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THE ROLE OF NUTRITION IN CANINE HIP DYSPLASIA

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Canine hip dysplasia (CHD) has been[48, 60] and continues to be one of the most common skeletal diseases seen in the practice of veterinary medicine. A review of medical records from 1985 through 1990 at a major university veterinary teaching hospital revealed that CHD and degenerative joint disease of the coxofemoral joint(s), account for 29% of the orthopedic cases.[52] The large and giant breeds are at greatest risk and have an increased incidence compared to the general population.[9, 60] CHD is frequently associated with degenerative joint disease in joints other than the hip,[44] raising questions regarding systemic factors in the disease process and the role of nutrition. Nutrition, particularly excesses of energy, protein, specific vitamins, and minerals affect bone development in a number of ways in many different species. Most of these affects are detrimental to normal skeletal growth.[31] Similarly, nutrition has been incriminated specifically in the development of CHD, a developmental disorder of the coxofemoral joint.[3, 29, 35, 36, 51, 53, 60]

GROWTH RATE MANIPULATIONS

A number of studies suggest an increased incidence of CHD in the rapidly growing large and giant breeds.[9, 25, 35, 53] Both the frequency and severity of the condition can be mitigated by growth rate manipulations.[28, 35, 53] This has led to the belief that nutrition plays a key role in this disease process. Although supporting the clinical observation that rapid growth is associated with increased incidence of CHD in the large

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and giant breeds, most studies fail to establish the specific role of nutrition in the pathogenesis of the disease.[48, 60] Simple questions such as feed quantity, composition, and quality can be difficult if not impossible to extract from retrospective studies. These same questions are difficult to quantitate in prospective efforts. There is a lack of repeatable studies in which growth rate, feeding methods, or specific nutrients have been shown to influence the disease.

OVERFEEDING AND GROWTH RATE

"Overfeeding" for maximal growth rate has been shown to be incompatible with optimal skeletal characteristics in rats,[54] children,[14] poultry,[67] pigs,[50] cattle,[49] and horses.[68] In dogs, an early study emphasized the role of nutrition in the development of skeletal disease and demonstrated a relationship between growth, breed, and age.[23] Early findings of CHD, such as joint laxity and anatomic changes, were documented within 2 weeks of birth in other studies.[24, 26] Rapid weight gain in German Shepherds during the first 60 days after birth had been associated with CHD at a later age.[53] Further evidence supporting this influential time period was demonstrated in a study comparing cesarean section, hand-reared puppies with normal birth, bitch-fed puppies. The incidence of CHD was reduced only by the severe growth reduction induced by cesarean section and hand-rearing. Vaginally delivered, bitch-fed puppies that grew "optimally" or somewhat "suboptimally" had a higher incidence of CHD.[35] Furthermore, this and other studies emphasized the importance of the period from 3 to 8 months of age in the development of CHD,[28, 35] with the first 6 months generally felt to be the most critical.[24] Further substantiating these findings, the frequency and severity of CHD was shown to be influenced by weight gain in growing dogs sired by parents with CHD or by parents with a high incidence of CHD in their offspring.[28] Dogs with weight gain above the standard weight curve of the breed had a higher frequency of CHD as well as more severe CHD than dogs with weight gain below the standard curve. This study further pointed out that palpation of the hip was of little to no value in predicting abnormal versus normal development of hip joints unless due consideration was given to nutrition during growth. A better correlation occurred between hip status at 30 weeks of age and weight gain from 12 to 30 weeks of age than occurred between hip status at 30 weeks and palpation findings at 7 to 12 weeks of age.[28] Similar lack of reliability in the subjective evaluation of hip joint laxity in puppies for predicting either normal or dysplastic hip joints in the adult dog has been noted.[35]

DIAGNOSIS

Determining the presence or absence of CHD is somewhat limited by diagnostic methodologies. Palpation in the very young is not an

adequate predictor of future disease,[28, 35] and significant cellular changes in synovium, cartilage and other structures around the joint can take place prior to radiographic changes.[15, 34, 36, 44] Improved diagnostic techniques are needed to assist in pinpointing causative mechanisms and factors. Although there are many points of difference, all of the previously mentioned studies support the early, critical time period in the development of CHD.

FEED CONSUMPTION

In an effort to study the influence of feed consumption on the incidence of skeletal disease, Hedhammer et al[23] performed an experiment comparing ad libitum versus restricted dietary intake in Great Dane puppies. The study was criticized for several factors: use of a breed expected to show an increased incidence of skeletal disease; the dogs were artificially reared in confinement with little or no exercise; their clinical behavior was dissimilar from naturally occurring cases of skeletal disease; and even though the diets were described as ad libitum versus restricted, both diets were in excess of the National Research Council's (NRC) 1974 recommendations in metabolizable energy, calcium, phosphorous, and protein.[43] Consequently, both diets represented "overnutrition." However, the resultant skeletal pathology markedly increased awareness of the critical role nutrition plays in the disease process. A similar study to evaluate ad libitum versus restricted intake was performed by Lavelle,[31] taking into account some of the variables unaccounted for in the Hedhammer paper. This study again used Great Dane puppies. Attempts were made to pair littermates, the diet was a commercially available growth diet, and the dogs were housed to encourage exercise. The restricted intake group received 60% of the paired littermates' ad libitum diet intake. The unrestricted group showed consistently more advanced skeletal development throughout the study; however, ultimate long bone length was similar in both groups after 30 weeks. The incidence of skeletal disease as seen in the study by Hedhammer et al was not reproduced in the Lavelle study. In both studies, the unrestricted dogs overate relative to the NRC standards (1974). This is further emphasized when it is noted the consumption of the "restricted" dogs in the Hedhammer group (fed ⅔ of the ad libitum group intake), relative to NRC, was as high as the Lavelle ad libitum dogs. The difference in activity levels may have resulted in significantly more energy availability for growth, and subsequent bone pathology, in the Hedhammer study as compared to the more active Lavelle study dogs.[31] Ad libitum versus time-restricted intake (2–30 minute daily feeding periods) was also evaluated in Labrador Retriever puppies. The restricted group consumed less (17%) of the caloric dense commercially available growth diet, had comparable growth (within 1.1 kg of ad libitum group at 34 weeks of age), and had less osteodystrophic changes. It was clear that more rapid growth in

the weeks following weaning does not necessarily assure a larger dog at maturity.[1]

In one colony of rapidly growing Labrador Retrievers, the growth plates of the acetabula fused at 5 months as determined by conventional radiography. Closure of epiphyseal plates was delayed until 7 months of age in puppies growing at a restricted rate. It was reported that normal closure of these growth plates occurs at 6 months in puppies growing at conventional rates. It was speculated that early fusion in the acetabulum may result in future bone and cartilage disparities and predispose to dysplastic changes.[36] None of these studies completely answer concerns of overconsumption in large and giant breeds, but they do point out the need to evaluate husbandry methods and observe potential overnutrition.

NUTRIENTS

It is extremely difficult to moderate any one nutritional component within the diet (e.g., carbohydrate) and not impart an effect on the overall characteristics (e.g., energy density) of the diet. As a result of this complexity, very few specific nutrients have been identified as having direct influence on CHD. Excess intake of carbohydrates, protein, and specific vitamins and minerals have been incriminated with anatomic changes compatible with CHD.[23] Severe alterations in the protein to carbohydrate ratio can alter bone growth relative to body weight.[47, 65] The role of fat in CHD or skeletal disease has not been established.

Carbohydrates and Calories

Carbohydrates have minimal to no influence on the production or prevention of CHD except when associated with reduction of overall food consumption. In a study using female Beagles, no statistically significant effect was seen on the incidence of CHD whether carbohydrate was included or excluded from an otherwise nutritionally adequate diet.[65] Radiographic evaluation in this study was performed at 10 months of age. This potentially may underestimate the incidence of CHD in this population. Similarly, variation in Beagle colony incidence of CHD[37, 41] may affect the statistical significance of presence or absence of the disease. Another study evaluated hip laxity prior to 12 weeks of age in purebred German Shepherd, Golden Retriever, and Labrador Retriever puppies. This study demonstrated that puppies without laxity in the hips at less than 12 weeks of age could develop CHD if kept on high caloric intake during growth. Conversely, puppies with hip joint laxity at less than 12 weeks of age could develop normal hip joints if kept on low caloric intake during growth.[28] Some studies would dispute that the diet fed is a significant influence on hip joint laxity.[65] It is

possible that excessive growth rate and body weight on a high calorie diet, regardless of calorie source, would stress the hip, resulting in potential for increased laxity around the joint and subsequent dysplastic changes.

Protein

Investigators have attempted to produce normal hip growth and reduce CHD in mixed-breed puppies by feeding a high- or all-meat diet.[51] Subsequent studies in purebred, known dysplastic breeds (German Shepherd, Golden Retriever, and Labrador Retriever)[28] and in female Beagles[65] have not shown similar results. Again, similar concerns can be raised in the Beagle study concerning age of radiographic evaluation (10 months), appropriateness of the Beagle as a research model for CHD, and Beagle colony variation in incidence of CHD. It can be concluded that high protein intake is less important for development of normal hip joints than previous studies might indicate. Current thinking is that as long as the amino acid and fatty acid contents of a diet meet growth requirements and the diet is acceptable, the proportion of energy supplied by carbohydrate, fat, and protein becomes less important as a consideration in the growing dog.[33] However, as we become more aware of dietary amino acid and endocrine interactions, such general statements may not hold true.

Vitamin C

L-ascorbic acid (vitamin C) plays an integral role in many of the body's homeostatic mechanisms. Probably its most important role is in hydroxylation of proline and lysine during biosynthesis of collagen, the most important structural protein in the body. Type I collagen is the most widely distributed in connective tissue, primarily in bone and ligaments. In 1976, an article[3] reported that megadoses of ascorbate fed to the bitch during pregnancy and provided to the offspring until young adulthood eliminated CHD. Ascorbate therapy was based on its major biochemical functions of being an antistressor, detoxicant, and necessary metabolite for maintaining biochemical homeostasis in the body, especially as it relates to collagen metabolism in and around joints. Eight litters of German Shepherd puppies from known dysplastic parents or parents that had produced dysplastic offspring were used for the study. The bitch received 2 to 4 g sodium ascorbate crystals/day during pregnancy. The puppies received calcium and vitamin supplements from birth to 3 weeks, 500 mg/day ascorbate from 3 weeks to 4 months, and 1 to 2g ascorbate/day from 4 months up to 2 years. No CHD was reported in any of the offspring. No radiographs were taken to document presence or absence of dysplastic changes, however, and no long term follow-up studies have been published. Neither this nor

any other study has verified ascorbic acid levels, much less deficiencies, in hip dysplastic dogs. One study measured vitamin C concentrations in the blood in a series of Labrador Retrievers.[59] They found higher (1.22 ± 0.05 mg/dL) levels of vitamin C concentrations in younger dogs than in adults (0.89 ± 0.03 mg/dL). If CHD were to be associated with a low vitamin C level, lower concentrations would be more likely in the younger animals undergoing the stresses of growth. Unfortunately, no mention was made of the presence or absence of CHD. No other studies have demonstrated a positive effect of oral supplementation of vitamin C in preventing CHD in growing dogs genetically at risk for the disease. Vitamin C supplementation in pigs has produced elevations in plasma levels; however, articular concentrations of hydroxyproline were unchanged.[42] Similar studies in dogs demonstrated transient elevation of plasma vitamin C concentrations with long-term supplementation not increasing concentrations much above normal.[11, 59]

Vitamin C has been studied as a possible contributor to osteochondrosis. Osteochondrosis of the acetabular rim has been proposed to lead to a shallow acetabulum and subsequent CHD.[45] Most of the studies evaluating the effect of vitamin C on osteochondrosis have used the pig as a research model and agree that vitamin C supplementation has no effect on the incidence of osteochondrosis.[42, 57, 66] The relationship between vitamin C, osteochondrosis, joint laxity, and CHD in the dog is as yet unproven.[4] If a decrease in vitamin C levels could be documented to produce joint laxity, it would be expected that other joints beside the hips would demonstrate laxity. There are reports relating CHD with degenerative disease in multiple joints.[44] However, joint laxity other than in the hips was not noted.

Excess vitamin C supplementation generally is considered to have little or no effect on the skeleton. However, there is experimental evidence in chickens to support the role of vitamin C in bone mineralization and resorption.[61, 62, 63, 64] Excess vitamin C has been shown to perpetuate hypercalcemia,[55] which may induce hypercalcitoninism, delaying cartilage maturation, reducing bone resorption, and subsequently affecting normal bone remodelling. A recent study[5] demonstrated a positive effect on the symptoms caused by chronic inflammation in the dog's various joints when treated with vitamin C (polyascorbic).

Calcium

Plasma calcium concentration is tightly regulated by the body and varies between 2.2 to 3.0 mmol/L in adult dogs[56] and 2.4 to 2.9 mmol/L in the young, growing dog.[18] This regulation is needed for the many calcium-dependent biologic processes such as muscle contraction, hormonal release, and blood coagulation. The three specific hormonal regulators of plasma calcium concentration (calciotropic hormones) are parathyroid hormone (PTH), calcitonin (CT), and 1,25 dihydroxycholecalciferol (1,25 vit D_3). Their release is influenced by plasma calcium

concentration, which they modify through action on their respective target organs. The three systems most concerned with calcium regulation are the intestines, kidneys, and bone.

Ingested calcium crosses the intestinal epithelium by active (carrier mediated) or passive transport.[2] The principle hormonal regulator is 1,25 vit D_3. It is synthesized in the mitochondria of the renal tubular cells in response to plasma calcium concentration.[17] It stimulates synthesis of transport and enzyme proteins, which increase calcium and phosphorous passage through the intestinal wall.[27]

The kidney plays a minor role in the overall scheme of calcium metabolism.[38] Under the influence of 1,25 vit D_3, it decreases the excretion of calcium and phosphorous.[27] Exposed to increased circulating PTH, the kidney decreases calcium excretion and increases the excretion of phosphorous.[58]

Bone is closely linked to serum calcium regulation. In the adult dog, under balanced conditions, accretion (deposition into bone) and resorption (loss from bone) values are 0.1 to 0.2 mmol/kg body weight/day.[16, 40] In the young, growing dog, both values are increased at least 100 times.[19, 22] Low calcium concentrations stimulate PTH synthesis and secretion, whereas high plasma calcium concentrations result in fragmentation of PTH into biologically inactive components.[39] PTH action on bone shrinks the osteoblasts, allowing the brush border of the osteoclast to contact the bone–matrix surface[6] with resultant dissociation of mineral from the matrix, increasing calcium availability to the plasma circulation. Calcitonin (CT) a hormone produced in C-cells located in the thyroid and internal parathyroid glands[7] and responding to increased intravenous or oral calcium load,[19] decreases bone resorption by decreasing the size of the brush border, and the number and motility of the osteoclasts.[6, 10] CT does not affect the kidney or intestine. However, it may influence the satiety centers and result in decreased food intake.[14, 32] 1,25 vit D_3 can act on bone to increase mineralization as well as increase resorption.[27, 46]

Chronic, high calcium intake in large breed dogs has been associated with hypercalcemia, concomitant hypophosphatemia, rise in serum alkaline phosphatase, retarded bone maturation, higher percentage of total bone volume, retarded bone remodeling, decrease in bone resorption cells, and retarded maturation of cartilage with disturbances in endochondral ossification (articular and epiphyseal).[18] Clinical disease associated with these changes are osteochondrosis, retained cartilage cones, radius curvus syndrome, and stunted growth.[18, 23] Elegant studies performed by Hazewinkel conclude that these young dogs do not have a mechanism to protect themselves against excessive calcium intake.[20] Calcium excess, through the influence of the calciotropic hormones on target organs, is routed primarily to bone. Coupled with relatively little absorption from bone, severe pathologic changes occur in the young, growing skeleton that is unable to respond by normal remodelling and endochondral ossification. Refinement on earlier studies has helped define calcium as a major causative or contributing factor in the

pathogenesis of skeletal disease in the growing giant breed dog.[18, 19] Further studies implicate the level of calcium excess, rather than the imbalance in the calcium: phosphorous ratio, as the incriminating factor influencing skeletal disease.[21] Recent investigations produced osteochondrosis in the fetuses of ewes fed high levels of dietary calcium.[8]

The role of calcium in skeletal disease is becoming well-substantiated. Owing to their rapid and profound growth, giant breed dogs become sentinels for nutritionally influenced skeletal disease such as is seen with excesses in dietary calcium. Although exaggerated in giant breeds, similar changes may be slower to surface and are not as easily identified in the smaller breeds. Regardless, dietary calcium is a highly influential nutrient for skeletal development.

Electrolyte Balance

Recent investigations have proposed the role of dietary electrolytes in CHD.[30] This study assumed joint laxity is a major predisposing factor in CHD, and reducing this laxity in the early growth periods will minimize the potential severity of CHD. As stated previously, however, hip joint laxity in puppies may not be a significant indicator in predicting eventual abnormal development of the hip joint.[28] The study[30] indicates that by controlling the balance of dietary electrolytes (Na^+, K^+ and Cl^-) the severity of hip joint laxity can be reduced in dogs with a high incidence of CHD. Based on the formula:

dietary electrolyte balance (DEB) (meq/100 g) = sodium (meq/100 g) + potassium (meq/100 g) − chloride (meq/100 g)

if the combination of dietary electrolytes was kept below 20 meq/100 g (preferably below 10 meq/100 g) in a nutritionally balanced dog food composition, a reduction in the severity of hip joint laxity was noted in dogs fed the diet during their formative years. Hip joint laxity was determined using the Norberg hip score computed from radiographs.[13] Significant correlation between radiographic findings (e.g., Norberg hip scores) and progression of hip dysplasia is not proven. All of the dogs in the dietary electrolyte studies had some degree of CHD when classified by the Norberg score. In one of the studies,[30] a DEB less than 10 meq/100 g in English Pointers fed from 6 to 30 weeks of age indicated a trend towards reduced Norberg hip scores compared to diets containing a higher DEB. Similar trends were seen in a group of St. Bernards during the same growth phase when low DEB diets were compared to a commercial diet with a DEB of 27 meq/100 g. A third study evaluated the effect of DEB on a group of St. Bernards fed from 8 to 10 months of age. The lower DEB diets again showed trends toward less of a drop in the Norberg hip score over the 2-month feeding trial. This was interpreted as a decrease in worsening of hip joint laxity. Other

investigators feel the degree of joint laxity is not significantly influenced by the diet fed.[65] These studies incriminating DEB with joint laxity did not prove a mechanism of action. There was speculation, however, that this electrolyte balance within the diet may, by some mechanism, influence the formation of hip synovial fluid with subsequent minimization of joint laxity during critical stages of growth.

CONCLUSIONS

The role of nutrition in CHD is as multifactoral as the disease itself. Rate of growth, feeding methods, feed consumption, and specific nutrients as well as the electrolyte balance within the diet have all been shown to influence CHD. The large and giant breeds are the most susceptible to skeletal disease. This apparent increased sensitivity makes these breeds somewhat of a sentinel to monitor dietary influences. We can assume similar processes are occurring in the smaller breeds, but they lack the tremendous growth rates seen in the large and giant breeds that probably magnify their presence. Maximizing the growth rate in young, growing puppies does not correlate to maximal adult size. It does, however, increase the risk of skeletal disease. The growth phase of 3 to 8 months, and possibly the phases prior to weaning, are integral to ultimate skeletal integrity. Dietary deficiencies are of minimal concern in this age of commercial diets specifically prepared for young, growing dogs. However, there is potential for harm resulting from oversupplementation with energy, vitamins, minerals, and possibly acid/base imbalance. The giant breeds may be limited in their ability to cope with excesses of minerals such as calcium, and the result is abnormal bone remodelling and skeletal disorders such as CHD. We leave a great many unanswered questions as to the role of nutrition in CHD. Known nutritional risk factors such as growth rate and oversupplementation can be addressed through good husbandry practice. Continued investigation, especially from a dietary formulation perspective, needs to be performed in order to identify and control the various nutritional factors in the diet that influence CHD.

References

1. Alexander JE, Wood LLH: Comparative Growth Study. Dayton, OH, Iams Company, Update No. 1003
2. Allen LH: Calcium bioavailability and absorption: A review. Am J Clin Nutr 35:783–808, 1982
3. Belfield WO: Chronic subclinical scurvy and canine hip dysplasia. Vet Med/Small Anim Clin 1399–1403, 1976
4. Bennett D: Hip dysplasia and ascorbate therapy: Fact or fancy? Semin Vet Med Surg (Small Anim) 2:2;152–157, 1987
5. Berge GE: Polyascorbate (C-Flex®), an interesting alternative by problems in the support and movement apparatus in dogs. Norwegian Vet J 102:582–583, 1990
6. Chambers TJ, Moore A: The sensitivity of isolated osteoclasts to morphological transformation by calcitonin. J Clin Endocrinol Metab 57:819–24, 1983

7. Copp DH, Cockcroft DW, Kueh Y: Calcitonin from ultimobranchial glands of dog, fishes and chickens. Science 158:924–926, 1967
8. Corbellini CN, Krook L, Nathanielsz PW, et al: Osteochondrosis in fetuses of ewes overfed calcium. Calcif Tissue Int 48:37–45, 1991
9. Corley EA, Hogan PM: Trends in hip dysplasia control: analysis of radiographs submitted to the Orthopedic Foundation for Animals, 1974 to 1984. J Am Vet Med Assoc 187:805–809, 1985
10. Cramer CF, Parkes CO, Copp DH: The effect of chicken and hog calcitonin on some parameters of Ca, P, and Mg metabolism in dogs. Can J Physiol Pharmacol 47:181–184, 1969
11. Cromwell GV, Hays VW, Overfield JR: Effect of dietary ascorbic acid on performance and plasma cholesterol levels of growing swine. J Anim Sci 31:63–66, 1970
12. Dluzniewska KA, Obtulowicz A, Koltek K: On the relationship between diet, rate of growth and skeletal deformities in school children (English summary). Folia Medica Craciviensia 7:115–126, 1965
13. Douglas SW, Williamson HD: Veterinary Radiological Interpretation. Philadelphia, Lea & Febiger, 1970, pp 109–111
14. Freed WJ, Perlow MJ, Wyatt RJ: Calcitonin: Inhibitory effect on eating in rats. Science 206:850–852, 1979
15. Greisen HA, Summers BA, Lust G: Ultrastructure of the articular cartilage and synovium in the early stages of degenerative joint disease in canine hip joints. Am J Vet Res 43:1963–1971, 1982
16. Goldman M: Skeletal mineralization. *In* Anderson AC (ed): The Beagle as an Experimental Dog. Ames, Iowa, Iowa State University Press, 1970, pp 216–225
17. Halloran BP, Hulter HN, Toto RD, et al: Regulation of the plasma concentration of 1,25 $(OH)_2D$ by parathyroid-hormone, calcium and phosphate. *In* Norman AW, Schaefer K, von Herrath D, et al (eds): Vitamin D, Chemical, Biochemical and Clinical Endocrinology of Calcium Metabolism. Berlin, HG de Gruyter, 1982, pp 467–469
18. Hazewinkel HAW, Goedegebuure SA, Poulos PW, et al: Influences of chronic calcium excess on the skeletal development of growing Great Danes. J Am Anim Hosp Assoc 21:377–391, 1885
19. Hazewinkel HAW: Influences of different calcium intakes on calcium metabolism and skeletal development in young Great Danes [Thesis] Utrecht, The Netherlands, Utrecht State University, 1985
20. Hazewinkel HAW: Calcium metabolism and skeletal development in dogs. *In* Burger IH, Rivers JPW (eds): Nutrition of the dog and cat. Waltham Symposium 7. Cambridge, Cambridge University Press, pp 293–302
21. Hazewinkel HAW, Van den Brom WE, Van'T Klooster AT, et al: Calcium metabolism in Great Dane dogs fed diets with various calcium and phosphorous levels. J Nutr (Suppl Waltham Symposium) 121:599, 1991
22. Hedhammer A, Krook L, Schrijver H, et al: Calcium balance in the dog. *In* Anderson RS (ed): Nutrition of the Dog and Cat. Oxford, Pergamon, 1980, pp 119–127
23. Hedhammer A, Wu FM, Krook L, et al: Overnutrition and skeletal disease: An experimental study in growing Great Dane dogs. Cornell Vet 64(suppl 5):11–160, 1974
24. Hedhammer A, Olsson SE, Andersson SA, et al: Canine hip dysplasia: study of heritability in 401 litters of German Shepherd dogs. J Am Vet Med Assoc 174:1012–1016, 1979
25. Hedhammer A: Nutrition as it relates to skeletal disease. *In* Proceedings of the Kal Kan Symposium, Columbus, OH, 1980, pp 41–44
26. Henricson B, Norberg I, Olsson S-E: On the etiology and pathogenesis of hip dysplasia: A comparative review. J Small Anim Pract 7:673–688, 1966
27. Kanis JA, Guillard-Cumming DF, Russell RGG: Comparative physiology and pharmacology of the metabolites and analogues of vitamin D. *In* Parson JA (ed): Endocrinology of Calcium Metabolism. New York, Raven, 1982, pp 321–362
28. Kasström H: Nutrition, weight gain and development of hip dysplasia. Acta Radiologica 334(suppl):135–179, 1975
29. Kealy RD, Lawler DF, Reutzel LF: Ralston Purina nutritional research on canine hip dysplasia. Industry Research Brochure, St. Louis, MO, 1985

30. Kealy RD, Lawler DF: Method for reducing the severity of hip joint laxity in dogs. United States Patent 4, 772, 476, Sept. 20, 1988
31. Lavelle RB: The effects of the overfeeding of a balanced complete commercial diet to a group of growing Great Danes. *In* Burger IH, Rivers JPW (eds): Nutrition of the Dog and Cat. Waltham Symposium 7. Cambridge, Cambridge University Press, 1989, pp 303–315
32. Levine BS, Morley JE: Reduction of feeding in rats by calcitonin. Brain Res 222:187–191, 1981
33. Lewis LD, Morris ML Jr, Hand MS: Dogs-feeding and care; diets for growth. *In* Small Animal Clinical Nutrition III. 1989, pp 3–13
34. Lust G, Beilman WT, Rendano VT: A relationship between degree of laxity and synovial fluid volume in coxofemoral joints of dogs predisposed for hip dysplasia. Am J Vet Res 41:55–60, 1980
35. Lust G, Geary JD, Sheffy BE: Development of hip dysplasia in dogs. Am J Vet Res 34:87–91, 1973
36. Lust G, Rendano VT, Summers BA: Canine hip dysplasia: Concepts and diagnosis. J Am Vet Med Assoc 187:638–640, 1985
37. Lust G, Roenigk WJ, Geary JC, et al: Clinical items: radiographic evaluation for evidence of hip dysplasia in three colonies of beagles. J Am Vet Med Assoc 166:497–499, 1975
38. Massry SG: Renal handling of calcium. *In* Bronner F, Coburn JW (eds): Disorders of Mineral Metabolism, vol 2. New York, Academic, 1982, pp 189–235
39. Mayer GP, Keaton JA, Hurst JG, et al: Effects of plasma calcium concentration on the relative proportion of hormone and carboxyl fragment in parathyroid venous blood. Endocrinology 104:1778–1784, 1979
40. Meyer H: Calcium and phosphorous requirement of the dog. Animal Nutrition, 6:31–54, 1978
41. Morgan JP: Hip dysplasia in the Beagle: A radiographic study. J Am Vet Med Assoc 164:496–498, 1974
42. Nakano T, Aherne FX, Thompson JR: Effect of dietary supplementation of vitamin C on pig performance and the incidence of osteochondrosis in elbow and stifle joints in young growing swine. Can J Anim Sci 63:421–428, 1983
43. National Research Council: Nutrient Requirements of Dogs. Washington DC, National Academy of Sciences, 1974
44. Olsewski JM, Lust G, Rendano VT, et al: Degenerative joint disease: multiple joint involvement in young and mature dogs. Am J Vet Res 44:1300–1308, 1983
45. Olsson S-E: Osteochondrosis—A Growing Problem to Dog Breeders. White Plains, NY, Progress, Gaines Dog Research Centre, 1976, pp 1–11
46. Ornoy A, Zusman J: Vitamin and cartilage, chapt. 8. *In* Hall BK (ed): Cartilage: Development, Differentiation and Growth, vol 2. New York, Academic, 1983, pp 297–326
47. Platt BS, Heard CRC, Steward RJC: Experimental protein-calorie deficiency. *In* Munro HN, Allison JB (eds): Mammalian Protein Metabolism. vol 2. New York, Academic, 1964, pp 445–521
48. Priester WA, Mulvihill JJ: Canine hip dysplasia: Relative risk by sex, size, and breed, and comparative aspects. J Am Vet Med Assoc 160:735–739, 1972
49. Reiland S, Stromberg B, Olsson S-E, et al: Osteochondrosis in growing bulls. Acta Radiologica 358(suppl):179–196, 1978
50. Reiland S: The effect of decreased growth rate on frequency and severity of osteochondrosis in pigs. An experimental investigation. Acta Radiologica 358(suppl):107–122, 1978
51. Resnick S: Effect of an all-meat diet and a high-carbohydrate diet on hip formation in dogs. Vet Med/Small Anim Clin 739–743, 1974
52. Richardson DC: Review of orthopedic case records. Raleigh, NC, North Carolina State University College of Veterinary Medicine, 1985–1990
53. Riser WH, Cohen D, Lindquist S, et al: Influence of early rapid growth and weight gain on hip dysplasia in the German Shepherd dog. J Am Vet Med Assoc 145:661–668, 1964
54. Saville PD, Lieber CS: Increases in skeletal calcium and femur thickness produced by undernutrition. J Nutr 99:141–144, 1969

55. Schalm OW: Veterinary Haemetology. London, Bailliere Tindall and Cassell, 1965
56. Schärer V: Die Bestimmung der Normalwerte von Calcium und Phosphor im Serum beim Hund, Bern (Switzerland), Hell & Co, 1970
57. Strittmater JE, Ellis DJ, Hogberg MG, et al: Effect of vitamin C (ascorbic acid) on degenerative arthritis (osteochondrosis) and growth of swine. Report of swine research. East Lansing, MI, Michigan State University Agricultural Experiment Station, 1977, pp 111–115
58. Sutton RAL, Wong NLM, Dirks JH: Effects of metabolic acidosis and alkalosis on sodium and calcium transport in the dog kidney. Kidney Int 15:520–533, 1976
59. Teare JA, Krook L, Kallfelz FA, et al: Ascorbic acid deficiency and hypertrophic osteodystrophy in the dog: A rebuttal. Cornell Vet 69:384–401, 1979
60. Teare JA, Hintz HF, Krock L: Rapid growth and skeletal disease in dogs. Petfood Industry, Jan/Feb: 12–15, 1981
61. Thornton PA, Brownrig D: Calcium utilisation and skeletal development in chicks as influenced by parenteral dietary ascorbic acid. J Nutr 75:351–360, 1961
62. Thornton PA, Omdahl JL: Further evidence of skeletal response to exogenous ascorbic acid. Proc Soc Exp Biol Med 132:618–621, 1969
63. Thornton PA: Bone salt mobilisation effected by ascorbic acid. Proc Soc Exp Biol Med 127:1096–1099, 1968
64. Thorton PA: Influence of exogenous ascorbic acid on calcium and phosphorus metabolism in the chick. J Nutr 100:1479–1486, 1970
65. Tvedten HW, Carrig CB, Flo GL, et al: Incidence of hip dysplasia in Beagle dogs fed different amounts of protein and carbohydrate. J Am Anim Hosp Assoc 13:595–598, 1977
66. Walker T: A study of bone development in the young pig with particular reference to calcium and phosphorus and leg weakness in boars [Thesis]. Aberdeen, Scotland, Aberdeen University
67. Wise DR, Jennings AR: Dyschondroplasia in domestic poultry. Vet Rec 91:285–286, 1972
68. Wyburn RS: A degenerative joint disease in the horse. NZ Vet J 25:321–322 & 335, 1977

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