Rickets in a litter of racing greyhounds

Rickets was diagnosed in six 14-week-old racing greyhound littermates presented with musculoskeletal disease. Physical findings included listlessness, profound muscle weakness, lameness, lateral bowing of the antebrachii and focal hard swellings proximal to the tarsi and carpi. Radiological findings included generalised osteopenia, axial and radial thickening of growth plates, and 'cupping' of the adjacent metaphyses; the distal ulnar growth plates were most severely and consistently affected. The diagnosis was confirmed by demonstrating subnormal concentrations of 25-hydroxycholecalciferol in serum samples collected at admission. The pups' diet consisted of an inexpensive generic kibble formulated for adult dogs, porridge, milk, pasta, minced beef, vegetables and a small quantity of calcium carbonate powder. The pups were successfully treated by feeding a nutritionally complete, vitamin D-containing ration formulated for growing pups. Bilateral growth retardation of distal ulnar physes occurred as a sequel in one pup.

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INTRODUCTION

The terms rickets and osteomalacia encompass a group of disorders in which there is defective mineralisation of the newly formed organic matrix of the skeleton. Rickets is a disease of the developing skeleton, where defective mineralisation occurs not only in bone, but also at the cartilaginous portion of the growth plate (Campbell 1964, Krane and Holick 1980). It is characterised by a defective calcification of epiphyseal cartilage, delay in maturation and arrangement of cartilage cells and a failure to remodel freshly deposited bone. Together these derangements result in enlargement of metaphyses and weakening of bone shafts that in turn lead to bending deformity, with bowing of the limbs. Osteomalacia refers to the equivalent disorder of the adult skeleton at a time when the growth plates have closed; bone remodelling is affected primarily, so unmineralised bone matrix accumulates in all parts of the skeleton (Krane and Holick 1980).

There are a number of conditions that can give rise to rickets, but they share as a common feature inadequate intake or endogenous production of vitamin D (cholecalciferol) in relation to the calcium content of the diet (Krane and Holick 1980, Carpenter 1991, Fraser 1995). Rickets can be diagnosed definitively by measuring reduced concentrations of the storage form of vitamin D, 25-hydroxycholecalciferol [25(OH)D], in blood. When there is an insufficient concentration of calcium at mineralisation sites in the growing skeleton, clinical and radiographic signs of rickets become apparent.

In humans, the clinical signs of rickets include skeletal deformity, susceptibility to fractures, listlessness, profound muscle weakness with hypotonia, and disturbed growth (Krane and Holick 1980). Characteristic radiological features are most prominent at epiphyseal growth plates. Physes are increased in thickness, metaphyseal borders are hazy due to decreased calcification of the hypertrophic zone, the calcification border becomes ragged and cup-shaped, the trabecular pattern of diaphyses may be thinned and bone shafts may be bowed (Krane and Holick 1980). Changes are most prominent at sites of maximum bone growth, so in neonates the skull and ribs are most affected, whereas in older children the distal end of the ulna, radius and femur are involved most severely.

Rickets was once a common nutritional disease of people, its diagnosis being straightforward based on characteristic clinical signs and radiological findings. No doubt rickets was also commonly seen in dogs and cats fed similar foods and kept under similar circumstances to affected human patients. Ashmount (1903) described rickets as 'a constitutional disease of puppyhood, characterised by general debility, chiefly in the bones and cartilages, but also in the muscles and other anatomical structures, causing imperfect development of the bones and consequent deformities'.The disease is now so rare, however, that few clinical descriptions of naturally affected dogs and cats exist,

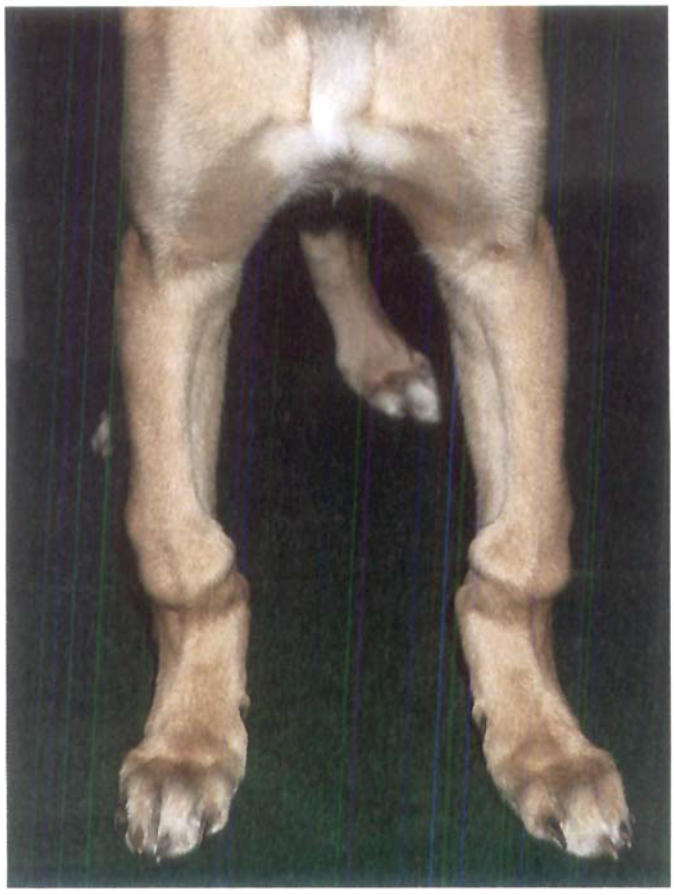

FIG 1. Thoracic limbs of a 14-week-old racing greyhound pup with rickets on the day of admission. Note the lateral bowing of the antebrachii, and the focal swelling of the radii and ulnae immediately above the carpi

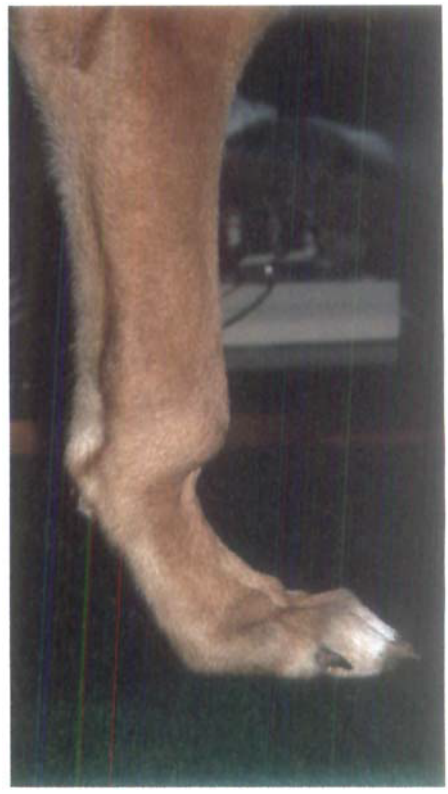

Fig 2. Lateral aspect of the thoracic limb of the pup in Fig 1. Note the hyperextended stance, and the focal bony swelling on the radius immediately proximal to the carpus

except for brief accounts in older reviews (Campbell 1964, Bennett 1976) and some textbooks (Watson 1990, Hazewinkel 1993, Johnson and others 1995).

Detailed contemporary reports of naturally occurring cases are lacking, with the exception of a radiological 'What is your diagnosis?' (Bruyere 1975), a brief abstract from a radiology meeting (Lavelle 1988) and a case study concerning a dog with a suspected inborn error of vitamin D metabolism (Johnson and others 1988). In only one case was the clinical and radiographic diagnosis of rickets confirmed by 25(OH)D determination (Hazewinkel 1993). Additional information can be gleaned from reports of rickets in foxes (Gorham and others 1970, Conlogue and others 1979) and laboratory studies in which the disease was induced experimentally (Campbell 1964, Campbell and Douglas 1965, Hazewinkel 1989).

There are two probable reasons for the paucity of veterinary reports. First, the widespread use of commercially formulated food has made nutritional bone disease much less common. Secondly, the most common inappropriate diet fed to growing pups consists exclusively of fresh meat and, or, offal, which typically results in nutritional secondary hyperparathyroidism (NSH) rather than rickets (Watson 1990).

The present report concerns a litter of greyhound pups in which a diagnosis of rickets was made based on characteristic clinical and radiological findings, and confirmed by demonstration of low concentrations of 25(OH)D in stored serum samples.

CASE HISTORIES

Physical findings

Six 14-week-old racing greyhound pups (four male, two female) were presented at the beginning of winter for investigation of skeletal abnormalities and locomotor impairment. Two remaining littermates were considered normal by the owner, although they were not examined. All the pups examined had similar abnormalities, although the severity of changes varied. The pups were unwell, weak and lame. Several had diarrhoea. Two were barely able to walk, and were so weak that they failed to reposition their legs in response to proprioceptive position testing. The antebrachii were bowed laterally, and the carpi and tarsi were hyperextended such that the pup's stance was palmargrade and plantigrade, respectively (Figs 1 and 2). Focal bony swellings that were neither hot nor painful on palpation were present proximal to the carpi and tarsi, and the costochondral junctions were of increased prominence (Figs 1 and 2).

The dam was also presented for examination, and was clinically normal.

Radiological findings

Radiographs taken of the distal thoracic and pelvic limbs of the pups showed similar findings in all cases although there was some variation in the extent, but not the nature, of the alterations. There was generalised osteopenia, with decreased radiodensity of cortical and cancellous bone. Growth plates were thickened markedly, and sometimes irregularly in both axial (longitudinal) and radial (transverse) directions, with cupping of the adjacent metaphyses (Fig 3). The enlarged physes evident radiographically corresponded to the focal bony swellings proximal to the carpi and tarsi.

The distal ulnar growth plate was most consistently and severely affected. Similar changes were evident in the distal radius and tibia, although in some instances the changes were not uniform across the full width of the physis, resulting in isolated

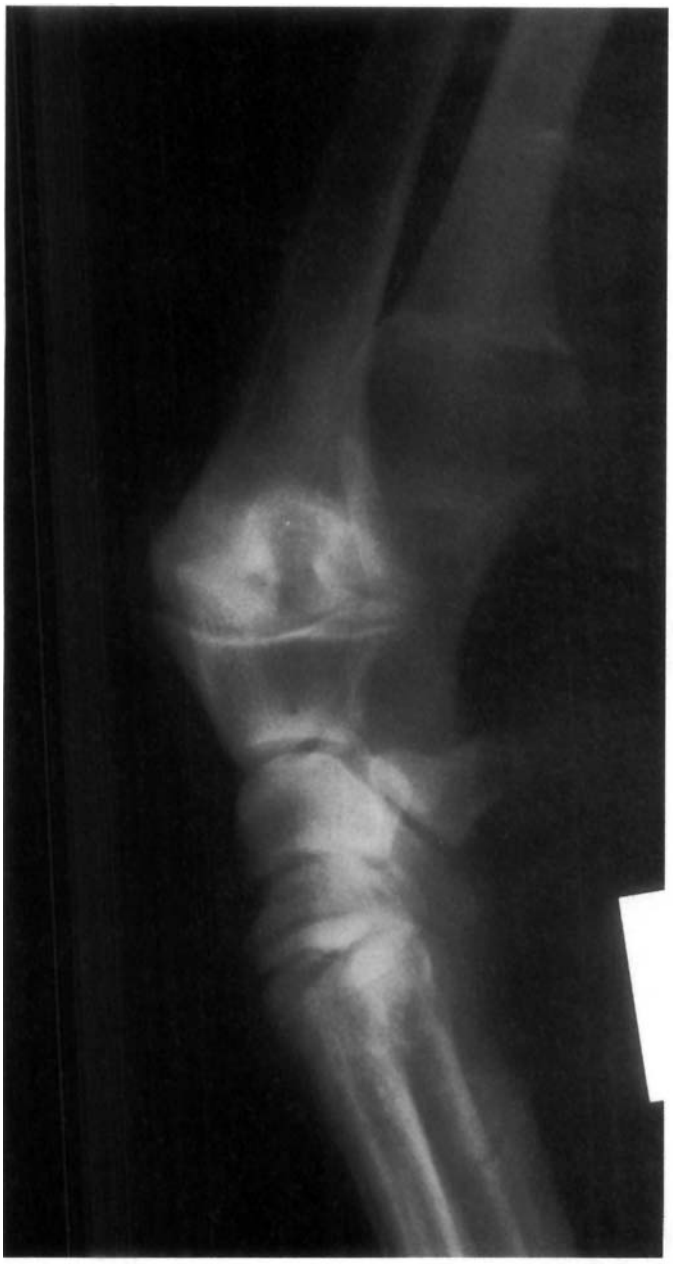

Fig 3. Lateral radiograph of the distal antebrachium in a greyhound pup with rickets. There is a generalised decrease in the radiodensity of bones, especially in the epiphyses and metaphyses. The distal growth plates of the radius and ulna are widened, this being especially prominent in the case of the ulna physis. An unmineralised 'peninsula' of cartilage emanates from the distal radial growth plate. Radial widening of growth plates has resulted in focal cartilaginous swellings and mushroomed metaphyses

'peninsulas' and 'islands' of unmineralised cartilage extending into the metaphysis (Fig 3). These radiological changes reflected on-going failure of mineralisation of cartilaginous matrix laid down at growth plates.

Radiographs of the corresponding regions of the litter's dam were unremarkable.

Dietary and environmental history

The bitch and pups had been housed in outdoor runs. Despite repeated and detailed questioning, it was not possible to obtain a consistent dietary history from the owner. The pups had been weaned between the ages of four and six weeks, in accordance with local custom in the greyhound industry. They were fed four times daily: the constituents of the diet included porridge, milk, pasta, minced beef, vegetables and an inexpensive generic kibble formulated for adult dogs made from wheatmeal and meatmeal derived from beef and, or, mutton. This was supplemented with two teaspoons of calcium carbonate powder divided among the daily rations provided for the whole litter.

Concentrations of 25(OH)D in affected pups and normal dogs

Method

Sera were collected from the six affected pups on the day of admission, and stored at −20°C. The levels of 25(OH)D were determined by a competitive protein binding assay (Mason and Posen 1977). Concentrations below 8 nmol/litre could not be measured accurately, and were thus reported as less than 8 nmol/litre.

Adequate quantities of serum were obtained for individual 25(OH)D determinations for four pups. In the two remaining pups, there was an inadequate sample volume so the sera were pooled prior to assay. Serum samples were also collected from two of the pups three weeks after admission, following therapy. Sera collected from 39 normal dogs, including 25 racing greyhounds, were assayed to determine a canine reference range for this method.

If adequate sample volume was available after assay of 25(OH)D, concentrations of total calcium and inorganic phosphate were determined using a commercial wet chemistry analyser (Cobas Mira).

Findings

The concentration of 25(OH)D in serum samples taken from 39 normal adult dogs throughout the year ranged from 7 to 91 nmol/litre, the 95 per cent confidence interval being 37 to 49 nmol/litre. For the subgroup of 25 adult racing greyhounds, 25(OH)D concentrations ranged from 15 to 91 nmol/litre, the 95 per cent confidence interval being 41 to 57 nmol/litre.

In the four pups for which a sufficient volume of serum was obtained to determine 25(OH)D, the concentrations were 24, 9, 15 and less than 8 nmol/litre, respectively. The pooled sample of serum from the two remaining pups had a 25(OH)D concentration of less than 8 nmol/litre. Thus the 25(OH)D concentrations in all pups were below the reference range.

In two cases only was sufficient serum left for measurement of total calcium and inorganic phosphate concentrations. In one pup, the calcium concentration was 0·4 mmol/litre (adult reference range 2·1 to 2·9) and the phosphate concentration was 2·1 mmol/litre (adult reference range 0·8 to 1·6). In the second pup, the calcium concentration was 2·8 mmol/litre and the phosphate concentration was 2·8 mmol/litre.

Treatment

The pups were treated by feeding a nutritionally complete commercial food formulated for growing pups (Eukanuba Puppy Food; Iams) three to four times a day, and housing outdoors in an open yard for several hours daily. The diet contained 1·3 per cent calcium, 1·0 per cent phosphorus and 1860 IU vitamin D/kg of food (414 IU/1000 kcal metabolisable energy). There was a prompt and dramatic improvement in the overall condition of the pups, which had ravenous appetites despite their poor constitutional status. Muscle strength improved rapidly over a few days, as reflected by increased desire for and tolerance of exercise, and resolution of distal limb hyperextension.

Within two weeks of starting the new diet, bowed limbs began to straighten, physeal swellings of the distal limbs became less evident as the pups grew skeletally and, in the majority of pups, lameness resolved. In two pups, intermittent shifting lameness persisted for many weeks, and one of these later developed 'greyhound polyarthritis' (Huxtable and Davis 1976). Following dietary correction, limb growth was commensurate with growth of the rest of the skeleton.

Radiological improvement was evident at two weeks although, qualitatively, it lagged behind the improvement in the pups' physical status. The first change evident was mineralisation of the widened cartilaginous growth plate, commencing at the portion of the physis immediately adjacent to the metaphysis. In most pups, the entire widened growth plate became mineralised and incorporated into growing metaphyseal and diaphyseal bone. In some individuals, however, portions of unmineralised growth plate persisted as retained cartilaginous cores or islands. Concurrently, there was an overall increase in the mineralisation of the appendicular skeleton, with increased radiodensity of cortical and cancellous bone. In the two most severely affected pups, which were 'donated' to the hospital and therefore could be followed over several months, the mushroom-like metaphyseal swellings became slowly but completely incorporated into a remodelled metaphyseal-diaphyseal region. In one pup there was some retardation in growth of the distal ulnar growth plates bilaterally, presumably because of the retained cartilage cores observed radiographically. This resulted in temporary constraint in the growth of the radius and some persisting deformity.

Serum samples collected from the two most severely affected pups three weeks after admission demonstrated increases in the 25(OH)D concentration from less than 8 to 48, and from 15 to 40 nmol/litre, respectively.

Further history

According to the owner, this was the bitch's fourth litter. The first litter comprised one normal male dog which grew to 34 kg. The second litter consisted of two pups afflicted with signs identical to the litter of this report. Pups from the third litter did not have signs suggestive of rickets, and included two bitches which went on to race with moderate success.

DISCUSSION

This litter of pups undoubtedly had rickets. Characteristic clinical signs were present, including lameness, disinclination to walk, bony swellings proximal to the carpi and tarsi, prominence of costochondral junctions, and bowing of limbs (Watson 1990). The physical appearance of the pups (Figs 1 and 2) was remarkably similar to that reported by Hazewinkel (1989, 1993) and, taken together with typical radiological changes, such physical findings are likely to be pathognomonic for canine rickets.

As in children with rickets, muscle weakness was a prominent feature in these pups and, coupled with loss of ligamentous support, gave rise to hyperextension of the distal limbs. Characteristic radiological changes were present also, with marked widening of the growth plates in axial and radial directions resulting in mushroomed metaphyses (Bennett 1976, Johnson and others 1988, Watson 1990). These features reflect accumulation of cartilage produced at the normal rate, but not mineralised. This change was most evident in the distal ulnar growth plate, presumably because endochondral ossification occurs more rapidly there compared with other growth plates as a result of its disproportionate contribution to the elongation of the ulna.

There was also a generalised decrease in the radiodensity of cortical and cancellous bone. Although similar changes have been reported in association with certain types of chondrodystrophy (Watson 1990, Johnson and others 1995), limb length in the rachitic pups was proportional to body size.

Concentrations of 25(OH)D were less than the 95 per cent confidence interval for adult dogs (and adult racing greyhounds) in all six pups, and markedly reduced in at least three. 25(OH)D represents the storage form of vitamin D compounds, and such markedly reduced levels indicate chronic vitamin D deficiency.

All clinical signs resolved promptly and completely following dietary modification using food containing approximately three times the Association of American Feed Control Officials' recommended vitamin D content (500 IU/kg of food; 143 IU/1000 kcal metabolisable energy) and a calcium to phosphorus ratio (1·3:1) appropriate for growth. Furthermore, 25(OH)D concentrations were normal after three weeks on this diet and regular access to exercise in a sunny outdoor run.

The question arises as to why these pups developed rickets, rather than the much more commonly observed condition, NSH. In rickets there is failure of mineralisation of newly formed osteoid, while in NSH normal bone is formed at the physis, but osteopenia occurs because of excessive bone resorption elsewhere (Bennett 1976, Watson 1990, Johnson and others 1995). In both conditions, circulating concentrations of parathyroid hormone are elevated markedly in an

attempt to maintain ionised calcium concentrations in plasma and interstitial fluid compatible with life. Neither rickets nor NSH will occur if the absolute and relative quantities of calcium and inorganic phosphate in the diet are adequate irrespective of its vitamin D content (Campbell 1964, Kealy and others 1991, Fraser 1995).

In Australia, the accepted dogma has been that pups do not develop rickets because, even in winter, there is sufficient sunlight for vitamin D production in the skin to provide for bodily needs. However, recent work has questioned the ability of the skin of dogs (and cats) to synthesise vitamin D (Hazewinkel 1989, How and others 1994, 1995); in any case, ultraviolet B exposure in the Australian winter may be insufficient to permit synthesis of adequate amounts of vitamin D, especially in the face of increased demand, even in those species so capable (D. R. Fraser, personal communication). Consequently, the most likely cause of rickets in the pups was a diet deficient in both bioavailable calcium and vitamin D (Watson 1990).

The pups' initial diet was unquestionably low in high quality protein, calcium and vitamin D, although the extent of these derangements would be critically dependent on the composition and amount of the generic biscuit given to the pups. Despite requests to the manufacturer and consultation with industry specialists (J. Kohnke, personal communication), we have been unable to determine the calcium, phosphorus, phytate and vitamin D content of this kibble. However, given its low cost and small market share, it seems unlikely that it was supplemented with vitamin D.

Furthermore, due to the phytate content of the cereal on which it is based, it is possible that the kibble was deficient in available calcium, because phytates bind dietary calcium thereby preventing its absorption from the gut. The generous contributions of milk and porridge to the diet may also have contributed to the development of rickets, for milk is virtually devoid of vitamin D (Hollis and others 1981), while porridge may also contain phytates (Mellanby 1949). Lastly, diarrhoea, whatever its cause, may have resulted in reduced efficiency of absorption of calcium from the gut.

Because milk has a very low concentration of vitamin D (Hollis and others 1981), newborn pups depend on stored vitamin D, presumably obtained across the placenta before birth, to meet requirements in early life (Clements and Fraser 1988, Fraser 1995). A low dietary intake of calcium and the resulting secondary hyperparathyroidism enhances the rate of loss of 25(OH)D from the circulation (Clements and others 1987a, b), so that if the supply of vitamin D is limited, deficiency develops. Vitamin D deficiency prevents the adaptive increase in the absorptive capacity of the gut for calcium when dietary calcium supply is low and physiological requirements (for growth) are increased. This is presumably how the clinical syndrome of rickets develops.

However, most pups fed generous quantities of fresh meat or meat by-products without adequate bone or calcium supplementation develop NSH rather than rickets (Campbell 1964, Campbell and Douglas 1965, Bennett 1976, Watson 1990). It could be that there is just enough blood and fat, and thus vitamin D analogues, in these animal tissues to prevent the development of rickets, but the relative and absolute calcium deficiency and phosphorus excess result in secondary hyperparathyroidism. We speculate that there may have been insufficient fresh meat and fat in the diet of the greyhound pups of the present report to provide this minimal amount of vitamin D required to prevent the development of rickets. Because the serum concentrations of 25(OH)D in mammalian offspring at birth are closely related to that of their dams (Goff and others 1984), low maternal vitamin D status in the bitch may have further predisposed the pups to rickets (Fraser 1995).

Greyhounds may be at increased risk of developing rickets in comparison with other breeds, either for genetic reasons and, or, because of the eclectic feeding practices which pervade the greyhound industry. The rapid skeletal growth of which this breed is capable may also predispose to the development of rickets, by analogy with the human situation where rachitic changes are most obvious in children who grow the fastest.

Lavelle (1988) briefly reported a litter of 10 10-week-old greyhound pups with rickets, three of which probably had symptomatic hypocalcaemia. A litter of 12-week-old greyhound pups with typical rachitic lesions evident radiographically was examined at the University of Queensland Veterinary Teaching Hospital; this litter had been fed a mixture of bread and meat, and was successfully treated by dietary correction and calcium supplementation, although some pups had residual growth plate damage (R.A. Read and G. Robins, personal communication). Another litter of greyhound pups with symptomatology and radiographs typical of rickets had been seen previously in our clinic; however, the detailed case notes could not be retrieved (P. E. Davis and K. A. Johnson, unpublished data).

Further work is required to determine whether vitamin D metabolism and calcium requirements in greyhounds are different from other dogs, and whether canine skin is indeed incapable of synthesis of vitamin D, as has been suggested (Hazewinkel 1989, How and others 1994, 1995).

Obviously the easiest way to prevent the development of nutritional bone disease in young dogs is by feeding a nutritionally complete food properly formulated for growth. However, where industry practice has resulted in the perpetuation of a plethora of home-made diets, it may be prudent to suggest routine supplementation of greyhound puppy diets with generous amounts of calcium carbonate and, or, raw, meaty bones for, even in the absence of vitamin D, rickets is unlikely to occur if the diet contains adequate calcium in relation to its phosphorus content (Campbell and Douglas 1965, Kealy and others 1991, Fraser 1995).

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