs and their legs. The within subjects coefficient of variation, indicating measurement error, was 0.8%.

**Study 3**     *Study to estimate the reliability of measurements by more than one person (inter-observer error).*

A total of 196 measurements was used in the data analysis. The mean ulna length was 9.9 cm (s.d. 0.4). Figure 5-5 presents a scatter diagram of the maximum difference between measurements on a particular leg and the average of these measurements.



**Figure 5-5:** Scatter diagram of average ulna length measurements against the maximum difference (range) between measurements as recorded by different observers.

On average, measurements have a range of 0.72cm +/-0.27 (N=28). Pearson's product moment correlation coefficient was 0.145 (p=0.45, N=28) suggesting that there is no relationship between the length of the ulna and the variation between measurements. The results of the two-way analysis of variance are presented in Table 5-3.

Source Term	DF	Sum of Squares	Mean Square	F-Ratio	P-Value
Dog	13	14.67	1.13	13.84	0.00
Leg	1	0.03	0.03	0.33	0.57
Observer	6	2.69	0.45	5.50	0.00
Error	175	14.27	0.08		
Total	195	31.65			

**Table 5-3 :** Results of two-way analysis of variance analysing the effect of dog, leg and observer on ulna length in the study assessing the reliability of measurements by multiple observers.

The main effects, observer and dog, were found to have a significant effect on the measurements of the ulna, but there was no difference between left and right leg. An intra-class correlation coefficient of 0.50 (95% CI 0.34-0.67;  $F_{27/162}=9, 29, p=0.000$ ), was estimated for the inter-observer variation, indicating that 50% of overall variation between measurements was caused by differences between observers. The within subjects coefficient of variation was estimated as 2.8%.

The interrater reliability analysis using Cronbach's alpha statistic (Table 5-4) shows that the overall variation between observers was small and that no one measurer could be singled out as the major contributor of the above variation.

Deleted Observer	one	two	three	four	five	six	seven
Alpha	0.861	0.883	0.875	0.881	0.871	0.878	0.883

**Table 5-4: Effect on deleting one observer on Cronbach's coefficient Alpha in the study assessing the reliability of measurements by different observers.**

### Discussion

The ulna was chosen as a suitable bone to measure skeletal growth in the live dog because it has distinct surface landmarks at either extremity. The first study verified the accuracy of this assumption by demonstrating the close correlation between the length of the ulna measured externally and that measured on its radiographic image. This bone is also considered to be accurately measurable in the live human (Valk, 1971). For most bones, measurements are considered more reliable when they are taken from radiographic images compared to those made on the live animal. This is because of the difficulty of identifying surface landmarks in the live animal and because measurements made on the living have to be made through overlying soft tissues (Roche, 1978). However, it should be emphasised that when using radiographs for this purpose, it is important to utilise standard radiographic projection and conditions and avoid magnification errors to achieve accurate and repeatable results. The disadvantage of this technique is the requirement for radiographic equipment and the potential health hazard associated with repeated exposure to x-rays.

Reliability studies, both "within observer" and "between observer" have been performed by anthropologists studying human growth (Kemper and Pieters, 1974; Jordan *et al*, 1975). These studies found inconsistencies existed "between observers". In general it is considered that consistency of measurement increases when i) the number of technicians decreases, ii) the experience of the technician increases and iii) the landmarks are clearly defined and easily located (Cameron, 1978). In this present study, the finding of very little variation (1%) attributable to repeated measurements recorded by a single observer compared to over 50% variation resulting from repeated measurements taken by seven different people agrees with these conclusions. The observers in this study were not trained and the task of measuring a defined distance on a puppy is probably more difficult than obtaining the equivalent measurements in a

human. It was, therefore, not surprising that variation occurred. However, the variation of measurement that occurred was shared homogeneously between all measurers and was not dependant on which leg was being measured. The importance of the amount of this variation should be regarded in relation to the absolute measurements and in relation to the increment of growth.

The reason to perform measurements on a subject is to provide information about that object of observation. For those measurements to be useful, the measurement procedure must be reliable. This implies that any measurement error should be a relatively small fraction of the possible range between absolute values. Assessment of the amount of such an error can be calculated in a number of ways. Analysis of variance, Pearson's product moment correlation coefficient, within subjects coefficient of variation, and reliability indices are all suitable methods (Bland, 1995). The reliability index is defined as the ratio of variability between subjects to the sum of the variability between subjects plus the measurement error.

In study one, an intra-class correlation coefficient (ICC2, 1) was used because it is a sensitive indicator of how similar the measurements E and R are (Streiner and Norman, 1995). In addition, an alternative method (Bland, 1995) was used for examining this relationship in more detail. The latter was designed as an absolute measure of agreement between two measuring instruments and separates the bias effect of the instrument from random error. Although frequently used for analyses of clinical results, the method is viewed by some authors as flawed because it does not explicitly relate the calculation of error variance to the range of observations (Streiner and Norman, 1995).

In studies two and three, the measurement of error "within" and "between" observers was calculated using the intraclass correlation statistical model ICC(2, 1) as recommended by Shrout and Fleiss (1979). This method has the advantage of including the error due to the measurer into the reliability coefficient.

Since measurement error can seriously affect the interpretation of results from statistical analyses, it is important to assess the amount of such error before judgements are made on the data

collected (Shrout and Fleiss, 1979). The concepts of reliability can only be applied to certain observations under specific conditions. Most studies on live animals involve some measurement error and whether the reliability of such measurements is considered to be acceptable is the decision of the investigator (Bland, 1995). In this study the “intra-observer” reliability of repeated measurements was high and was, therefore, considered acceptable. However, by comparison, when multiple observers were involved the reliability of measurements became unsatisfactory. There are several ways to reduce this error variance, such as providing training for the people performing the measurements and by eliminating those whose measurements are consistently at the extremity of the acceptable range.

From this study, it can be concluded that i) the distance between the surface landmarks, point of *tuber olecrani* and proximal aspect of the stopper pad, does accurately record the length of the ulna bone and ii) that if such measurements are to be used for investigating long bone growth then they should, ideally, be taken by one person only.

### A comparison of body weight and skeletal growth in puppies of three different breeds

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#### Abstract

The purpose of this study was to evaluate and compare the growth of three breeds of dogs from birth to 16 weeks of age by the weekly measurement of body weight and ulna length. In addition, the quantity and types of food given to the puppies were recorded and using computer analysis the mean concentration of nutrients estimated on a weekly basis. The puppies studied were 15 Dobermanns, 10 Labrador retrievers and 15 Heading Dogs. The relationships between the weekly measured growth parameters and the variables age, breed, dams nested within breed, gender and diet were investigated. A statistical model describing the mean growth rate over the 16 week period was formulated for the parameters, body weight and length of ulna for each breed. The data was analysed using repeated measures analysis of variance methodology.

Dobermann puppies gained significantly more body weight and increased the length of their ulnas over most of the growth period, when compared to the other breeds. Labrador retriever puppies also gained significantly more body weight, but not ulna length when compared to the Heading Dog puppies. Over the period 10 to 16 weeks of age, males puppies significantly increased in body weight compared to females. A short period of accelerated growth occurred in both Dobermann and Labrador retriever puppies between six to seven weeks of age. The effect of diet was insignificant. The relationship between the average of the standardised measures of the two parameters body weight and ulna length for each breed initially showed a consistent bias which became more variable with increasing age.

It was concluded that the larger breeds showed more rapid growth over the study time period. However, measurement of both body weight and increase in bone length was required to characterise the growth, since there was a poor predictive relationship between each of these two parameters as the puppies age.

**Introduction**

Growth is a complex, highly integrated process involving a host of interactions between genotype, hormones and their receptors, nutrients and the environment. Information accumulated from serial measurements of physical growth, such as body weight or dimension, can be used to study growth patterns for a particular individual or breed. In addition, the influence of some of the factors which affect growth can be investigated. Such studies may be of particular relevance for examining the relationship between skeletal growth rate and the development of bone disease.

Anthropometrical studies on somatic growth of humans have been numerous. The first documented longitudinal growth study has been credited to Philibert Gueneau de Montbeillard who measured the growth of his son from 1759-1777 (Scammon, 1927). Since that time a multitude of papers and books on the subject has been published and the information can now be reliably used to detect and evaluate growth disorders in children and assess the nutritional status of communities (Cameron, 1978).

Fewer and less comprehensive anthropometrical studies are available for other animal species. In particular, there is a paucity of published information on growth patterns of dogs. This is surprising, considering the wealth of information regarding the nutrition and health of puppies. Studies that have been conducted using measurement data other than body weight alone include those investigating growth and skeletal development in Great Danes (Hedhammar *et. al.*, 1974; Hazewinkel *et. al.*, 1985; Nap, 1993) Greyhounds (Riser, 1975) and Labrador retrievers (Alexander and Wood, 1987).

For a number of years, several skeletal disorders of young medium-large breed dogs have been linked to over-nutrition ( in terms of both energy and nutrients) and rapid growth. These disorders which develop within the first few months of life, include hip and elbow dysplasia, osteochondrosis and canine wobbler syndrome. Much of the evidence for this link has been established through experimental studies where the levels of nutrients such as energy and calcium far exceeded those recommended by the National Research Council's Nutrient Requirements of Dogs, 1974. (Hedhammer *et. al.*, 1974; Hazewinkel *et. al.*, 1985). These diseases are commonly

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seen within the dog population and, by inference, over-nutrition has been cited as one of the causes, despite the fact that there is limited information in the literature regarding the diets chosen by owners for their growing dogs.

The aims of this paper are to measure somatic growth of puppies in three different medium-large breeds of dog from birth to 16 weeks of age, and to investigate the effects of breed, diet, gender and litter on this growth pattern. The diets fed to the puppies, as selected by owners, were analysed to assess any deviation from that recommended by the Canine Nutrition Expert Committee of the Association of American Feed Control Officials (1997) in order to ascertain if over-nutrition occurred.

### **Materials and Methods**

The growth of 45 puppies from birth to 16 weeks of age was measured. The litters originated from eight unrelated dam-sire matings. Twenty of the puppies originated from two dams, both Heading Dogs, a New Zealand working breed derived from Border Collies, with 10 puppies in each litter. Another ten puppies were born to three working Labrador retriever dams with litter sizes of three, three and four puppies, respectively. The remaining 15 puppies were born to three Dobermann pinscher dams (litter size, three, five and seven). The puppies were vaccinated against canine distemper, infectious hepatitis and canine parvovirus at eight, 12 and 16 weeks of age and dewormed with a broad spectrum anthelmintic<sup>†</sup> at four, six, 10 and 12 weeks of age. Although owned by different people, the puppies lived in similar environments with kennel and run accommodation at night and access to outside areas during the day. At 16 weeks of age, the puppies were homed with new owners and were no longer available for study. All puppies remained healthy throughout the study as judged by owners' reports and weekly veterinary health inspections.

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<sup>†</sup> Drontal Plus, Bayer AG, Leverkusen, Germany

The growth of the puppies was recorded by weekly measurements of body weights and length of the ulna bone. This length was taken to be the distance between the palpable point of the tuber olecrani and the proximal junction of the stopper pad to the hairy skin as measured externally along the caudal aspect of the antebrachium (Chapter 5). To facilitate palpation of the tuber olecrani, the leg was held with the elbow joint flexed at a 90° angle whilst the carpus remained straight. The body weight and length of both ulnas was also measured in each of the dams. All linear measurements were taken by the same person using the same calipers. Each measurement was repeated twice and the average length recorded. Weight gain and the increase in the length of the ulna in the puppies was calculated by subtracting the respective measurements for successive weeks.

In addition, the quantity and type of food given to individual puppies was recorded on a daily basis. All puppies were weaned between four and five weeks of age. The owners were not instructed in the choice of food fed to the puppies and most litters received a mixture of various commercial diets (such as dog food roll, canned and dried dog food). The nutrient content of the diets fed each week were estimated using the Animal Nutritionist software (N-squared and Durango Software, Silverton, Oregon) and then expressed as percentage of estimated daily requirements for growth, i.e. % daily allowance as recommended by the Canine Nutrition Expert Committee of the Association of American Feed Control Officials (1997). Depending on the results of this analysis the diets were categorised on a week by week basis as either balanced or unbalanced, with respect to the content of macronutrients (protein, fat and carbohydrate), as well as calcium, phosphorous, magnesium, zinc and Vitamin A. The nutrient content of the commercial diets fed were supplied by the manufacturer. Vitamin D content of the diets could not be assessed due to incomplete information from the manufacturers.

The data was stored using the database management software Microsoft Access for Windows 95 (Microsoft Corporation, Redmond, Washington) and analysed using the statistical software packages SPSS for Windows version 7.5 (SPSS, Chicago, Illinois) and SAS for Windows Version 6.12 (SAS Institute, Cary, North Carolina).

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Line plots including error bars were used to graphically present the relationship between weekly measured growth parameters and the variables age and breed category. The plots present the averages for each of the measurements including their 95% confidence limits.

The growth data representing repeated measures of body weight and ulna length were analysed using a single mixed model with special parametric structures of the covariance matrices. Age was modelled as a within-subjects effect and breed, dams nested within breed, gender and diet were modelled as between-subject effects. This analysis was conducted using the SAS procedure PROC MIXED (Anon, 1996). Restricted maximum likelihood (REML) was used to fit either compound symmetry or first order autoregressive covariance structures. The appropriate covariance structure for modelling within-subject variation was selected on the basis of a maximum value for Akaike's Information Criterion (AIC) as described in Littell *et al* (1996). Pairwise multiple comparisons of least squares means between individual groups were conducted using the Bonferroni adjustment for 95% confidence limits.

A single mixed model for repeated measures data based on the above approach was used to fit quadratic regression models to the growth parameters body weight and ulna length for the 16 week period, following the procedure described by Littell *et al* (1996). In addition, the mean body weight and the mean length of the ulna for the puppies of each breed at 16 weeks of age was compared as a percentage of the mean body weight and the mean length of the ulna of their respective dams.

A single mixed model analysis for repeated measures data was also used to examine the relationship between the growth parameters body weight gain and increase in ulna length and the fixed effects age, breed and gender.

Lastly, the relationship between body weight and ulna length was investigated by estimating the Spearman rank correlation coefficient between the two variables, for each of the three breeds. In addition, a scatter plot of the relationship between the average of the standardised measures

of the two growth parameters and their differences was produced in order to assess if there was a progressive non-linear pattern (Bland, 1995).

The abbreviation S.D. was used to represent standard deviation, 95% CL for 95% confidence limits and SEM for standard error of the mean.

## Results

The diets were estimated to be balanced for all the Heading Dog puppies for the whole 16 week period. For the Labrador puppies, the diets were also balanced for the whole study period for one litter, but not for the seven puppies from the other two litters. The unbalanced diets fed during weeks 4 to 7 and 12 to 16 were marginally deficient in protein, calcium, and phosphorus and moderately deficient in zinc (Table 6-1).

Dietary component	Age (weeks)			
	4	5 - 7	12 - 14	15-16
Protein	85%	90%	114%	85%
Calcium	63%	80%	94%	75%
Phosphorus	65%	84%	90%	64%
Zinc	32%	42%	164%	42%

\* As recommended by the Canine Nutrition Expert Committee at the Association of American Feed Control Officials.

\* Average percent over time period.

**Table 6-1: Percent of recommended daily dry matter intake of nutrients\* in Labrador diets.**

Unbalanced diets were also fed to some of the Dobermann puppies during the 16 week study period. These periods were during week 4 only (seven puppies), 11 to 16 (three puppies), weeks 5 to 7 (eight puppies) and 13 and 14 (three puppies). The unbalanced diets were transiently deficient in protein, calcium, phosphorus, and/or magnesium (Table 6-2).

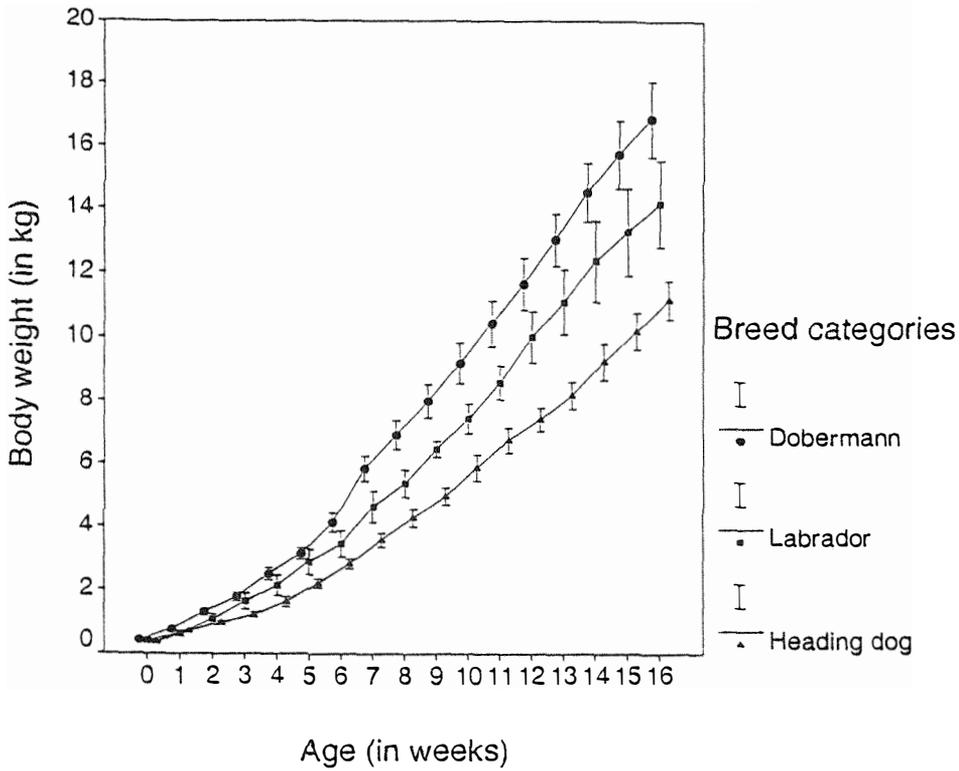
Dietary component	Age (weeks)			
	4	5 - 7	11 - 16	15 - 16
Protein	111%	96%	100%	80%
Calcium	64%	94%	80%	167%
Phosphorus	71%	76%	80%	53%
Zinc	143%	48%	260%	20%

- \* As recommended by the Canine Nutrition Expert Committee at the Association of American Feed Control Officials.
- \* Average percent over time period.

**Table 6-2: Percent of recommended daily dry matter intake of nutrients in Doberman diets\*.**

***Body weights***

The line plot for mean body weight of puppies shows curves for all three breeds of puppies, with Dobermanns attaining the greatest weight and the Heading Dogs the least over the 16 week period (Figure6-1).



**Figure 6-1 :** Line chart for average body weight in puppies by week of age and breed (error bars represent 95% confidence limits).

The appropriate single mixed model included a first-order autoregressive covariance structure suggesting that the correlation between repeated observations decreases with increasing time between them. The model contained the significant fixed effects age, breed and gender as well as their first order interaction terms (Table 6-3).

<b>Fixed effect</b>	<b>Numerator degrees of freedom</b>	<b>Denominator degrees of freedom</b>	<b>Type III F-statistic</b>	<b>P-value</b>
Age	16	656	466.3	0.0001
Breed	2	41	29.31	0.0001
Breed* Age	32	656	10.33	0.0001
Gender	1	31	3.14	0.084
Age* Gender	16	656	1.79	0.0283

**Table 6-3 : Fixed effects included in mixed model for body weight in puppies.**

The effects of diet and dams nested within breed were not statistically significant. There was a significant difference in body weight between the Dobermann and Heading Dog puppies from seven to 16 weeks of age, Dobermann and Labrador puppies from 15 to 16 weeks of age and between Labrador and Heading Dog puppies from 11 to 16 weeks of age. Initially there was no significant difference between the genders, but a significant difference was seen with the repeated measures analyses of variance from 10 weeks of age ( $p=0.04$ ) to 16 weeks of age ( $p=0.0001$ ), as the bodyweight of the male puppies gradually surpassed that of the female puppies.

The statistical model describing the initial growth rate for body weight for each breed is:

Dobermanns	<b>body weight (kg)</b>	=	<b>0.41</b>	+	<b>0.48</b>	*	<b>age</b>	+	<b>0.03</b>	*	<b>age<sup>2</sup></b>
	SEM		0.36		0.05				0.002		
	df,		41,		713,				713,		
	t-statistic		1.12,		10.6,				12.7,		
	P-value		0.27		0.0001				0.0001		

Labradors	<b>body weight (kg)</b>	=	<b>0.38</b>	+	<b>0.39</b>	*	<b>age</b>	+	<b>0.03</b>	*	<b>age<sup>2</sup></b>
	SEM		0.37		0.05				0.002		
	df,		41,		713,				713,		
	t-statistic		1.01,		6.34,				9.16,		
	P-value		0.32		0.0001				0.0001		

Heading Dogs	<b>body weight (kg)</b>	=	<b>0.36</b>	+	<b>0.25</b>	*	<b>age</b>	+	<b>0.02</b>	*	<b>age<sup>2</sup></b>
	SEM		0.29		0.04				0.002		
	df,		41,		713,				713,		
	t-statistic		1.24,		6.47,				11.8,		
	P-value		0.22		0.0001				0.0001		

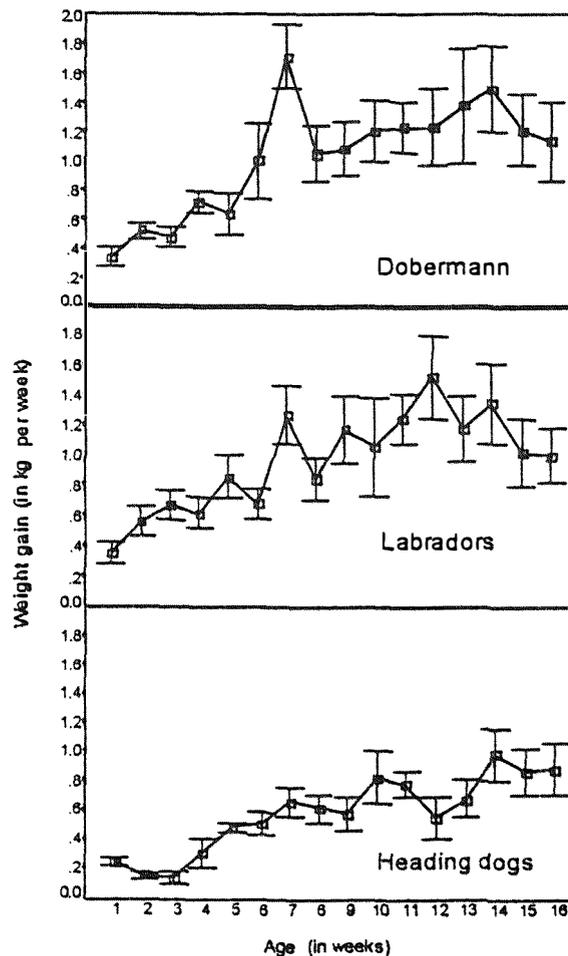
If the puppy is male then the following additions should be added to the model equations:

		<b>-0.002</b>	+	<b>0.078</b>	x	<b>age</b>
	SEM	0.33		0.02		
	df	41,		713,		
	t-statistic	-0.07,		3.49,		
	p-value	0.95		0.0005		

For the individual breeds in the statistical model, the average birth weights of the puppies from each breed were similar (mean measured birth weight: - Dobermann 0.4 kg, Labrador 0.4 kg and Heading Dog 0.35 kg). The coefficients for the variable age show that the Dobermanns gained more weight at a faster rate than did the Labradors which, in turn, gained more weight at a faster rate than the Heading Dogs. The significant positive coefficient for the quadratic terms suggests that growth rate increases with age during the observation period. This is particularly so for male puppies as evidenced by the coefficients for the variables age and gender.

At 16 weeks of age the mean body weight of the puppies for the different breeds expressed as a percentage of the average of their dam's body weight was approximately 50% for the Dobermanns, 47% for the Labradors and 44% for the Heading Dogs.

The line plot showing the mean weekly weight gain of the puppies is shown in Figure 6-2. The single mixed model for body weight gain with the best model fit included a compound symmetry covariance structure indicating that the covariance between any two observations on the same animal did not vary across time. The model contained the fixed effects age, breed and gender as well as the interaction term between breed and age (Table 6- 4).



**Figure 6-2:** Line chart for body weight gain between successive measurements in puppies by week of age and breed (error bars represent 95% confidence limits).

Fixed effect	Numerator degrees of freedom	Denominator degrees of freedom	Type III F-statistic	P-value
Age	15	630	44.79	0.0001
Breed	1	41	45.67	0.0001
Breed* Age	30	630	4.18	0.0001
Gender	1	41	6.02	0.0185

**Table 6-4 :** Fixed effects included in mixed model for body weight gain in puppies.

The Dobermann puppies showed a significant gain in body weight during the period six to seven weeks of age when compared with the prior (difference between average gains: +0.71, 95% CL:0.29 to 1.14) and the following weeks (difference between average gains: -0.66, 95% CL:-1.09 to -0.23), indicating a short period of accelerated growth. Likewise, within the Labrador breed there was a significant gain in body weight during the period six to seven weeks of age when compared with the prior (difference between average gains: +0.61, 95% CL: 0.21 to 1.15) and following weeks (difference between average gains: -0.44, 95% CL -0.85 to -0.11). No such accelerated growth was identified in the Heading Dog puppies.

### ***Ulna length***

The line plot for ulna length of the puppies for the three breeds over the 16 week study period shows similar curves for all three breeds (Figure 6-3).

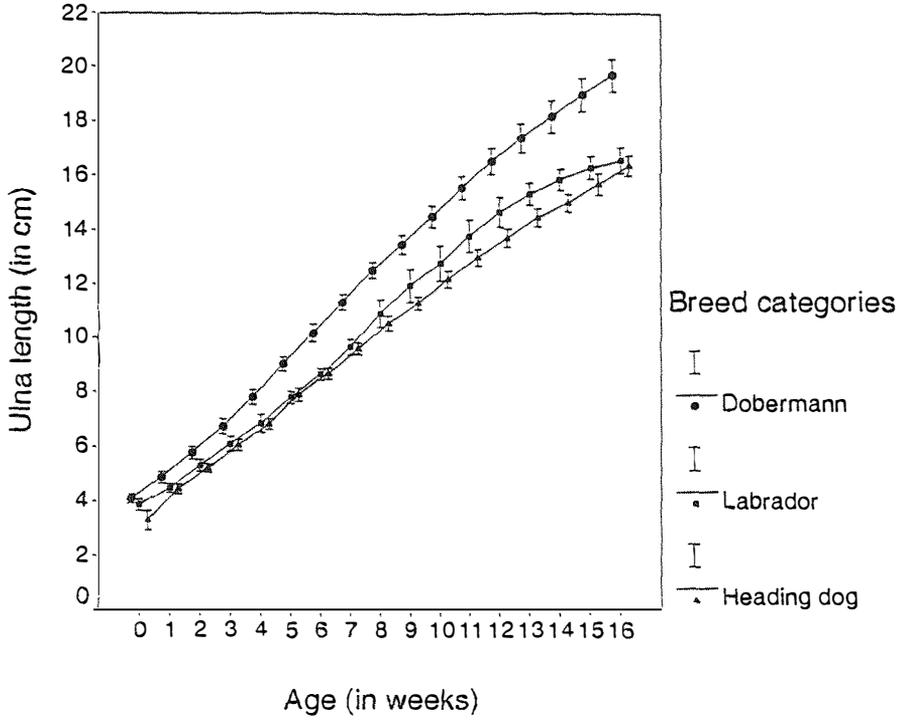


Figure 6-3: Line chart for average ulna length in puppies by week of age and breed (error bars represent 95% confidence limits).

A first-order autoregressive covariance structure provided the best fit for the single mixed model. It included the significant fixed effects breed, dams nested within breed, age and gender as well as their first order interaction term (Table 6-5).

<b>Fixed effect</b>	<b>Numerator degrees of freedom</b>	<b>Denominator degrees of freedom</b>	<b>Type III F-statistic</b>	<b>P-value</b>
Age	2	36	74.1	0.0001
Breed	16	672	973.65	0.0001
Breed* Age	32	672	7.76	0.001
Gender	1	36	6.12	0.0182
Dams within breed	5	36	7.35	0.0001

**Table 6-5: Fixed effects included in mixed model for ulna length in puppies.**

The effect of diet was not significant. There was a significant difference in average ulna length between Dobermanns and Labradors from five to 16 weeks of age and between Dobermanns and Heading Dogs from four to 16 weeks of age. There was no such significant difference between the Labradors and Heading Dog puppies. Males had significantly longer ulna lengths than females

( $p = 0.02$ ). The only significant dams nested within breed factor was between the two Heading Dog litters ( $p=0.0001$ ).

The statistical model describing the initial growth rate for ulna length for each breed is:

Dobermanns	<b>ulna length (cm)</b>	=	<b>3.83</b>	+	<b>1.08</b>	x	<b>age</b>	-	<b>0.006</b>	x	<b>age<sup>2</sup></b>
	SEM		0.22		0.34				0.002		
	df,		41,		714,				714,		
	t-statistic		17.52,		31.47,				3.21,		
	P-value		0.0001		0.0001				0.0014		

Labradors	<b>ulna length (cm)</b>	=	<b>3.64</b>	+	<b>0.97</b>	x	<b>age</b>	-	<b>0.01</b>	x	<b>age<sup>2</sup></b>
	SEM		0.24		0.04				0.002		
	df,		41,		714,				714,		
	t-statistic		15.3,		23,				-4.4,		
	P-value		0.0001		0.0001				0.0001		

Heading Dogs	<b>ulna length (cm)</b>	=	<b>3.12</b>	+	<b>0.99</b>	x	<b>age</b>	-	<b>0.01</b>	x	<b>age<sup>2</sup></b>
	SEM		0.17		0.03				0.002		
	df,		41,		714,				714,		
	t-statistic		17.5,		33.2,				-6.3,		
	P-value		0.0001		0.0001				0.0001		

If the puppy is male then the following constant should be added to the above model equations.

	+	<b>0.33</b>
SEM		0.17
df		41
t-statistic		2.0
P-value		0.0530

The statistical model shows that the mean ulna length in Dobermann puppies is longer at birth, and with increasing age, grows faster than the ulna of the other two breeds. Although Labradors are born with slightly longer mean ulna length than Heading Dogs, the rate of growth is similar in both breeds. The statistical model indicates that the growth rate in the puppies is slowing towards the end of the observed growth period.

At 16 weeks of age the mean ulna length of puppies for the different breeds expressed as a percentage of the average of their dam's ulna length was approximately 80% for the Dobermanns, 80% for the Labradors and 72% for the Heading Dogs (Table 6-6).

Breed		Average body weight (kg)	Number of Observations	Average ulna length (cm)	Number of Observations
Dobermanns	Dams	34.8 SD 2.9	3	24.4 SD 0.3	6
	Puppies	16.0 SD 2.1	15	19.7 SD 1.1	30
Labradors	Dams	29.3 SD 3.2	3	20.3 SD 0.3	6
	Puppies	14.1 SD 2.1	10	16.6 SD 0.8	20
Heading Dog	Dams	25.5 SD 4.5	2	22.4 SD 0.2	4
	Puppies	11.3 SD 1.3	20	16.3 SD 0.7	40

Legend : SD - Standard Deviation

**Table 6-6 : Average (+/- S.D.) body weight and ulna length in dams and 16 week old puppies.**

The line plot showing the mean weekly ulna length gain for the three breeds is shown in Figure 6- 4. The single mixed model for increase in ulna length provided the best fit when a compound symmetry covariance structure was included. The main effects included in the model were age and breed as well as their interaction (Table 6-7).

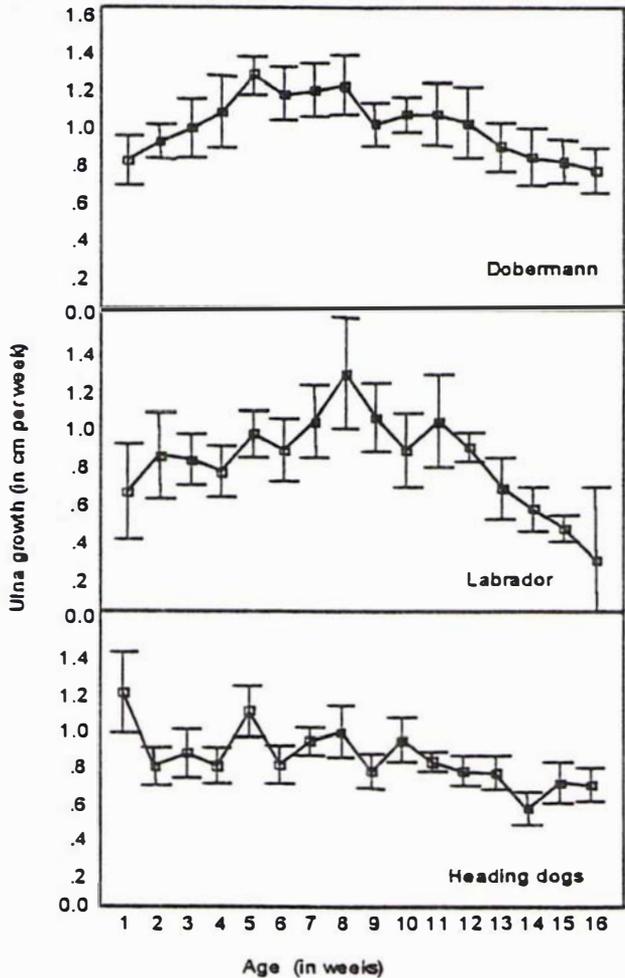


Figure 6-4 : Line chart for change in ulna length between successive ulna length measurements individual puppies by week of age and breed (error bars represent 95% confidence limits).

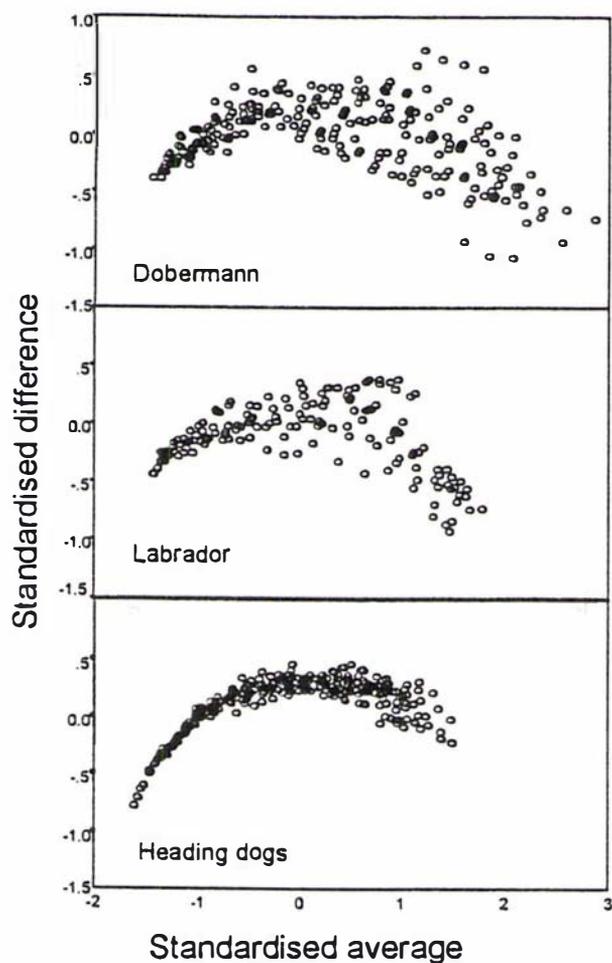
Fixed effect	Numerator degrees of freedom	Denominator degrees of freedom	Type III F-statistic	P-value
Age	15	630	15.58	0.0001
Breed	2	42	50.97	0.0001
Breed* Age	30	630	3.6	0.0001

**Table 6-7: Fixed effects included in mixed model for increase in ulna length between successive measurements.**

There was no statistically significant difference when comparing the increase in ulna length between successive weeks from birth to 16 weeks of age for the two breeds Dobermann and Labrador. Within Heading Dogs there was a significant difference in average ulna growth as measured between the periods defined by birth and one week of age and by one to two weeks of age (-0.4 cm, 95% CL: -0.73 to -0.07).

### ***Body weight and ulna length***

The Spearman's rank correlation coefficients for the three breeds were 0.981, 0.98 and 0.997 for Dobermanns, Labradors and Heading Dogs respectively, indicating a strong correlation between body weight and ulna length for all three breeds. The scatter plot pattern presented in Figure 6-5 demonstrates that in the younger puppies both growth parameters showed consistent bias. However, with increasing age the bias becomes more variable between dogs. Variability was greatest in Dobermann and Labrador and least in Heading Dog puppies.



**Figure 6-5 :** Scatter plot of relationship between standardised values of the average of both growth parameters and their difference. In the young puppies, the two growth parameters body weight and ulna length show a consistent bias. However, as the puppies age, the predictive relationship between these two parameters becomes less accurate (as demonstrated by the increased scattered arrangement of values). This variability is more marked in the Dobermann and Laborador puppies than in the Heading Dog puppies.

**Discussion**

Although the pattern of growth is an individual characteristic, grouped data from most animal populations show that it follows a well defined curve from birth to maturity (Parks, 1982). The data from this study illustrate and quantify the initial part of this growth curve for both body weight and ulna length for the three breeds studied. Growth curves can be estimated using mixed model analysis or nonlinear regression curve fitting. The latter is the preferred technique to fit growth data which reach a horizontal asymptote. In this case the logistic or the Gompertz curve can be used (Krzanowski and Marriott, 1995). The puppy growth data in this paper covered a period from birth to 16 weeks during which there is continuing growth. Under such circumstances mixed model analysis including autoregressive covariance structures provides a useful analytical technique for estimation of growth rate and for assessment of the impact of other factors of interest such as breed, litter, gender and diet.

Despite the small number of dogs studied, significant differences between the breeds were found. The Dobermann breed is the largest of the three breeds and hence it was not surprising that these puppies had significantly greater growth in terms of both body weight and ulna length for most of the time period studied. However, adults of the other two breeds are of similar height, but the Heading Dog is of a less thickset stature than the Labrador. This appears to be reflected in the resulting growth data since the Labrador puppy body weight increased significantly more over the time period examined, compared with that of the Heading Dog puppies, yet the growth rate of the ulna was found to be similar. Since it is known that larger breeds take longer to reach their adult body weight and size than smaller ones (Legrand-Defretin and Munday, 1993; Nap, 1993), different growth curves should be expected for the various breeds of dogs.

The significant effect of gender on body weight growth rate was unexpected. This is because it was assumed that growth of the puppies would be similar in prepubescent animals. The observation that the males gained more weight as they aged has been found in other species (Hintz *et al*, 1979) and is supported by other recent work (Booles *et al*, 1994). These latter authors performed a study on Labrador retriever puppies at 20 weeks of age and found that their

body composition consisted of approximately 78% lean tissue, 19.5% fat and 2.4% bone mineral with males having a slightly higher total solid content and hence body weight than females. This phenomenon could be due to the effect of male sex hormones on growth rate or the result of behavioural differences, with male puppies competing for, and obtaining more food than females. This study also demonstrated that male puppies on average were born with longer ulnas than the females.

The observation that by 16 weeks of age the puppies had achieved between 70-80% of the adult ulna length was not surprising since it is known that the growth plates of this bone fuse at six to nine months of age. Such fast bone growth has been documented by Riser (1975), who reported that the femurs of 30 week old Greyhound puppies measured 95% of the total adult femoral length. By comparison, the body weight of the puppies was only 40 to 50% that of their dams. The measurement of body weight is probably a less reliable comparison between dam and puppies because it is reliant on total body composition which can be quite variable depending on the degree of obesity, muscle mass etc.

The lack of a significant effect of the type of diet on these growth rates was expected since most of the puppies were fed diets that were either balanced or only marginally or transiently deficient or in excess of nutrients known to affect skeletal development.

Although the massed data of measurements of weight and ulna length can be represented by a continuous growth curve, undulations in the weekly gain charts for both parameters illustrate that the growth of the puppies was non-uniform. A short period of accelerated mean body weight gain was identified in the Dobermann and Labrador puppies between the periods of six and seven weeks of age. This variation in mean growth rate between consecutive time periods in individual animals has been recorded before (Alexander and Wood, 1987). Some of this variation could be due to measurement error. A recent study examining the reliability of measurement for ulna length in the dog showed an intra-observer error of 0.8% (Burbidge and Pfeiffer, 1998). Therefore, although some of the variation may be due to technical errors, it does not account for

all of it. Similar observations of discontinuous, aperiodic growth spurts have been made in studies of growth in individual humans (Lampl *et al*, 1992). These authors suggest that 90-95% of normal development during infancy is growth free and length accretion is a distinctly saltatory process of incremental bursts punctuating background status. However, this viewpoint has been contested in favour of the more traditional assumption that growth is a regular continuous process (Heinrichs *et al*, 1995). In comparison with humans, the dogs grow rapidly and no periods of stasis were identified in this study. Shortening the measurement period to daily measurements may well have isolated periods of growth stasis in individual animals. The cause of the growth spurt in the weaned Dobermanns and Labradors was not determined, but coincided with weaning and the puppies eating a full solid food diet.

The significant decrease in rate of ulna growth in the Heading Dog puppies during period one to two weeks of age could have been due to the fact that both Heading Dog litter sizes were large and therefore the puppies could have been undernourished in this early period. In such circumstances, a phenomenon termed “catch-up” or compensatory growth can occur (Tanner, 1986).

The relationship between paired observations of body weight and ulna growth, as found in this study, indicates that both parameters should be used to assess growth. This is because as the puppies age, the predictive relationship between the two parameters becomes less accurate. The observation that the Dobermanns and the Labradors had the greatest variability as they aged could be due to their bulkier body stature. The growth of the soft tissues in these breeds would contribute more to the total body weight than that of the thinner Heading Dogs. It may be that there is greater variation in this soft tissue growth between the puppies than there is for skeletal growth.

Sources of error and variation in this study include observer technique, measurement error, equipment, cooperation and the small genetic sample for each breed. Although the number of litters for each breed studied was small the results are likely to be reasonably representative due

to the adherence by breeders to certain set breed standards, giving rise to limited variation within each breed. The potential error factors relating to measurement were minimised in this study by using the same observer and equipment (Burbidge and Pfeiffer, 1998). The resulting growth curves over the 16 week period were similar in shape to those reported by Alexander and Wood (1987). However, since the landmarks measured were different, no comparison could be made of the actual values. If normal growth dynamics of dogs are to be studied it is important to standardize measurement techniques and growth records in order that data can be used for meaningful individual or inter-breed comparisons and for the detection of growth disorders.

## Chapter Seven

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### **The presence of caudal cervical vertebral malformation in Dobermann puppies and the effects of diet and growth rate**

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#### **Abstract**

This prospective study investigated the relationship between diet, growth rate and the presence of caudal cervical vertebral malformation in 15 Dobermann puppies. The Dobermann puppies originated from three litters, and were studied from birth to 16 weeks of age. The sires and dams of each litter were unrelated.

The growth rate, in terms of body weight gain and increase in ulna length, was measured weekly for all puppies. In addition, the nutritional quality of their diets was assessed. Radiographs of the cervical spine were taken at six weeks and between 12 and 16 weeks of age and examined for the presence of caudal cervical vertebral malformation. A mixed model for repeated measures data was used to investigate the relationship between the growth rate of the puppies and the fixed effects age, dam, diet, gender and presence of caudal cervical vertebral malformation.

Five of the puppies had changes consistent with caudal cervical vertebral malformation. The diets were either balanced or transiently deficient in protein, calcium, phosphorus and/or magnesium. There was no significant association between the growth rate and the variables dam, gender and the presence of caudal cervical vertebral malformation. There was no significant association between the diet and increase in ulna length, but a trend existed between body weight gain and the feeding of a balanced diet ( $p=0.0672$ ).

It was concluded that evidence of caudal cervical vertebral malformation can be detected radiographically as early as six weeks of age in some Dobermanns, and that the puppies' diet and their growth rate were not significant factors in its initial development.

**Introduction**

Caudal cervical spondylomyelopathy refers to the most common cause of cervical spinal cord compression in large-breed dogs (Seim and Withrow, 1982; Sharp *et al*, 1992). Affected Dobermann pinschers have abnormal caudal cervical vertebrae (Seim and Withrow, 1982; Lewis, 1989; Mason, 1979; Read *et al*, 1983). These vertebral malformations consist of stenosis and/or asymmetry of the cranial opening of the neural canal, and deformation of the articular facets and dorsal spinous processes. Malalignment with tilting of one or more of the vertebral bodies can occur (Wright, *et al* 1973; Trotter, *et al* 1976; Chambers and Betts, 1977; Read *et al*, 1983; Lewis, 1991). It is thought that such bony abnormalities either directly or indirectly (via secondary ligamentous and/or intervertebral disc changes) cause the spinal cord compression that results in the characteristic clinical signs of wobbler syndrome (Seim and Withrow, 1982; Van Gundy, 1988; Seim and Bruecker, 1993; McKee *et al*, 1990).

There has been much debate over the cause of these vertebral changes. Several factors have been implicated, including genotype, body conformation, overfeeding and rapid growth rate. Evidence that the condition may be heritable within the Dobermann pinscher breed is scanty (Lewis, 1989). Some authors have, however, indicated that certain breed lines appear to be predisposed to the syndrome (Mason, 1977; Lewis, 1991).

In 1973, Wright *et al* proposed that the cervical vertebral malformations that occur in caudal cervical spondylomyelopathy could develop as a result of abnormal forces influencing the growth of these vertebral bones. It was hypothesised that dogs with heavy heads and long necks were predisposed due to the imbalance of forces between this type of head and neck conformation and the action of muscles and ligaments acting on the cervical vertebrae (Parker *et al*, 1973; Lewis, 1989). However, a recent epidemiological study of the disease in Dobermann pinschers failed to find any relationship between the size of the head and the length of the neck and the presence of cervical vertebral malformation as judged by radiological examination (Burbidge *et al*, 1994).

The role of over-feeding and rapid growth rate in the development of the disease is also unclear. Some authors have suggested that rapid growth rate in puppies predisposes to the development of cervical vertebral deformities (Selcer and Oliver, 1975; Lewis, 1989; Lewis, 1992). Evidence that excessive food intake (in particular of calories, protein and calcium) and rapid weight gain adversely affected skeletal development was provided by the work of Hedhammer *et al* (1974) and Hazelwinkel *et al* (1985). These authors found more abnormal changes in the growing bones of dogs fed excessively than in those on a restricted diet. Such changes included increased frequency of the development of osteochondrosis dissecans, radius curvature and cervical vertebral neural canal stenosis. The authors suggested these changes were due to abnormal and delayed bone remodelling. However the study investigating the influence of chronic dietary calcium excess in the skeletal development of growing Great Danes, showed that cervical vertebral changes and/or spinal cord lesions occurred in both control and non-control groups of dogs (Hazewinkel *et al*, 1985; Goodegebuure and Hazewinkel, 1986). Such findings gave rise to speculation that excess dietary calcium alone did not play a fundamental role in the development of canine cervical vertebral malformation.

Despite the fact that cervical vertebral malformations occur quite commonly in Dobermanns, (Lewis, 1989; Burbidge *et al*, 1994) to my knowledge there have been no published studies investigating if such changes are indeed the result of over-feeding and rapid growth rate.

The aims of this study were firstly, to identify the possible presence of cervical vertebral malformation in young Dobermann puppies; secondly to investigate the nutritional quality of the diets fed to these puppies and, thirdly to determine if any relationship existed between such diets, the growth rate of the puppies and the presence of caudal cervical vertebral malformation.

## **Materials and Methods**

Fifteen Dobermann pinscher puppies (11 male and four female) aged from birth to 16 weeks were used in this study. The puppies originated from three unrelated dam-sire matings. The litter size

consisted of three, five and seven puppies. Close relatives (i.e. dam, or siblings) of the three dams of the puppies were known to have clinical signs consistent with a diagnosis of caudal cervical spondylomyelopathy (wobbler syndrome). These particulars on the sires were unknown. The puppies were vaccinated against canine distemper, infectious hepatitis and parvovirus at eight, 12 and 16 weeks of age and treated with a broad spectrum anthelmintic<sup>1</sup> at four, six, 10 and 12 weeks of age. Although each litter was owned by different people, the puppies lived in a similar environment with housed accommodation at night and unrestricted access to outside areas during the day. At 16 weeks of age the puppies from each litter were sold to different individuals, and follow-up either lost or access denied.

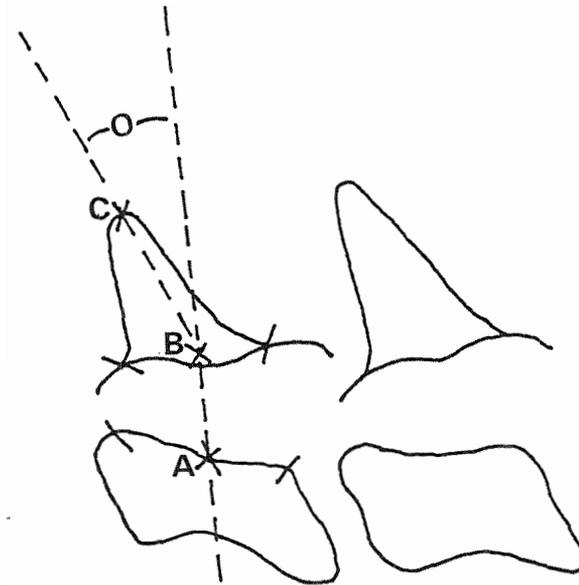
A lateral radiograph of the cervical spine with the primary beam centred over the caudal cervical vertebrae was taken of each puppy at six weeks and between 12 and 16 weeks of age. Each puppy was categorised on this latter radiograph, as having either normal or malformed sixth and/or seventh cervical vertebra according to the following criteria.

- whether the vertebral body of the sixth and/or seventh vertebra was rectangular in shape (normal) or abnormally shaped.
- whether the angle of the dorsal spinous process in relation to the vertebral body was greater than 20°. This angle has been shown to increase in Dobermanns with caudal cervical vertebral malformation compared to other breeds of dogs (Burbidge and Pfeiffer, unpublished data, Appendix A). It is measured by the following method. Firstly, the mid-point of a line drawn between the dorso-cranial and dorso-caudal points of the vertebral body was found (point A) (Figure 7-1). Then the mid-point of a line drawn between the most cranial and caudal junction of the dorsal spinous process to the neural arches was established (point B). A third line was drawn between A and B. Next a line was drawn between the most dorsal point of the dorsal spinal process and point B. The angle between these two latter lines was then

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<sup>1</sup> Drontal Plus, Bayer AG, Leverkusen, Germany

measured. This angle was recorded for the sixth and seventh cervical vertebra in all of the dogs (Figure 7-1).



**Figure 7- 1** Diagram illustrating the methodology in the measurement of the angulation of the dorsal spinous process. **A** = midpoint of the dorsal aspect of the vertebral body; **B** = mid point of dorsal spinous process attachment to neural arch; **C** = dorsal point of the dorsal spinous process.

The quantity and type of the food given to the puppies was selected by the owners and recorded daily for each puppy. The puppies were weaned between four and five weeks of age and subsequently received a mixture of various commercial and homemade diets. The nutrient content of the diets fed each week were estimated using the Animal Nutritionist software (N-squared and Durango software, Silverton, Oregon). These details of the commercial diets were supplied by the manufacturers and

added to the nutrient database of the Animal Nutritionist software. The nutrient content of the diets were then expressed as a percentage of estimated daily requirements for growth, i.e. % daily allowance as recommended by the Canine Nutrition Expert Committee of the Association of American Feed Control Officials (1997). Depending on the results of this analysis the diets were categorised week by week as being either balanced or unbalanced, with respect to the content of macronutrients, and calcium, phosphorous, magnesium, zinc and vitamin A. The exact vitamin D content of the diets could not be accurately assessed due to incomplete information being available from the food manufacturers.

The growth of each puppy was assessed weekly by recording body weight and by measuring the length of both ulnas and recording the average. The length of the ulna was taken to be the distance between the palpable point of the tuber olecrani and the junction of the stopper pad to the foreleg, as measured externally along the caudal aspect of the antebrachium (Burbidge and Pfeiffer, 1998). All weight and linear measurements were taken using the same equipment and by the same person.

The data were stored using the database management software Microsoft Access for Windows 95 (Microsoft Corporation, Redmond, Washington) and analysed with the statistical software packages SPSS for Windows version 7.5 (SPSS, Chicago, Illinois) and SAS for Windows Version 6.12 (SAS Institute, Cary, North Carolina).

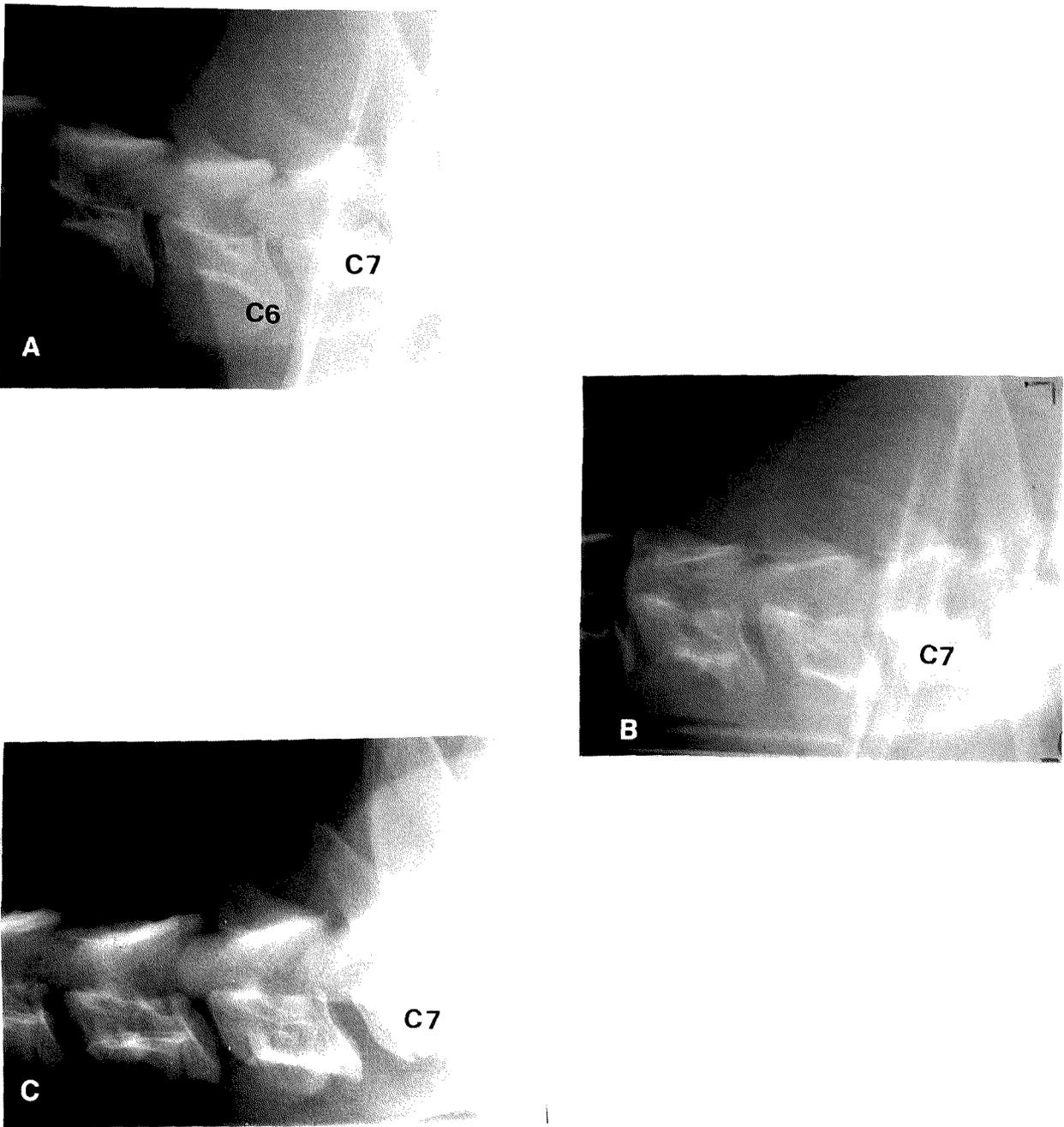
Line plots were used to graphically present the relationship between the average of the measured growth parameters, body weight and ulna length and the variables age and presence of caudal cervical malformation for the puppies in each litter.

The relationship between growth rate, as indicated by body weight gain and increase in ulna length and the fixed effects age, dam, diet, gender and the presence of caudal cervical malformation was examined using a mixed model analysis for repeated measures data. This analysis was conducted using the SAS procedure PROC MIXED (Anon, 1996). Restricted maximum likelihood (REML)

was used to fit compound symmetry and first order autoregressive covariance structures. The appropriate covariance structure for modelling within-subject variation was selected on the basis of a maximum value for Akaike's Information Criterion (AIC) as described by Littell *et al* (1996). Pairwise multiple comparisons of the least squares means between individual groups were conducted using the Bonferroni adjustment for 95% confidence limits.

## **Results**

All puppies remained clinically healthy for the duration of the study. Five of the 15 puppies had abnormal caudal cervical vertebrae based on the criteria set down above. In two of the five puppies these abnormalities were detected at six weeks of age. Each litter was represented by at least one affected puppy. Radiographically, the ossified centrum of the either sixth or seventh cervical vertebral body of these puppies was abnormal, often being trapezoid instead of rectangular in shape (Figure 7- 2). In addition, angle A was greater than 20° in three puppies, and angle B greater than 20° in the remaining two (Table 7-1).



**Figure 7-2 :** Lateral radiographs of the caudal cervical spines of Dobermann puppies (C6 = sixth, C7 = seventh cervical vertebra) : A) Normal; B) Abnormal shaped vertebral bodies and dorsal spinous process C7; C) Abnormal shaped vertebral body C7.

<b>Vertebral body shape C6/C7</b>	<b>Angle A</b>	<b>Angle B</b>
R	0	0
R	16	0
R	0	0
R	18	0
R	12	0
R	14	0
R	18	0
R	16	0
R	20	0
T	32	10
T	15	24
T	26	5
T	15	25
T	32	0

**Legend:**

R = rectangular  
T = trapezoid/abnormal  
Angle A = angle of dorsal spinous process, sixth vertebra.  
Angle B = angle of dorsal spinous process, seventh vertebra.

**Table 7-1: Radiological results of caudal cervical vertebral changes in 15 Doberman puppies.**

All puppies had at least one week where their diet was unbalanced in one or more of the nutrients measured. This varied from one week only (three puppies) to eight weeks (five puppies). The periods occurred at week 4 only (seven puppies), weeks 11 to 16 (three puppies), 5 to 7 (eight puppies) and 13 and 14 (three puppies). The unbalanced diets were transiently deficient in protein, calcium, phosphorus, and/or magnesium (Table 7-2).

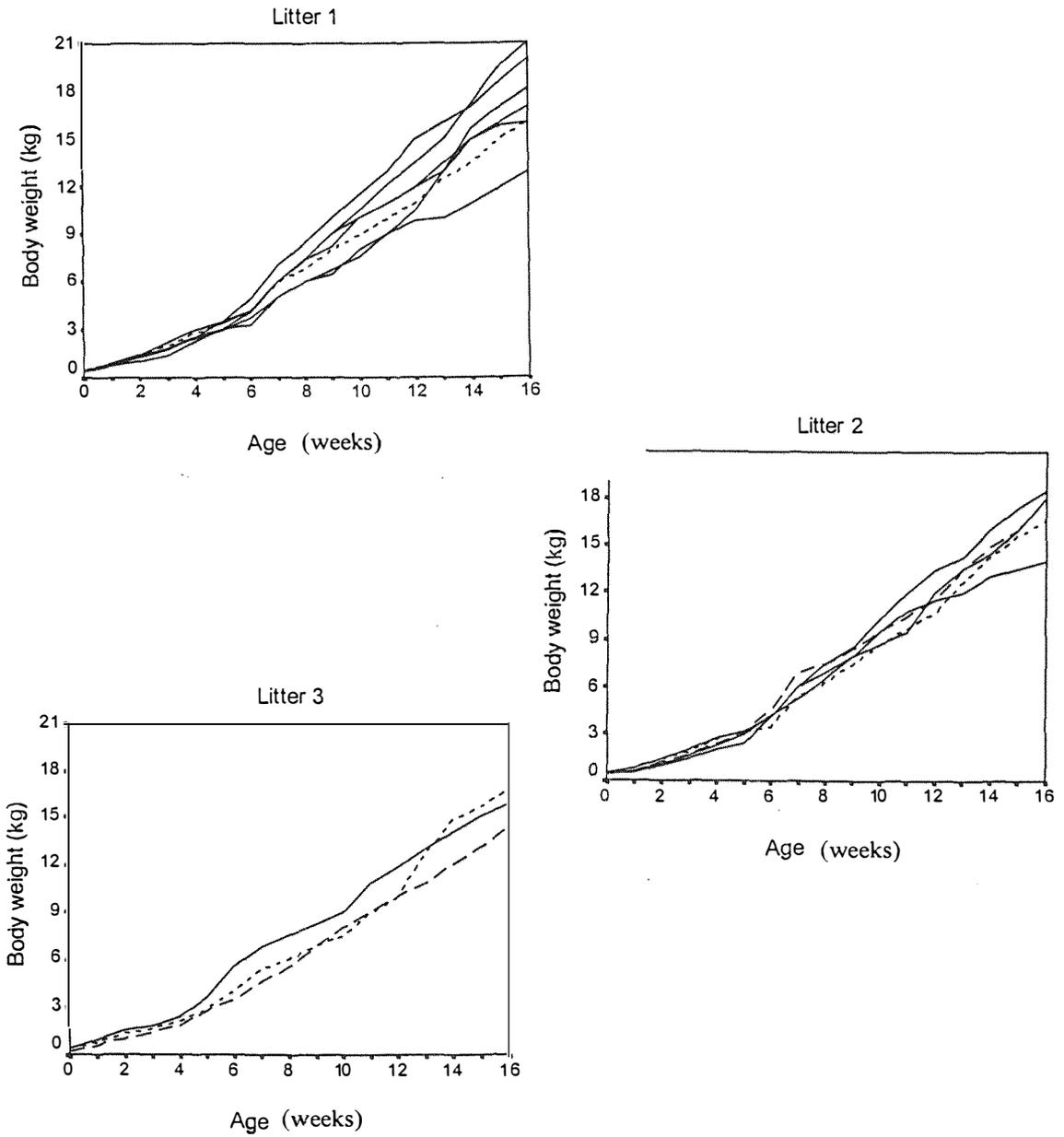
Dietary component	Age (weeks)			
	4	5-7	11-16	13-14
Protein		96% <sup>1</sup>		80%
Calcium	64%	94% <sup>1</sup>	80%	
Phosphorus	71%	76% <sup>1</sup>	80%	53%
Magnesium		48%		20% <sup>1</sup>

\* As recommended by the Canine Nutrition Expert Committee of the Association of American Feed Control Officials

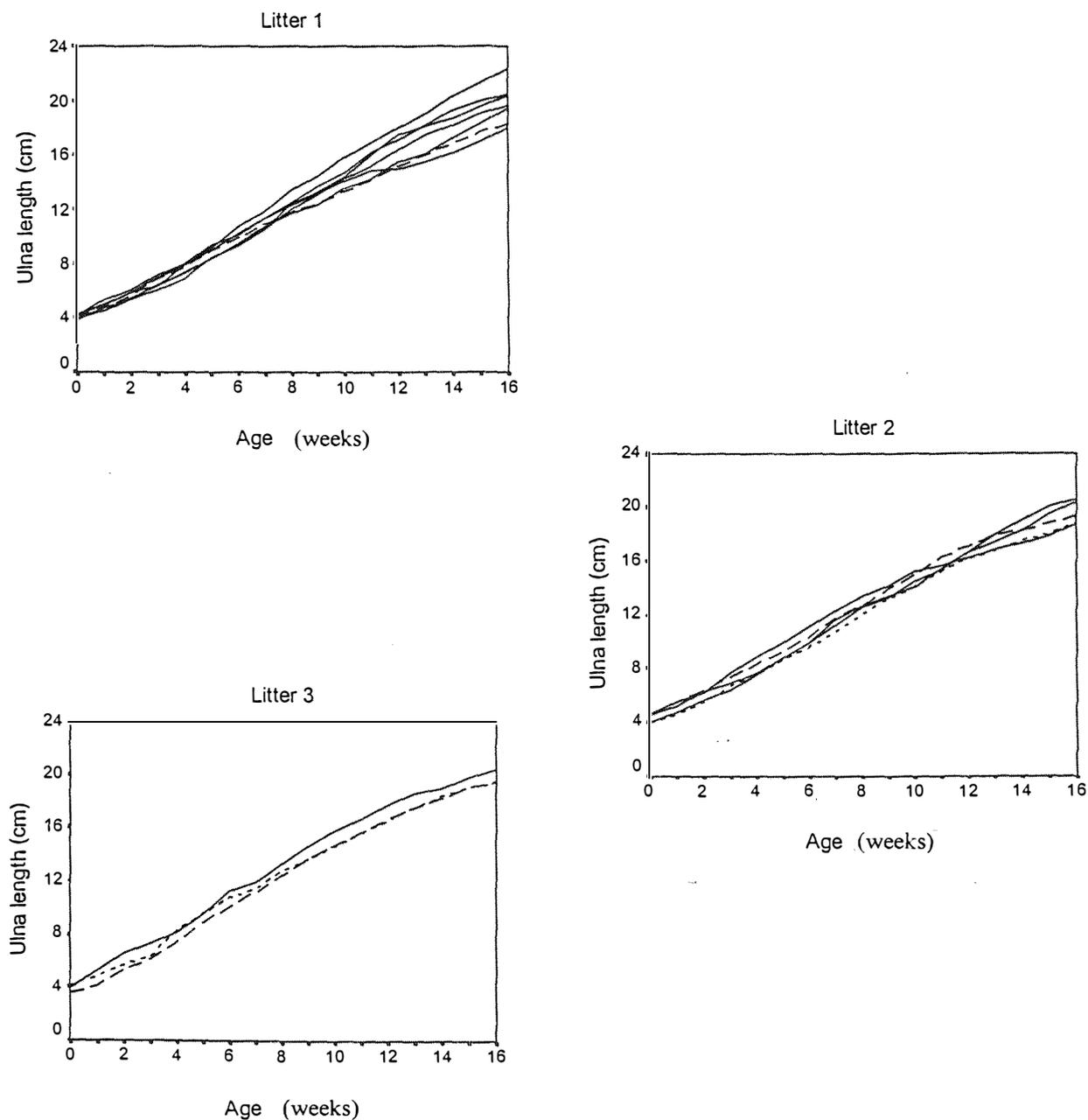
<sup>1</sup> Average percent over time period

**Table 7-2: Percent of recommended daily intake of dry matter nutrients in Dobermann diets\*.**

The line plots for the growth in terms of body weight and ulna length and the variables age and presence of caudal cervical malformation for the puppies in each litter are shown in Figure 7-3 and 7- 4.



**Figure 7-3:** Line plot of body weight against age for the three litters of puppies. (legend: solid lines = unaffected, dotted lines = presence of caudal cervical vertebral malformation).



**Figure 7-4:** Line plot of ulna length against age for the three litters of puppies (legend: solid lines = unaffected, dotted lines = presence of caudal cervical vertebral malformation)

The mixed models for body weight gain and increase in ulna length showing the best fit included a compound symmetry covariance structure. There was no significant association between these growth characteristics and the variables, dam, gender or presence of caudal cervical malformation. As expected in growing animals, there was a significant association between body weight gain and age ( $F=10.34$ , 15/207 df.,  $p=0.0001$ ) and increase in ulna length and age ( $F=5.8$ , 15/207 df.  $p=0.0001$ ). There was no significant association between balanced or unbalanced diet and increase in ulna length but there was a trend towards statistical significance for the relationship between diet and body weight gain ( $F=3.39$ , 1/2 07 df.  $p=0.0672$ ). The trend indicated that dogs on a balanced diet gained more body weight.

## **Discussion**

The observation that five of the 15 Dobermann puppies had abnormally shaped caudal cervical vertebrae before 16 weeks of age supports the previous observations that these changes occur early in life (Wright *et al*, 1973; Lewis, 1989). Vertebral ossification in the dog begins in the sixth week of gestation with primary ossification centres appearing laterally in the base of each pedicle of the neural arch and in the middle of each centrum (Noden and de Lahunta, 1985). After birth, the cervical vertebrae continue to develop by the process of active endochondral ossification at the chondro-osseous surfaces of the primary and secondary ossification centres, as well as by intramembranous ossification beneath the periosteum. By one month of age the laminae of the neural arches of the caudal cervical vertebra have fused, so that the shape of the neural canal can be influenced only by changes within the physes between the vertebral body and the neural arch and/or

by the modelling of bone formed by intramembranous ossification (Burbidge *et al*, 1995). In this study, subtle vertebral changes were detected in some of the puppies at six weeks of age, indicating that these changes either existed prior to birth or occurred during the early post-natal development.

The distinguishing radiological features of caudal cervical vertebral malformation in adult dogs have been recorded in several papers (Trotter *et al*, 1976; Wright *et al*, 1973; Shores, 1984; Cappello, 1997; Burbidge, unpublished data). These include: tilting of the vertebral body, a change in shape and opacity, vertebral canal malalignment, subluxation, a stenotic cranial neural canal, deformed articular facets and abnormal angulation of the dorsal spinous processes. Many of these features cannot be seen on radiographs of immature dogs because of the lack of ossified tissue. However, altered shape of the ossified centrum of the cervical vertebral body was detectable and abnormal angulation between the dorsal spinal process and the vertebral body identified in some of the puppies. It is hypothesized by the present author that both of these changes are likely to progress and result in the abnormal vertebral body and the neural canal shape seen in affected adults.

The observation that a third of the Dobermann puppies studied had vertebral changes supports the findings of radiological surveys in adult Dobermanns where vertebral abnormalities were detected in a high proportion of the population (Lewis, 1991; Burbidge *et al* 1994). Due to the limited information, and the small number of dams and puppies in this present study, little can be concluded as regards heritability of the condition. Unfortunately the owners of the dams and sires refused to give permission for radiographs of the cervical spine of these dogs so the conformation of their

vertebrae remains unknown. Surveys of Dobermann pinscher populations have indicated that caudal cervical vertebral malformation, based on radiographic evidence, occurs in approximately 50% of dogs studied and has a significant association with the development or presence of wobbler syndrome ( Lewis, 1991; Burbidge *et al*, 1994).

The finding that diet was not a significant factor in the development of caudal cervical vertebral abnormalities in the puppies studied could be explained in two ways. Firstly, the development of vertebral changes in some puppies at six weeks of age gave little time for diet (other than dam's nutrition to the puppies whilst they were *in utero* and later, dam's milk) to have an effect on skeletal development. Secondly, the diets fed to the puppies were either balanced or transiently deficient or excessive in the nutrients measured, including calcium. Thus in this study an over-supplemented diet was not a factor in the development of abnormal cervical vertebrae in the puppies. This finding is further supported by two inferences. Firstly, one other study (Hazewinkel *et al*, 1985) also questioned the association between calcium over-supplementation and the development of cervical vertebral malformation since these changes also occurred in both the control and over supplemented groups of dogs. Secondly, the diets fed and the nutritional deficiencies that occurred are likely to be more representative of the typical feeding patterns chosen by owners than the experimental diets fed in the earlier studies (Hedhammer *et al*, 1974; Hazewinkel *et al*, 1985). Thus the conditions of this study more accurately represent those within the Dobermann population.

There was no indication in this small data sample to suggest that there was a difference in growth

rate (both in terms of body weight gain and increase in ulna length) between dogs with abnormal cervical vertebrae and those with normally shaped vertebrae.

The results from this study indicate that some of the vertebral changes associated with caudal cervical vertebral malformation are present at six weeks of age in some Dobermanns and that these changes are unlikely to result from over-feeding or abnormally rapid growth rate. Further investigations are required to ascertain if any vertebral changes are present at birth or develop during the early post partum period.

### **Caudal cervical vertebral malformation in Dobermanns - are abnormalities present at birth?**

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#### **Abstract**

The aim of this study was to examine the cervical spines from deceased neonatal Dobermann puppies for the possible presence of caudal cervical vertebral malformation. The features looked for included those vertebral changes typically found in Dobermanns affected with caudal cervical spondylomyelopathy, namely: stenosis of the cranial vertebral canal opening, mishapened vertebral bodies, vertebral tilting and articular facet abnormalities.

The cervical spines from 27 unrelated neonatal Dobermann puppies (group D) and six from puppies of other large breeds (group O) were collected, and their morphology examined and compared using computerized tomography scans (CT) of the whole cervical spine, and gross, radiographic, and CT of the individual fifth, sixth and seventh cervical vertebra. The CT images of the individual vertebra were quantitatively assessed for the presence of stenosis of the cranial neural canal and vertebral body asymmetry. Statistical analysis examining the relationship and differences between these vertebral measurements, and the effects variables, breed group, gender and body weight was performed using multivariate analysis of variance.

No differences were detected between the two groups of puppies upon CT scanning of the whole cervical spine, nor upon gross and radiographic comparison of the individual fifth, sixth and seventh vertebra. However, statistically significant differences were found between the two puppy breed groups upon analysis of the measurements taken from the CT images of the individual vertebra. These differences consisted of a relatively narrowed cranial neural canal opening ( $p = 0.0001$ ) and evidence of vertebral body asymmetry ( $p = 0.04$ ) in the fifth, sixth and seventh cervical vertebrae of the Dobermann group. In addition, further analysis indicated that the most marked changes in morphology occurred in the seventh cervical vertebra.

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It was concluded that the caudal cervical vertebral changes, typical of those found in Dobermanns affected with caudal cervical spondylomyelopathy, are congenital malformations and that the seventh vertebra has the most marked deformities.

### **Introduction**

One of the features invariably present in Dobermanns affected with caudal cervical spondylomyelopathy is that of malformed caudal cervical vertebrae. These vertebral malformations can include stenosis of the cranial opening of the neural canal, misshapen vertebral bodies, vertebral tilting and degenerative joint disease of the articular facets (Trotter *et al*, 1976; Wright, 1977; Shores, 1984; Lewis, 1989; Sharp *et al*, 1992). The severity of these changes vary in individual dogs and their clinical significance in terms of existing and future neurological status is still debated.

There have been several theories suggested for the development of the vertebral changes in Dobermanns ( Hedhammer *et al*, 1974; Mason, 1977; Wright *et al*, 1973; Hazewinkel *et al*, 1985; Van Gundy, 1989; Lewis, 1989; Lewis, 1991; Lewis, 1992; Sharp *et al*, 1995). These include inherited factors, body conformation, (in particular the possible biomechanical effect on the developing caudal cervical vertebrae of a long neck, large head and angle of carriage) and nutritional influences of a diet rich in energy, protein and calcium (compared to the U.S. National Research Council's Nutrient Requirement of Dogs, 1974). Such over-feeding results in rapid skeletal growth and abnormal bony remodeling. Despite these differing opinions, most authors consider that the vertebral malformations are present and/or develop in the immature dog.

This study explores the possible presence of cervical vertebral malformation in Dobermann less than four days old.

### **Materials and Methods**

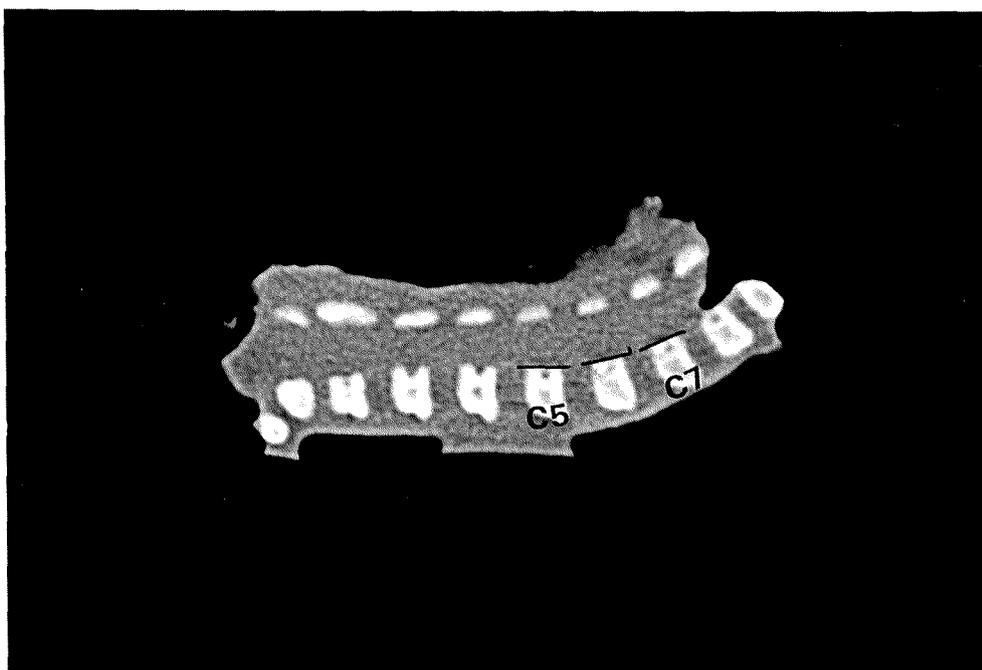
The cervical spines from 27 neonatal Dobermann puppies (group D) and six from puppies of other large breeds (group O) were harvested over a four-year period, and fixed and preserved in 10% formalin. Each puppy originated from a different litter and had either died at or within four days of

birth. The gender and weight of each puppy were recorded and for the Dobermanns their colour was also noted.

Four studies were performed on the caudal cervical vertebrae. These were CT of the whole cervical spine, and gross inspection, radiographic and CT examination of the fifth (C5), sixth (C6) and seventh (C7) individual vertebrae.

### *CT cervical spine*

A mid-sagittal 1 mm CT scan slice (Somatom Plus, Siemens Medical Systems, Erlangen, Germany) of the whole cervical spine was collected in a single 50mm by 20mm field of view to assess the alignment of the vertebrae with each other. This was measured by drawing a line along the dorsal aspect of the vertebral body and recording the change in the level of one vertebra relative to that of its' adjacent vertebrae at the intervening disc space (Figure 8-1). If adjacent lines were parallel or less than 20°, then the alignment of the vertebrae was regarded as being normal (Wright, 1977).



**Figure 8-1 :** Photograph of CT of cervical spine of newborn Dobermann. The ventral surface of the neural canal is marked by a horizontal line. The vertebral alignment appears normal.

***Gross anatomy***

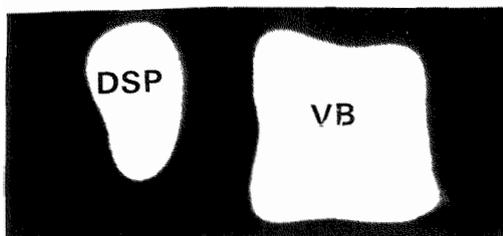
The spines were immersed in 1% potassium hydroxide solution for 48 hours to facilitate the removal of the soft tissues. The majority of this tissue was then carefully dissected from the vertebrae. Any residual muscle was removed using bacterial maceration. Once this had occurred, the fifth, sixth and seventh cervical vertebrae were separated by sharp dissection. The gross anatomy of each vertebra and the adjoining intervertebral disc structure was inspected using a bright light and microscope (magnification times 5). The gross appearance of the neural arches, dorsal spinous processes, articular facets and vertebral bodies was recorded.

***Radiography***

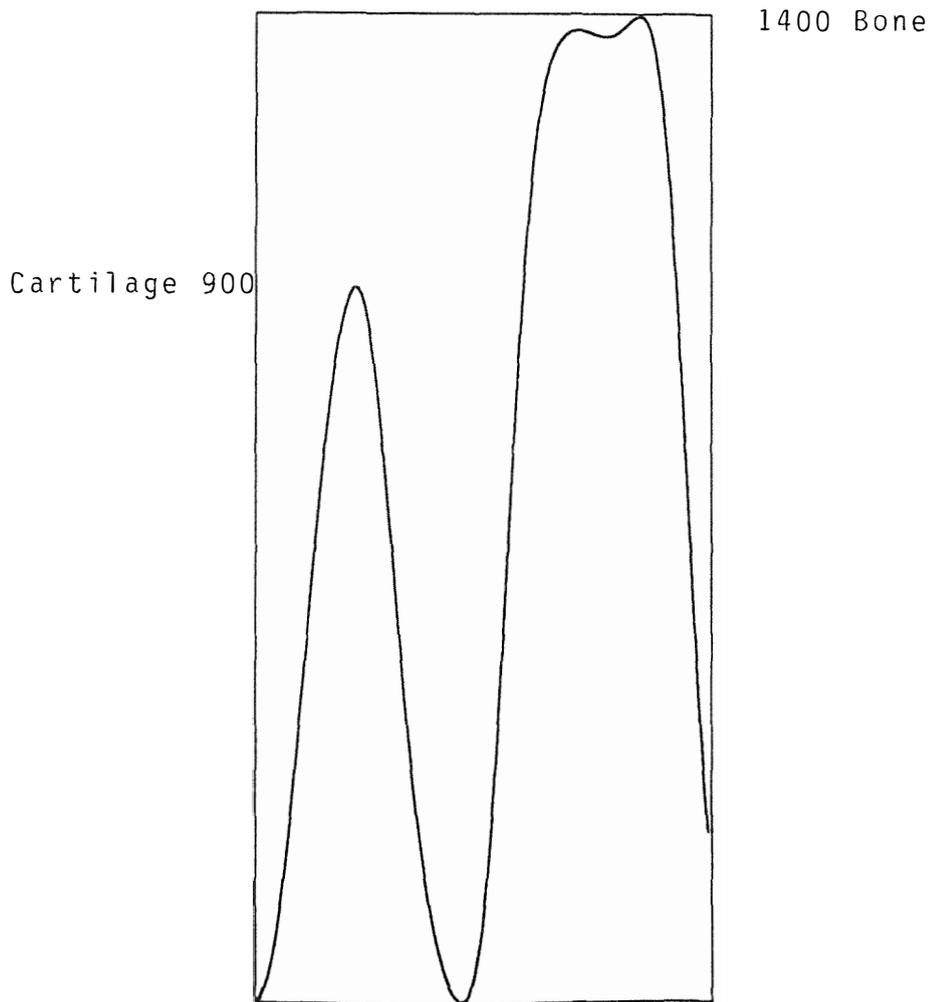
Cranio-caudal radiographs of each vertebra were taken using non screen film (Fuji medical X-ray film, Super HR-G, Fuji Photo Film Co Ltd., Japan) and a cabinet X-ray with a fluoroscopic inspection system (0.5 focal spot) (Torrex 150, Torr X-ray Corporation, Harbour City, California). The presence or absence of the three normal ossification centres, one in each of the neural arches and one in the vertebral body, was recorded.

***CT of individual vertebra***

A mid-sagittal 2mm CT scan slice (Somatom AR.C, Siemens Medical Systems, Erlangen, Germany) of each of the three separated vertebrae from each puppy was collected in a single 60mm by 60mm field of view. These images were examined and analysis performed using the UTHSCSA Image Tool Program, 1998 (developed at the University of Texas Health Science Center at San Antonio, Texas and available from the Internet by anonymous FTP from <ftp://maxradb.uthscsa.edu>). Firstly a CT gray scale threshold was found for bone and cartilage by analyzing areas on the image known to be cartilage (e.g. the dorsal spinous process) and known to be bone (e.g. the central portion of the vertebral body) (Figure 8-2). This was repeated on ten different vertebrae and the average gray scale threshold values for bone and cartilage were then used to create two images of each vertebra.

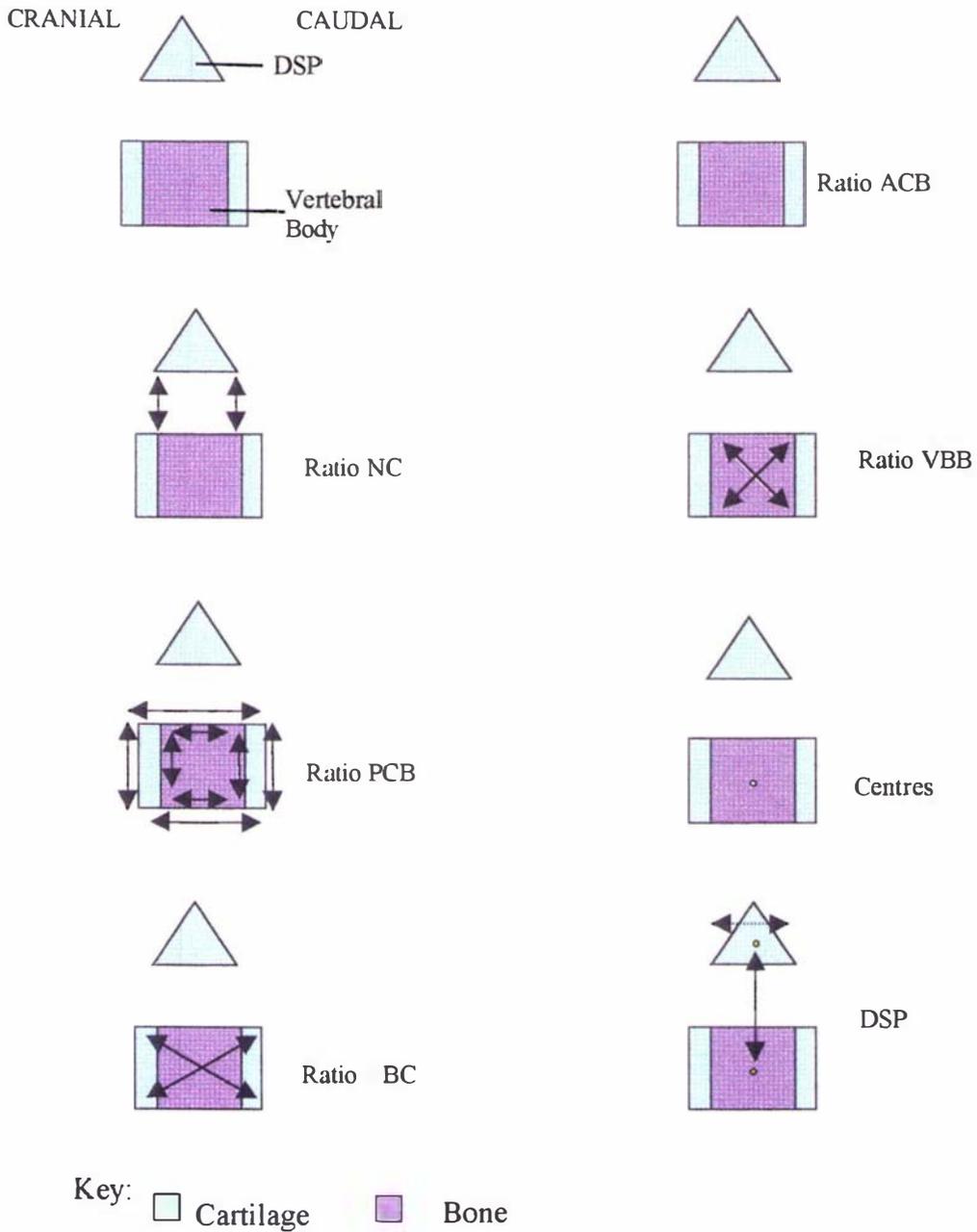


### Line Profile



**Figure 8-2:** The line profile of the CT threshold values for bone and cartilage as traced by a line passing through the mid point of the dorsal spinous process and through the vertebral body of one of the cervical vertebra.

The first image contained both bone and cartilage (whole image) and the second image consisted only of bone. Each of these vertebral images was evaluated for the following measurements: (Figure 8-3)



**Figure 8-3:** A diagrammatic representation of the measurements made on the vertebral images.

*Assessment of the neural canal*

Using the unaltered image of the vertebra, the cranial and caudal sagittal diameters of the neural canal for each vertebra were determined by measuring the distances between the most cranio-ventral point of the dorsal spinous process and the most cranio-dorsal edge of the vertebral body (cranial neural canal) and the distance between the most caudo-ventral point of the dorsal spinous process and the most caudo-dorsal edge of the vertebral body (caudal neural canal). The ratio of the cranial neural canal to the caudal neural canal distances was recorded (NC).

*Assessment of vertebral symmetry*

The measurements used to assess this were:

- a) the ratio of the area of the whole image of the vertebral body to that of the bone (ACB)
- b) the ratio of the perimeter of the peripheral cartilage of the whole image of the vertebral body to the perimeter of the bony centre (PCB)
- c) the ratio of the distance between the most cranio-dorsal point and the caudo-ventral point of the whole image of the vertebral body ( i.e. bone and cartilage ) to the distance between the most caudo-dorsal point of the vertebral body and the cranio- ventral point (VBC)
- d) the ratio of the distance measured between the most cranio-dorsal point of the bony portion of the vertebral body to the caudo-ventral point to the distance between the most caudo-dorsal point of the bony portion of the vertebral body to the cranio-ventral point ( VBB)
- e) the distance between the centre (as measured from the average of all the pixels in the object) of the whole vertebral body and that of the bony portion of the vertebral body ( Centres)
- f) the cranial or caudal distance difference between the centre of the whole image of the vertebral body and the centre of the cartilaginous dorsal spinous process (DSP).

*Statistical Analysis*

The data were stored and manipulated using the spreadsheet software Microsoft Excel for Windows 95 (Microsoft Corporation, Redmond, Washington) and analyzed using the statistical package SPSS for Windows version 8.0 (SPSS Inc, Chicago, IL 60611.)

Multivariate analysis of variance was used to analyze the relationship between the different measurements on the three vertebrae and the effect variables breed, vertebra, gender and the covariate body weight and their interaction terms. A between-subjects effects test was used to identify which of the dependent variables, (i.e. vertebral measurements) showed a difference between the breed groups D and O, genders, and body weight. In addition, the marginal means and 95% confidence intervals were examined to look for differences between the individual vertebrae C5, C6 and C7. Box plots were drawn of the distribution of the measurements for the dependent variables for each vertebra for both groups of dogs.

Using only the data from the Dobermann cervical spines, a hierarchical cluster analysis (using the Ward method) of the measurements for each vertebra was performed. The objective was to identify a group of puppies that were different from the others and had the characteristics of a relative narrowed cranial neural canal opening and asymmetry of the vertebra. Three combination groups of variables were used for separate cluster analyses. These were a) using all of the measurements, b) using the parameters ratio NC, VBB, VBC and Centres, and c) using the parameters ratio NC, ACB, PCB and VBB.

## Results

The descriptive statistics of the dogs are presented in Table 8-1.

Group	No.	Body Weight Average	Gender	Colour
Dobermann	27	325g (min 230 - max 409)	19M	18 B+T
			8F	9 RED
Other	6	371g (min 276 - max 456)	4M	
			2F	

**Table 8-1: Descriptive Statistics of the Puppies.**

***CT of cervical spine***

Examination of the CT scans of the whole cervical spine did not reveal any distinguishable differences between the breed groups D and O. This was due, in part, to the difficulty in positioning the entire cervical spine correctly to scan in a true sagittal plane, thus making the measurements inaccurate. However, there was no evidence of obvious tilting of individual vertebrae that is commonly observed on the radiographs of the cervical spines of adult Dobermanns affected with caudal cervical spondylomyelopathy.

***Gross anatomy***

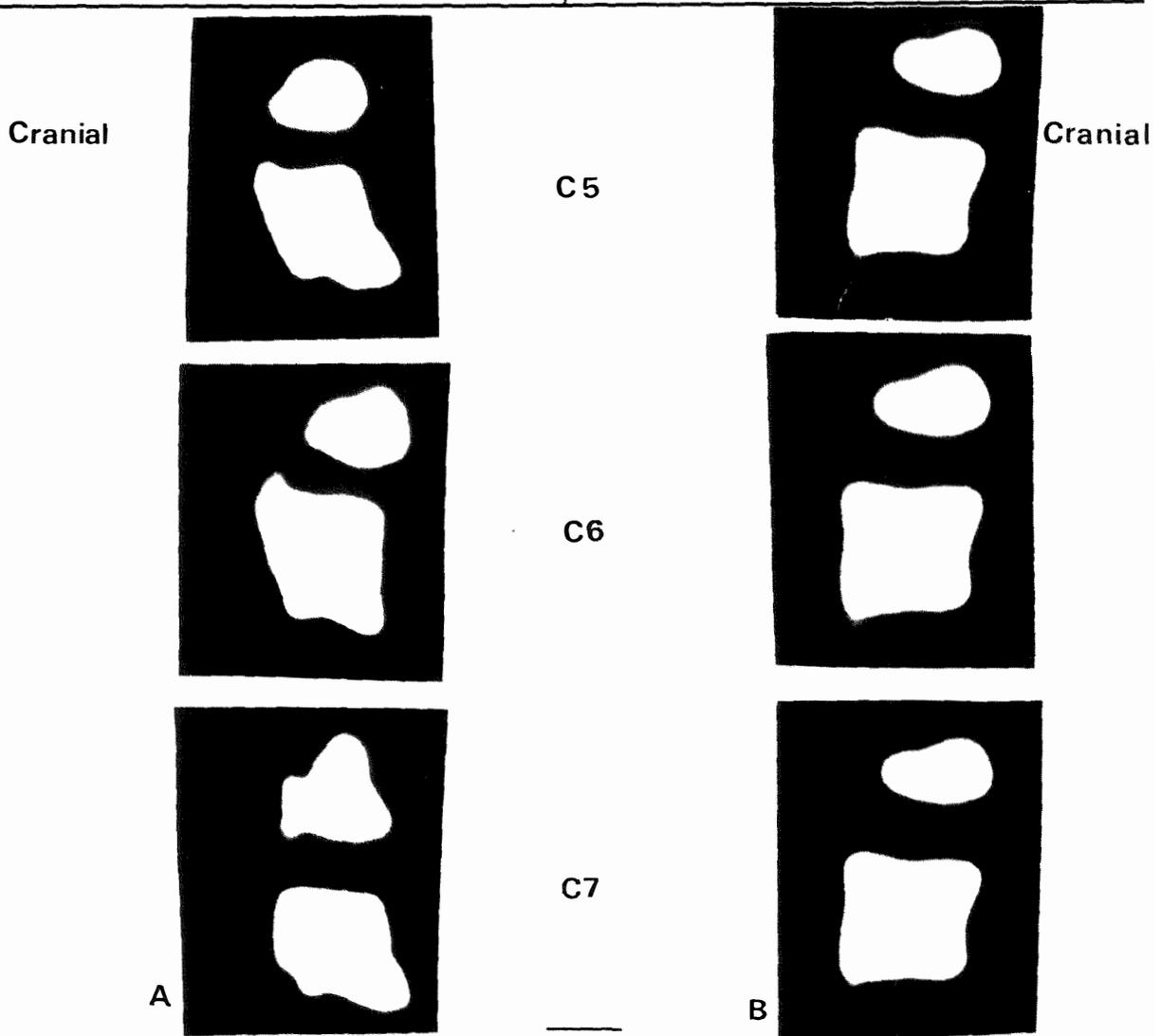
No differences in the gross anatomy could be detected between the breed groups O and D on the individual vertebrae, C5, C6 and C7. Their appearance was similar to that described for normal canine neonates (Burbidge *et al*, 1995).

***Radiography***

Examination of the radiographs of individual vertebrae failed to identify any significant differences between the two groups of dogs. Each vertebra had three separate ossification centres, one in the pedicle of each neural arch and one in the vertebral body.

***CT of individual vertebrae***

The average CT gray scale threshold value for cartilage was found to be 900 and that for bone 1400. The CT images from the two groups did, subjectively, appear to differ. The images from the Dobermann puppies were more varied in appearance and the vertebral bodies were less rectangular in shape (Figure 8-4).



**Figure 8-4:** CT images of the fifth, sixth and seventh cervical vertebrae of a neonatal Dobermann (A) and other large dog breed (B).  
Bar --0.25cm

#### *Statistical Analysis of CT images*

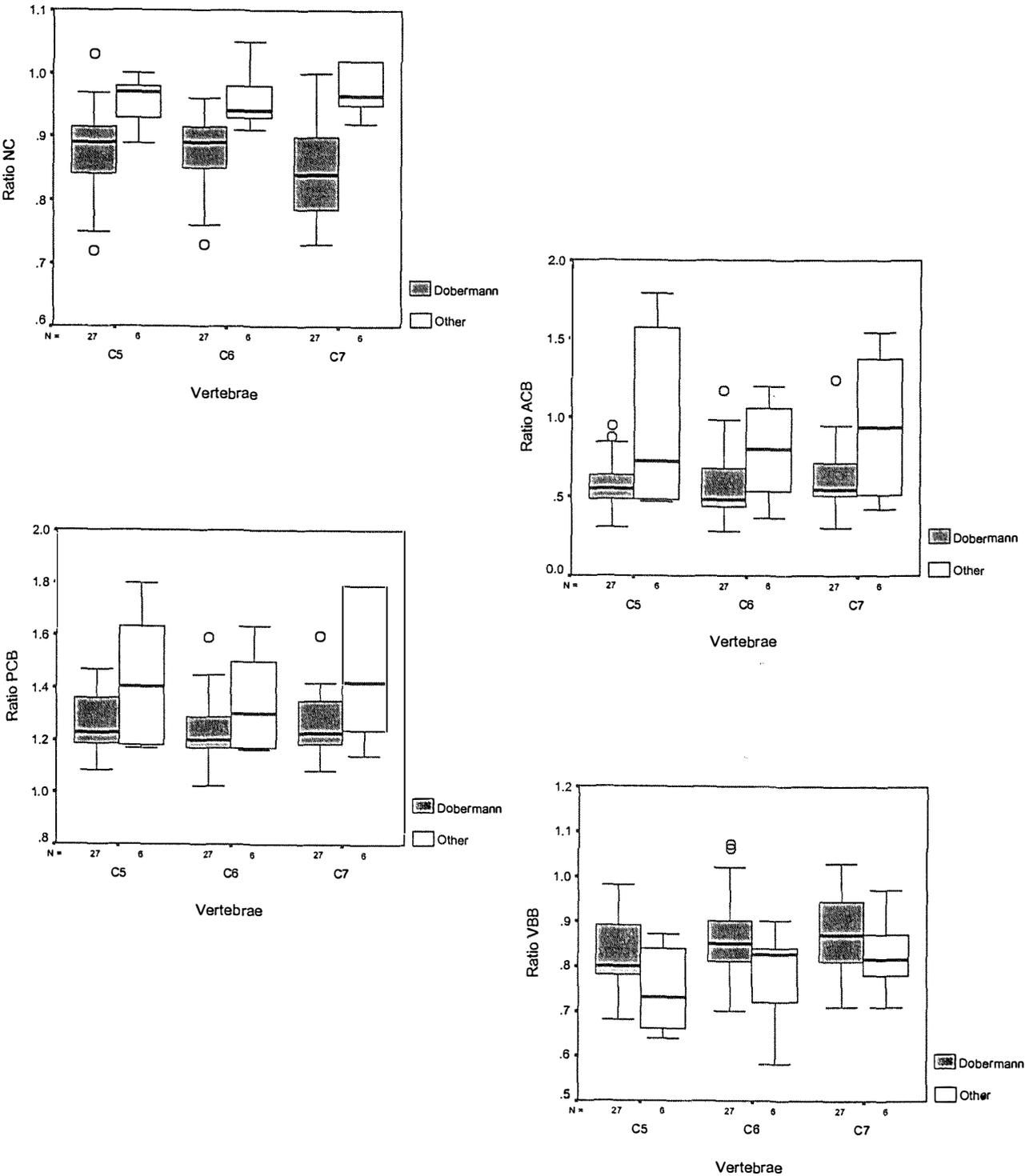
The multivariate analysis of variance using Pillai's trace, as a multivariate test for within subjects effects, demonstrated a significant difference for the variable breed ( $V=0.45$ ,  $F=9.5$ ,  $DF=7/80$ ,  $p=0.0001$ ), gender ( $V=0.26$ ,  $F=4.0$ ,  $DF=7/80$ ,  $p=0.001$ ), body weight ( $V=0.26$ ,  $F=4$ ,  $DF=7/80$ ,  $p=0.001$ ) and the first order interaction term, breed\* gender ( $V=0.4$ ,  $F=7.6$ ,  $DF=7/80$ ,  $p=0.0001$ ) but not for the other variables.

The between-subject effects test showed a significant difference between the breed categories, Groups D and O, for the measurements ratio NC ( $p=0.0001$ ), ratio ACB ( $p=0.0001$ ), ratio PCB ( $p=0.0001$ ) and ratio VBB ( $p=0.04$ ). This test also found there to be a significant difference between the genders for the measurements ratio ACB ( $p=0.002$ ) and PCB ( $p=0.0001$ ), for the co-variate bodyweight for the measurements ratio ACB ( $p=0.0001$ ) and for the breed\*gender interaction for the measurements ratio ACB ( $p=0.0001$ ) and PCB ( $p=0.0001$ ). Thus the only measurements that were solely breed dependent were the ratios NC and VBB.

Although the breed\* vertebra interaction was not significant in the above analysis, differences for the breed effect for the individual vertebrae were found upon examining the mean and 95% confidence interval for the measurements ratio NC, ratio ACB and PCB. The indication that a difference existed for C7, but not for C5 or C6, was derived from that fact that the confidence intervals did not overlap for these measurements. (Table 8-2). The box plots of the distribution of the measurements for the ratios NC, ACB, PCB and VBB for C5, C6 and C7 for both groups of dogs are shown in Figure 8-5.

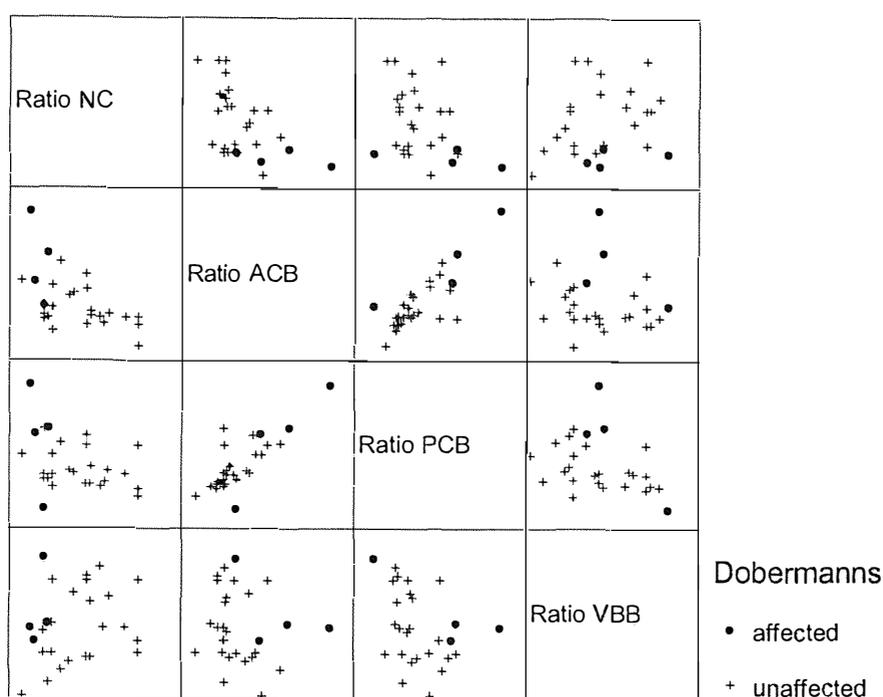
<b>Vertebra measurement</b>	<b>Breed</b>	<b>Mean</b>	<b>Std Error</b>	<b>95%</b>	<b>Confidence interval</b>
Ratio NC	D	0.860	0.014	0.831	0.888
	O	0.978	0.030	0.918	1.037
Ratio ACB	D	0.604	0.045	0.514	0.694
	O	1.258	0.026	0.803	1.181
Ratio PCB	D	1.258	0.026	1.208	1.309
	O	1.528	0.054	1.418	1.631

**Table 8-2 :** The mean and the 95% confidence intervals for the measurement ratios NC, ACB and PCB for the vertebra C7.



**Figure 8-5:** Box plots of the distributions of the measurements on the vertebral images for the ratios NC, ACB, PCB and VBB for C5, C6 and C7 for both groups of dogs.

The hierarchical cluster analysis failed to identify a separate sub-group of Dobermann puppies with characteristics consistent with cervical vertebral malformation for the individual vertebrae C5 and C6. However, this analysis did identify a distinct cluster consisting of a group of four Dobermann puppies that had these changes in the C7 vertebra. These changes consisted of relative cranial neural canal stenosis and some features of vertebral asymmetry. A scatter plot matrix was generated using four of the vertebral measurements for C7 (ratios NC, ACB, PCB and VBB) to demonstrate how these four puppies differed from the others (Figure 8-6).



**Figure 8-6:** A scatter plot of the vertebral measurements, ratios NC, ACB, PCB and VBB for C7 from the Dobermann puppies.

It showed that these four puppies were grouped with a similar value for the measurement ratio NC. However, for the other measurements, only three of these puppies were grouped closely together. This variation seen with the three vertebral ratio measurements ACB, PCB, and VBB may be due to the effect of the gender and bodyweight interactions. The phenotypic characteristics of the four

puppies in the cluster were that they were all male, weighing between 295 and 340g and coloured, three black and tans and one red.

### **Discussion**

The results from this study indicate that the vertebral malformations commonly associated with caudal cervical spondylomyelopathy are present in the neonatal Dobermann and are therefore congenital in origin. The greatest morphological abnormalities for all the caudal vertebrae in the Dobermann spines was the presence of stenosis of the cranial neural canal orifice and asymmetry of the bony portion of the vertebral body. These effects were consistent across gender and body weight variables. In addition, for C7, there was evidence of vertebral body asymmetry in terms of ratios of the area and perimeter of cartilage to bone. These changes are similar to those found in adults, where all three of the caudal cervical vertebrae may have stenosis of the cranial neural canal opening, but C7 often has the greatest morphological vertebral body abnormalities (Lewis, 1991; Sharp *et al*, 1992). The characteristic “tilting” of C6, which is commonly seen in adults, was not identified in the neonates on either the whole cervical spine or the individual vertebra studies. This change may occur as a consequence of the malformed C7 possibly resulting in abnormal stresses being placed on the adjacent vertebrae and the disc space between them.

The significant effect of gender on some of the vertebral ratios and the finding that all four of the puppies identified as having an abnormal C7 vertebra were male was interesting. Adult male Dobermanns are more commonly presented with caudal cervical spondylomyelopathy according to some authors ( Trotter *et al*, 1976; Denny *et al*, 1977; Chambers and Betts, 1977; Raffe and Knecht, 1980).

The examination criteria made on the neonate vertebrae were broad and designed to encompass any possible abnormality or potential difference between the two breed groups, D and O. The reason for this was that it was likely that any differences would be slight, since each individual vertebra is very small. There was sufficient difference between the two groups to show a significant difference in morphology when all three cervical vertebrae were included in the model. However, this was not so

when only the individual vertebra from each breed group were compared. Given that there were differences found upon examining the mean and 95% confidence intervals for C7, it is likely that the lack of significance for the individual vertebra comparison is due to insufficient numbers rather than lack of true differences. In order to minimize errors in classifying a vertebra as abnormal (i.e. false positives), the author tried to identify several puppies with a consistent number of similar changes before describing them as having caudal cervical vertebral malformation. Within the group of 27 Dobermann puppies there may well have been more vertebrae with abnormalities that were perhaps too subtle for detection using the above methodology. This is likely since the range of severity of vertebral malformations varies markedly in adult Dobermanns (Trotter *et al*, 1976; Lewis, 1989; Sharp *et al*, 1992). The use of dead puppies meant that there was no possibility of follow through of the puppies to an age where clinical signs of wobbler syndrome might be expressed. It also meant that the population studied was biased to those puppies that died at or near term. Another interesting investigation would be a longitudinal study following through the vertebral changes with age and correlating such changes with the occurrence and severity of neurological signs.

The predisposition of the Dobermann breed to caudal cervical vertebral malformation and the finding that it is congenital suggests that heritability is a likely causative factor. Since this vertebral abnormality is associated with caudal cervical spondylomyelopathy and the success of treatment of this condition remains inconsistent (Rusbridge, 1998), perhaps the focus of future investigations should be on verifying and establishing this potential causative factor. Such studies should be aimed at obtaining an accurate indication of the phenotype, designing a breeding programme to search for Mendelian transmission and lastly identifying molecular markers so that affected or carrier breeding animals can be detected. The level of gene expression for caudal cervical vertebral malformation is an important determining factor as to the success of such schemes. It may be that the condition has a high heritability factor or this factor may be low with other environmental effects playing a greater role in the development of the structural changes that occur.

## General Discussion

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Caudal cervical spondylomyelopathy (wobbler syndrome) is a common problem in the Dobermann pinscher breed (Seim and Withrow, 1982; Lewis, 1989). Descriptions of the caudal cervical spine in clinical cases consistently record the presence of vertebral malformation of the fifth, sixth and seventh cervical vertebrae, as well as intervertebral disc and ligament changes that result in compression of the spinal cord. The series of studies in this thesis were designed to determine if the proposed hypothesis “caudal cervical vertebral malformation, a predisposing factor for caudal cervical spondylomyelopathy (wobbler syndrome) in Dobermanns, is a deformity that is present in the very young dog,” was true. In addition, some of the previously suggested causative factors for the bony changes (namely body conformation, over-supplementation of food and comparatively rapid growth rate) were investigated.

### **Caudal cervical vertebral malformation in puppies**

Prior to the studies in this thesis, evidence that Dobermann puppies (aged three to 12 months) could have cervical vertebral malformation and exhibit neurological signs consistent with wobbler syndrome was provided in two papers (Parker *et al*, 1973; Lewis, 1989). Two distinct entities were recorded. Some affected puppies were found to have malformation of the seventh cervical vertebra, similar to those found in adult Dobermanns, although the exact details of the malformation were not recorded. Other affected puppies (approximately 75% of the cases) had articular facet, *ligamentum flavum* and dorsal annulus abnormalities in the mid-cervical region. Myelographic studies on these latter puppies demonstrated multiple sites of spinal cord compression at the third and fourth and/or fourth and fifth cervical intervertebral articulations. The radiological features of these latter puppies differ from those typically found in adult Dobermanns affected with caudal cervical spondylomyelopathy and may represent a different form of spondylomyelopathy, being more consistent with the changes reported in young Great Danes ( Hedhammer *et al*, 1974; Lewis, 1989)

and Basset hounds (Palmer and Wallace, 1967).

The evidence presented in this thesis shows that caudal cervical vertebral malformation does occur in the young Dobermann. The changes were similar to those found in adult Dobermanns affected with caudal cervical spondylomyelopathy. These changes consisted of stenosis of the cranial neural canal opening and a misshapened vertebral body, in particular of the seventh vertebra. Once it was found that the shape of the neural canal during normal development could be influenced only by changes within the physes between the vertebral body and each neural arch or by remodelling of bone formed by intramembranous ossification from four weeks of age onwards, (Chapter 4), it was suspected that vertebral malformation might occur at a young age or be congenital. The radiological changes of a malformed sixth and/or seventh cervical vertebral body, stenosis of the cranial neural canal and abnormal angulation of the dorsal spinous process recorded in affected puppies between six and 16 weeks of age, are similar to those found in adults affected with caudal cervical spondylomyelopathy (Chapter 7). Subtler, but similar changes could be detected using CT scan and image analysis techniques in the fifth, sixth and seventh cervical vertebrae of neonatal Dobermann puppies (Chapter 8). Of the fifth, sixth and seventh cervical vertebrae, the seventh had the most marked changes. Lewis (1989), also reported this finding in young (three to 12 months of age) Dobermanns. From the findings of the studies in this thesis, it is concluded that in Dobermanns, cervical vertebral malformation is congenital in origin.

Both plain radiography and CT scanning provide reliable diagnostic tools for the detection of vertebral malformation in adult dogs (Sharp *et al*, 1992). Both methods were used in the studies of this thesis. The sensitivity of radiography is likely to be less in puppies due to the lack of calcified tissue in the vertebrae. However, although vertebral malformation was identified in some of the puppies studied, it is possible that some went undetected for the above reason, and because the changes can be subtle and can vary in severity between individuals. In the neonatal puppies, CT scanning was the most reliable and sensitive method available. It demonstrated a number of individual variations (such as vertebral body asymmetry and cranial canal stenosis) in the Dobermann cervical vertebrae, which individually may have been subtle evidence of vertebral

malformation. However, it was decided that identification of more than one variation in each vertebra was required before classifying the vertebra as malformed. The reason for this was to minimize the misclassification of a normal vertebra for a malformed one (i.e. false positives). The objective was to be assured that cervical vertebral malformation was present in the neonatal spines.

In dogs affected with wobbler syndrome, myelography is required to reliably diagnose the extent and site of the spinal cord compression (Seim and Withrow, 1982). CT myelography can provide even more information, such as the presence of cord atrophy (Sharp *et al*, 1992; Sharp *et al*, 1995). Myelography was not used in any of the studies of this thesis. This was firstly because the procedure requires the patient to be anaesthetized and can be associated with significant morbidity, such as post-myelographic seizures (Widmer and Blevins, 1991). This was an unacceptable risk, particularly as most of the Dobermanns did not exhibit any neurological signs. Secondly, the focus of this thesis was to identify the presence of cervical vertebral malformation in the Dobermanns, rather than characterize any possible compressive myelopathy.

The presence of vertebral malformation in puppies was not synonymous with the existence of clinical and neurological signs of wobbler syndrome. Some puppies did have vertebral malformation in the absence of neurological signs. Alternatively, neurological signs of hindlimb ataxia with loss of conscious proprioception and exaggerated patellar reflexes can develop in the young dog, as recorded in this thesis (Chapter 3) and by others (Lewis, 1989). These neurological signs may be secondary to spinal cord compression typical of caudal cervical spondylomyelopathy or could be due to a concomitant primary spinal cord disease. However, neck pain, a common feature of affected adult Dobermanns was not present in these young dogs, presumably because of the absence of intervertebral disc disease.

## **Causative factors for caudal cervical vertebral malformation**

### **a) Heritability**

No study has solely investigated the heritability of caudal cervical vertebral malformation in Dobermanns. An attempt to identify any simple mechanism of inheritance from affected pedigree lines in Chapter 3 of this thesis failed because insufficient lineage data were available. Analyses of pedigrees of dogs affected with caudal cervical spondylmyelopathy by Mason (1977) and Lewis (1991) suggested a familial origin, and it is known that the incidence of the disorder is higher in the Dobermann and Great Dane than in other breeds (Seim and Withrow, 1982; Lewis, 1991). One possible explanation therefore, is that there is a genetic contribution to the aetiology of the condition. However, shared environmental factors or a combination of shared environmental and gene factors could also be important. The latter combined effect of both environmental and genetic factors that render an animal more or less likely to develop a certain condition is termed “liability” (Nicholas, 1996). This leads to the concept that above a certain threshold of liability all animals develop the condition and below it all animals are normal.

Due to the difficulty experienced in the comprehensive collection of pedigree data, further investigations of the possible genetic influence should include specifically planned matings and segregation analyses to test for agreement with a particular mode of inheritance by comparing the expected segregation frequencies of the Mendelian mode of inheritance with those observed. The segregation analyses could also be used to test for single gene inheritance, and to test for the presence of one or more genes making a relatively large contribution to the variation in liability. This latter information would be useful if the cause was multifactorial in origin. In addition, members of affected Dobermann families could be genotyped for DNA markers enabling linkage analysis to be conducted between the markers and the presence of cervical vertebral malformation. This would lead to the identification of DNA markers that are associated with the malformation, and ultimately, to the identification of genes that play an important role in determining liability. This information could then be used to increase the effectiveness of any control programme.

Identifying Dobermanns with vertebral malformation rather than caudal cervical spondylomyelopathy would be more useful and reliable for two reasons. Firstly, the animals could be identified at a young age (e.g. one year), and secondly, it seems that recognition of vertebral malformation provides a more reliable phenotype than the occurrence of neurological signs. The population study in Chapter 3 shows that radiological signs of vertebral malformation were present across the whole age range (3 to 156 months) of dogs studied, but the neurological signs were much less consistent. However, a further study is required correlating the presence and severity of vertebral malformation in young dogs with the later occurrence of neurological signs.

#### **b) Body conformation**

The possible influence of body conformation, such as heavy head, long neck and angle of carriage on the development of vertebral malformation remains contentious. It was first hypothesized by Wright *et al* (1973) and has since been commented on by several authors (Lewis, 1989; Sharp *et al*, 1995), however, no objective data has been presented by these authors to verify such suppositions. Two findings in the studies of this thesis cast doubt that body conformation is an influencing factor on the development of cervical vertebral malformation in Dobermanns. The first is that the study undertaken in Chapter 3 found no correlation between body conformation (head size, neck length, body length and height at withers) and radiographic evidence of cervical vertebral malformation in dogs aged between one and thirteen years of age. The second is the evidence that cervical vertebral malformation is present in neonatal Dobermanns. Therefore, from this objective data it appears that body conformation, in terms of the parameters measured, is not an influencing factor in the post-natal development of caudal cervical vertebral malformation.

#### **c) Nutrition**

The effect of feeding an *ad libitum* diet, (ie. providing up to 50% extra food compared to dogs on a restricted diet), on the growing skeleton of Great Danes was initially investigated by Hedhammer *et al*, (1974). One of the authors' conclusions was that there was an association between this excessive food intake (in particular energy, protein and calcium) and the development of cervical vertebral malformation, in particular, reduced neural canal diameter. The explanation for the failure

of the normal expansion of the vertebral foramen was that there was inadequate osteocytic osteolysis of the surrounding bone. This effect was thought to be secondary to the excess calcium in the diet and consequent hypercalcaemia and hypercalcitonaemia. However, there are now several reasons to doubt the veracity of this explanation. Firstly, when the effect of calcium alone in the diet (three times the recommended value) was further investigated in Great Danes by Hazewinkel *et al* (1985), no association was found between the feeding of excess calcium and the development of caudal cervical vertebral malformation. Secondly, it is thought that the theory that excessive calcium in the diet leads to hypercalcaemia and hypercalcitonaemia, which as a consequence leads to the retardation of bone maturation and remodelling, may be untrue. This is because it is now known that where high calcium diets are fed to dogs, they are able to regulate uptake by the intestine by decreasing the calcium coefficient to as low as 30 to 40% (Hazewinkel *et al*, 1991). Also, although calcitonin is a potent inhibitor of osteoclastic bone resorption, the effect is transient. This is because osteoclasts are able to escape from the influence of calcitonin following continued exposure to the hormone (Wiesbrode and Capen, 1982; Chambers and Mangus, 1982; Chambers and Moore, 1983).

Furthermore, work by Nap (1993) demonstrated that diets containing from 14 to 31% protein dry matter had no clinical, radiographic or histological effects on the developing skeleton or calcium kinetics. Thus these later studies do not support the original claim of an association between excess calcium and protein in the diet and the development of malformed cervical vertebrae.

The studies in this thesis also added supportive evidence that diet does not play a fundamental role in cervical vertebral malformation. Firstly, radiologically evident cervical vertebral malformation was found in five of fifteen Dobermann puppies studied in Chapter 7. Unlike the experimental diets of the above studies, diets fed by owners tended to be either balanced or transiently above or below the nutrient levels recommended by the Canine Nutrition Expert Committee at the Association of American Feed Control Officials (1997). Thus, excessive dietary concentration of nutrients such as calcium and protein, were not factors in the presence of the vertebral malformation in these puppies. Secondly, the finding that some of the vertebral changes could be detected as early as six weeks of age in two of the puppies meant that diet, other than dam's milk and diet "in *utero*" had little time

to effect such changes.

It is plausible, however, that marked dietary imbalances could exacerbate the severity of already existing vertebral malformations. This may explain the severe changes seen in the excessively fed experimental dogs in the studies of Hedhammer *et al* (1974). The long bones of the dogs in those studies were also abnormal, showing early epiphyseal closure, broadening of the metaphysis, increased density and further extension of the secondary spongiosa, and roughening of the endosteal and periosteal surfaces.

#### **d) Growth rate**

Rapid growth rate has been linked to a number of skeletal disorders such as osteochondrosis, hip dysplasia, retained cartilagenous cores, radius curvature and cervical vertebral malformation (Hedhammer *et al*,1974; Kasstrom, 1975; Hazewinkel *et al*, 1985). Experimental data on growth are often combined with nutritional studies: few studies in dogs have actually measured growth as a single variable. The term “fast growth rate” has therefore not been defined between and within breeds, and is a rather loosely applied term alluding to the greater growth rate of larger breeds of dogs compared to small. This faster growth rate of larger breeds is believed to be one of the predisposing factors for osteochondrosis ( Hedhammer *et al*, 1974). However, the comparison of growth between breeds in this thesis (Chapter 6) showed that Labrador retrievers, which have a high incidence of osteochondrosis (Fox and Walker, 1993) compared to Dobermanns (Lewis,1989) had a slower growth rate than Dobermanns. One growth study (Nap,1993) concluded that one of the most important influences on the differing growth rate between large and small dogs was the amount of circulating growth hormone. The studies from this thesis (Chapter 6) showed that dogs of different breeds had differing growth rates, both for body weight and skeletal growth. Therefore the growth curves and growth rate for each breed need to be determined before abnormally fast growth can be reliably detected for an individual of that breed. In addition, the measurement of skeletal growth requires accurate and consistent methodology to give reliable results (Chapter 5). The effect of fast growth rate in dogs is suspected rather than known, and in this study (Chapter 7) no correlation was found between growth rate and the presence of caudal cervical vertebral

malformation in Dobermann puppies.

### **Caudal cervical vertebral malformation as a predisposing factor for wobbler syndrome**

#### **a) Adults**

The only prospective study assessing the clinical significance of cervical vertebral malformation in adult Dobermanns is that of Lewis (1991). As part of a larger study, he followed 28 Dobermanns (aged one to eight years) that had obvious radiological signs of vertebral malformation, but were free from neurological signs at the time of the initial examination. Over the subsequent five to six years, 20 of these dogs developed clinical signs of wobbler syndrome. The Dobermann population study in this thesis (Chapter 3) also showed a significant association between the radiological presence of cervical vertebral malformation and neurological signs. The severity of the neurological signs increased significantly with age. In both of these studies, there were Dobermanns (some of which were over ten years of age) that had radiological evidence of caudal cervical vertebral malformation, but remained free from neurological signs. Therefore, although the presence of caudal cervical vertebral malformation does appear to be a predisposing factor for the later occurrence of neurological signs typical of wobbler syndrome, this progression does not always eventuate. However, the diagnosis of caudal cervical spondylomyelopathy does require that vertebral malformation is present as part of the disease process.

It is known from necropsy findings and myelographic studies in adult Dobermanns affected with caudal cervical spondylomyelopathy, that chronic degenerative disc disease with displacement of the dorsal annulus and *nucleus pulposus* into the neural canal contributes significantly to the spinal cord compression (Seim and Withrow, 1982; Sharp *et al*, 1992). Exactly how the presence of the malformed vertebrae affect the adjacent intervertebral disc spaces and the sequence of events that leads to chronic degenerative disc changes and neurological signs are unknown. The studies in this thesis indicate that the vertebral malformation was present at birth, but that the intervertebral disc appeared grossly normal (Chapter 8). It may be that the malformed vertebrae lead to chronic cyclic stress on the ligaments of the disc, causing rupture of some of the fibres and secondary fibroid

degeneration of the nucleus with subsequent protrusion or extrusion. However, descriptions of the intervertebral disc changes of affected Dobermanns differ from that typically found in other breeds of dog with cervical disc disease. In Dobermanns the compressive component is often primarily ligament (dorsal annulus or *ligamentum flavum*) i.e. a disc protrusion and not overt *nucleus pulposus* herniation or disc extrusion (Seim and Withrow, 1982). In addition, spinal cord atrophy may be present, presumably an indication of the chronicity of the compression (Sharp *et al*, 1992). Other factors, such as trauma or extension injuries of the neck may also play a part in the occurrence and progression of the intervertebral disc protrusion/extrusion and neurological signs, particularly for those cases which are acute in onset. This is because it is common for clinical cases to present with an acute onset of neurological signs (of varying severity) after minor traumatic events, such as crawling under a fence or playing with other dogs (Burbidge, personal observation). Some of these dogs may have had prior subtle neurological signs which were not noticed by the owner, as found in some of the Dobermanns (Group B) surveyed in Chapter 3. It may also explain the recorded predominance of clinical signs in males (Mason, 1977; Denny *et al*, 1977; Seim and Withrow, 1982), since these tend to be of more boisterous nature. However, possible influencing factors such as these are random events and therefore extremely difficult to study scientifically.

## **b) Puppies**

The clinical significance of caudal cervical vertebral malformation in puppies appears to be variable. Some puppies do have neurological signs (Lewis, 1989; Burbidge *et al*, 1994), but whether these are secondary to compression by the malformed caudal cervical vertebrae, or whether these puppies have additional spinal cord disease, is unknown. Since caudal cervical vertebral malformation is common within the Dobermann population (Chapter 3) and since the studies of this thesis indicate that it is congenital in origin (Chapter 8), it can be deduced that for most puppies the presence of caudal cervical vertebral malformation is usually of little immediate clinical significance.

## CONCLUSIONS

1. Morphological evidence of caudal cervical vertebral malformation (as judged by radiography and CT scanning) was present in the neonatal and young Dobermann puppy.
2. There was no significant association between the diet fed to the Dobermann puppies and the presence of caudal cervical vertebral malformation.
3. There was no significant association between the growth rate of individual Dobermann puppies and the presence of caudal cervical vertebral malformation.
4. The presence of radiographically evident caudal cervical vertebral malformation and age are important risk factors in the occurrence of clinical signs of wobbler syndrome in Dobermanns.
5. Body conformation of the adult, in terms of head size, neck length, body length and height at withers was not a significant factor for the presence of caudal cervical vertebral malformation in the Dobermann breed.
6. Growth rate varies between different breeds of dog, and both body weight and increase in bone length should be measured to more completely characterize that growth.

## RECOMMENDATIONS FOR FUTURE RESEARCH

As with most research, the new findings should be substantiated, refuted or added to by further experiments and observations. In particular, further investigations should be aimed firstly at further defining the aetiology of caudal cervical vertebral malformation and secondly, isolating other risk factors which contribute to the occurrence of clinical and neurological signs.

Such studies could include:

1. A prospective linear study following a large group of Dobermanns from birth to adulthood, aimed at investigating the presence of caudal cervical vertebral malformation, (as judged by radiographic or preferably CT examination), and determining if there is any correlation to possible body conformation and growth rate characteristics.
2. A prospective study following a group of Dobermanns from birth to death to evaluate and correlate the severity of the caudal cervical vertebral malformation, as judged by radiographic examination, with the development and severity of neurological signs. One aim might be to develop a plausible scoring system in young dogs that could be used to predict possible future clinical outcome. Such a scheme might be used as a selection criterium in breeding control programmes.
3. An investigation into the heritability of caudal cervical vertebral malformation by breeding experiments and detection of DNA markers.
4. Additional studies of growth in individual breeds, and the possible correlation between growth rate and the development of skeletal abnormalities such as osteochondrosis and hip dysplasia.

### Dorsal spinous process angulation in Dobermanns with caudal cervical spondylomyelopathy as compared with other breeds

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#### Abstract:

The objective of this study was to identify another reliable radiological feature for the recognition of caudal cervical vertebral malformation, a feature of cervical spondylomyelopathy in Dobermanns. The angulation of the dorsal spinous process in relation to the vertebral body of the sixth ( $C_6$ ) and seventh ( $C_7$ ) cervical vertebrae was compared between 25 Dobermanns affected with caudal cervical spondylomyelopathy (wobbler syndrome) and 25 other medium to large breed (non-wobbler) dogs. This angle was measured on lateral radiographs of the caudal cervical spine for both groups of dogs and compared using the Mann-Whitney U-test. In addition, an inter-rater reliability study was performed to assess the repeatability of the angle measurement. It was found that there was a significant difference in the angulation of the dorsal spinous process between the two groups of dogs for  $C_6$  ( $p < 0.0001$ ) and for  $C_7$  ( $p < 0.0001$ ). An intraclass correlation coefficient of 0.98 was estimated for the inter-observer variation for the angle measurements in both cervical vertebrae. An inter-rater reliability analysis using Cronbach's coefficient Alpha statistic indicated that there was 0.99 reliability for the angle measurements across observers.

It was concluded the angle of the dorsal spinous process relative to the neural canal of  $C_6$  and  $C_7$  provided a reliable quantitative parameter in the recognition of caudal cervical malformation in Dobermanns.

#### Introduction

Caudal cervical spondylomyelopathy (wobbler syndrome) in Dobermann pinschers results from malformed caudal cervical vertebrae and/or the associated soft tissue structures causing compression of the spinal cord. The radiographic features of the syndrome in this breed are

well documented (Wright et al, 1973; Trotter et al, 1976; Chambers and Betts, 1977; Raffé and Knecht, 1980; Read et al, 1983). The recorded cervical vertebral abnormalities or malformations include stenosis of the cranial aspect of the neural canal opening, proliferative exostoses of the dorsal articular facets, vertebral body malformation of varying severity, dorsal tilting of the cranio-dorsal aspect of the vertebral body and various signs of intervertebral disc disease. Further imaging techniques such as myelography and CAT scans have been recommended to better define the nature of the spinal cord compression in clinical cases ( Seim and Withrow, 1982; Sharp *et al*, 1992).

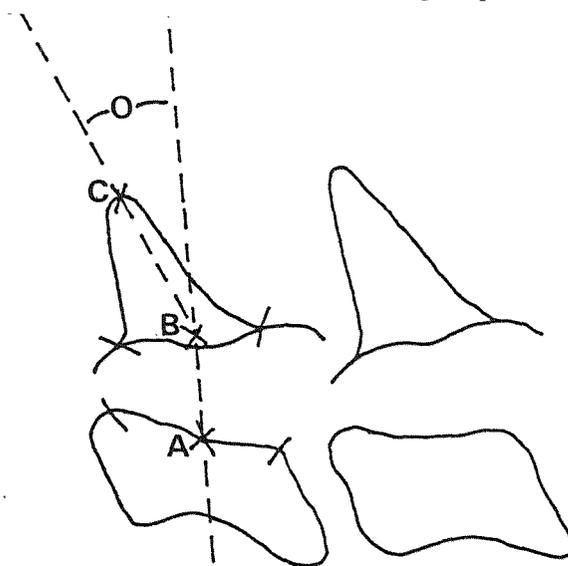
The radiological features of the abnormal caudal cervical vertebrae have been used to identify potential “wobblers”. Such assessment is reliant on the identification and subjective evaluation of the above criteria. The only reliable quantitative dimension is the measurement of the sagittal diameter of the spinal canal (Wright, 1977). This measurement has been shown to give an accurate estimation of the stenosis that occurs in the cranial opening of the neural canal of affected vertebrae. Lewis (1991) also used the degree of stepping between adjacent vertebrae as an additional parameter. However, this latter measurement has been shown to be highly dependent on the positioning of the neck, with significant variation occurring within and between breeds (Wright, 1977).

The present study was performed to identify one other reliable measurement that might be used to distinguish between normal shaped vertebrae and those characteristic of caudal cervical vertebral malformation in Dobermanns.

### **Material and Methods**

Radiographs of the caudal cervical spine of 25 adult Dobermanns with confirmed caudal cervical spondylomyelopathy (wobbler syndrome) and those of 25 adult medium to large breed dogs ( non-wobbler) were reviewed. Caudal cervical spondylomyelopathy in the Dobermanns was identified by the characteristic clinical, radiological and myelographic

signs. Radiographs were selected on the basis of the neck being in a true neutral lateral position, as assessed by the overlapping of the transverse processes of the sixth cervical vertebra ( $C_6$ ), and lack of extension or flexion. The angle of the dorsal spinous process in relation to the dorsal and ventral walls of the neural canal was measured by the following method. Firstly, the mid-point of a line drawn between the dorso-cranial and dorso-caudal points of the vertebral body was found (point A) (Figure 1). Then the mid-point of a line drawn between the most cranial and caudal junction of the dorsal spinous process to the neural arches was identified. (point B). A third line was drawn linking these two mid-points. Next a line was drawn between the most dorsal point of the dorsal spinal process and point B. The angle between these two latter lines was then measured. This angle was recorded for the sixth ( $C_6$ ) and seventh cervical vertebra ( $C_7$ ) in both groups of dogs.



**Figure 1 :** Diagram illustrating methodology in the measurement of the angulation of the dorsal spinous process.

**A = mid point dorsal aspect vertebral body**

**B = mid point dorsal spinous process attachment**

**C = dorsal point of spinous process**

**O = angle measured**

Statistical analysis of this data was performed using the statistical software package Statview 4.0 (Abacus Concepts, Inc. Berkeley, CA 1992). The distribution of the angle measurements for C<sub>6</sub> and C<sub>7</sub> was compared between the two groups of dogs using the Mann-Whitney U-test.

In addition, a blinded trial was performed to estimate the inter-rater reliability of the angle measurements. Five veterinarians applied the technique, described above, to obtain the angle O for C<sub>6</sub> and C<sub>7</sub> using 10 radiographs of Dobermanns and 10 of the other breeds. A two way analysis of variance was performed to explore the relationship between the angle measurement and the random effects, observer and dog. An intraclass correlation coefficient for the model ICC(2,1), following the notation by Shrout and Fleiss (1979), was calculated to quantify the importance of inter-observer variation. Furthermore, an inter-rater reliability analysis was conducted using Cronbach's coefficient Alpha to identify any inconsistent individual measurers (MacLennan, 1993). The statistical analysis was performed using the computer software packages SAS for Windows Version 6.12 ( SAS Institute, Cary, North Carolina, U.S.A. ) using SAS macro INTRACC.

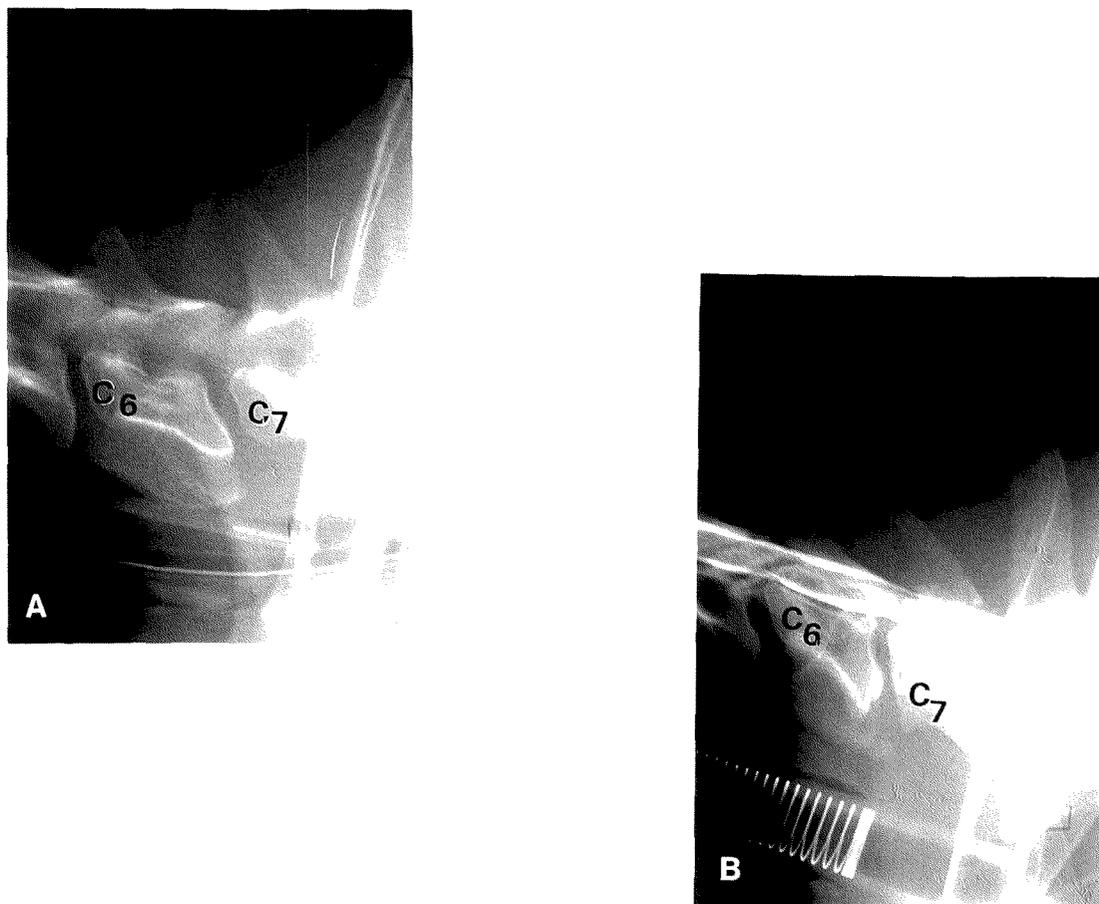
## **Results**

A summary of the data for the differences of the angulation of the dorsal spinous processes of C<sub>6</sub> and C<sub>7</sub> between Dobermanns and the other breeds is shown in Table 1.

	Mean	S.D.	S.E.	Min.	Max.
C <sub>6</sub> Dobermann	39	13.8	2.7	15	68
C <sub>6</sub> Other	21	9.5	1.9	2	36
C <sub>7</sub> Dobermann	35	7.1	1.4	20	45
C <sub>7</sub> Other	19	8.0	1.6	5	38

**Table 1** Summary of dorsal spinal process angle measurements of the sixth cervical vertebra (C<sub>6</sub>) and the seventh cervical vertebra (C<sub>7</sub>) from Dobermanns affected with caudal cervical spondylomyelopathy and unaffected dogs (Other) (S.D. Standard deviation, S.E. Standard error).

The Mann -Whitney U-test demonstrated a significant difference in the angulation of the dorsal spinous process between the two groups of dogs for C<sub>6</sub> (p <0.0001) and for C<sub>7</sub> (p < 0.0001). For both C<sub>6</sub> and C<sub>7</sub> the measured angle was significantly greater in the Dobermann group.



**Figure 2 :** Lateral view radiograph of the caudal cervical vertebrae in A) “non-wobbler” dog and B) Doberman affected with caudal cervical spondylomyelopathy. Note the increased angulation of the dorsal spinous process in the latter.

A total of 100 measurements were used in the data analysis for the inter-rater reliability study. The results of the two way analysis of variance for C<sub>6</sub> and C<sub>7</sub> are presented in Table 2.

	DF		Sum of Squares		Mean Square		F - ratio		P - value	
	C <sub>6</sub>	C <sub>7</sub>								
Dog	19	19	15150. 8	17462. 2	797.4	919.1	441.5	358. 8	0.000 1	
Observer	4	4	15.5	22.6	3.9	5.6	2.2	2.2	0.08	0.07 6
Error	76	76	137.3	194.6	1.8	2.6				
Total	99	99	15303. 6	17679. 4						

**Table 2 Results of two-way analysis of variance assessing the effect of between dog and between observer variation on the angle measurement of the sixth (C<sub>6</sub>) and seventh (C<sub>7</sub>) cervical vertebrae.**

The main effect, dog was found to have a significant effect on the angle measurement for both C6 and C7, but not the observer. An intraclass correlation coefficient of 0.98 was estimated for the inter-observer variation for the angle measurements in both cervical vertebrae. This indicates that only 2% of overall variation of the measurements was caused by differences between observers. The inter-rater reliability analysis using Cronbach's coefficient Alpha statistic indicated that there was 0.99 reliability for the angle measure in C<sub>6</sub> and C<sub>7</sub> across observers.

**Discussion**

The angulation of the dorsal spinous process relative to the neural canal does provide another reliable quantitative parameter in recognizing abnormal shaped vertebrae of Dobermann affected with caudal cervical spondylomyelopathy, and distinguishing them from the cervical

vertebrae of other breeds of similar sized dogs that do not have features of caudal cervical vertebral malformation. This increase in angulation of the dorsal spinal processes in affected Dobermanns' has not been, to the author's knowledge, described before. It is possibly a result of the "flattening" or "collapse" of the neural arches which also contribute to the characteristic stenosis of the cranial neural canal opening in affected dogs.

This feature could be used, in addition to the aforementioned radiological changes, to identify Dobermanns that have caudal cervical vertebral malformation. Whilst the presence of cervical vertebral malformation has been recognized as being a predisposing factor to the subsequent development of wobbler syndrome, not all Dobermanns with these changes develop clinical signs (Lewis, 1991, Burbidge *et al*, 1994; Sharp *et al*, 1992). Hence, in this study it was decided to compare measurements from the radiographs of Dobermanns with confirmed caudal cervical spondylomyelopathy with unaffected, but similar sized breeds of dogs.

Although this radiographic feature is not particularly useful to the clinician dealing with clinical cases of caudal cervical spondylomyelopathy, it is important to document as many abnormalities of cervical vertebral malformation as possible. The heritable basis of the syndrome still remains unclear, but should this become established, then the vertebral abnormalities seen on plain radiographs would become of paramount importance for use in possible screening programmes.

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## ERRATA

- Page 10 line 9 ..... **hypercalcitoninaemia**
- Page 20 line 5 ..... degrees of **necrosis** of the grey matter
- Page 22 line 2 ..... disruption **of** the dorsal annulus
- Page 23 line 11 ..... that **paresis** with
- Page 23 line 18 ..... and gracile tracts leading to proprioceptive deficits.
- Page 26 Figure 2-8 ..... Figure acknowledgement, Joe Trumpey. Reprinted from Wheeler S.J. and Sharp N.J. In *Small Animal Animal Spinal Disorders* p78. Mosby Wolfe, London.
- Page 29 line 18 ..... Additional distraction-stabilization technique: **Dixon, B.C., Tomlinson, J.L., Kraus, K.H.** (1996) Modified distraction-stabilization technique using an interbody polymethyl methacrylate plug with caudal cervical spondylomyelopathy. *Journal of the American Veterinary Medical Association* **208**,61-68.
- Page 37 line 10 ..... flexor, **cross**-extensor and patellar reflexes
- Page 41 Figure 3-4 ..... no dogs had a radiological score of 111 and a neurological score of A.
- Page 47 line 8 ..... on more than **one** occasion
- Page 55 line 5 ..... **sagittal** plane
- Page 55 line 6 ..... **sagittal** plane
- Page 55 line 7 ..... each of the caudal
- Page 68 ..... the term anthropometry applies to human measurement, perhaps a more appropriate term for the studies in this chapter would be "theriometry"
- Page 68 line 13..... can **be** applied
- Page 98 Figure 6-4 ..... measurements **in** individual puppies
- Page 111 line 4 ..... individual **groups**
- Page 111 line 9 ..... of **either the** sixth
- Page 122 line 20 ..... Dobermann **puppies** less
- Page 123 line 12 ..... or **intersected at** less than
- Page 139 line 6 ..... cervical **spondylomyelopathy**
- Page 141 line 24 ..... concentration of
- Page 144 line 4 ..... **ligamentous**
- Page 151 line 4 ..... Since the mean angle of the non-Dobermann group of dogs was 20 degrees, this angulation can be used as a baseline value to identify abnormal angulation of the dorsal spinous process.
- Page 153 line 11 ..... with caudal