Effects of diet restriction on life span and age-related changes in dogs

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Objective—To evaluate the effects of 25% diet restriction on life span of dogs and on markers of aging.

Design—Paired feeding study.

Animals—48 Labrador Retrievers.

Procedures—Dogs were paired, and 1 dog in each pair was fed 25% less food than its pair-mate from 8 weeks of age until death. Serum biochemical analyses were performed, body condition was scored, and body composition was measured annually until 12 years of age. Age at onset of chronic disease and median (age when 50% of the dogs were deceased) and maximum (age when 90% of the dogs were deceased) life spans were evaluated.

Results—Compared with control dogs, food-restricted dogs weighed less and had lower body fat content and lower serum triglycerides, triiodothyronine, insulin, and glucose concentrations. Median life span was significantly longer for dogs in which food was restricted. The onset of clinical signs of chronic disease generally was delayed for food-restricted dogs.

Conclusions and Clinical Relevance—Results suggest that 25% restriction in food intake increased median life span and delayed the onset of signs of chronic disease in these dogs. (*J Am Vet Med Assoc* 2002;220:1315–1320)

Diet restriction has been documented to have a positive effect on the life span of rodents and various invertebrate species.[1] In fact, research spanning more than 60 years has shown that diet restriction is the only nutritional intervention that consistently extends the life span of animals.[1,2] In previous studies, diet restriction increased median and maximum life span (ie, survival time of the longest-lived decile) of rodents, despite differences in species, strains, experimental designs, nutritional variables, environmental conditions, and predispositions for naturally occurring causes of death.[1] To our knowledge, the effect of diet restriction on life span of larger mammals has not been determined. Studies involving the effects of diet restriction on life span of primates are ongoing, but concluding data are not yet available because these species are so long-lived. Nonetheless, investigators have found that diet restriction does have a mitigating effect on a number of age-related diseases of primates.[3]

Studies of diet restriction and life span also have facilitated evaluation of aging markers that may have value as signals for preventive medical intervention or treatment earlier in life.[4] Markers that have been evaluated in these types of studies include body fat content[5] and serum or plasma concentration of glucose,[6] insulin,[6] triglycerides,[1] cholesterol,[1] and **triiodothyronine (T_3)**.[7]

In a previous 2-year study[8] of the effect of restricted food intake on development of orthopedic disease in Labrador Retrievers, we found that limiting food intake had a beneficial effect on the development of hip joints. The study subsequently was extended and directed toward determining the effect of diet restriction on the life span of this group of dogs and evaluating potential markers of aging.

Materials and Methods

Forty-eight Labrador Retrievers from 7 litters were used in the study, which consisted of a paired feeding design. Dogs in each litter were paired at 6 weeks of age on the basis of sex and body weight and assigned at random to 1 of 2 feeding groups. Beginning at 8 weeks of age, 1 dog in each pair was fed ad libitum, and the other dog in each pair was fed 75% of the amount of food that its pair-mate had consumed the previous day. The same formula was fed to both groups of dogs; only the quantity provided was different.

When the dogs were 3.25 years old, 2 adjustments were made to the feeding protocol. All dogs were switched from a growth formula diet (27% protein content) to an adult formula diet (21% protein content). In addition, the amount of food that was fed was reduced and held constant to prevent insidious development of obesity in the dogs that were fed ad libitum. The amount offered to the 24 dogs that previously had been fed ad libitum was calculated by estimating the ideal body weight for each dog on the basis of skeletal size in reference to other dogs of the same breed. These dogs then were fed 62.1 Kcal of **metabolizable energy (ME)**/kg of estimated ideal body weight (ie, the estimated maintenance requirement for large breed dogs[a]). This group of dogs was designated as the controlled-feeding group. The remaining 24 dogs each continued to be given 25% less than the amount fed to their respective pair-mates. This group of dogs was designated as the restricted-feeding group. Details of the experimental design and procedures have been described.[8-10]

Dogs were weighed weekly as puppies, periodically as adolescents, and weekly as adults. Beginning at 6 years of age, body condition was evaluated annually to assess degree

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of leanness or obesity, and a body condition score ranging from 1 (emaciated) to 9 (severely obese) was assigned.[a] Also beginning at 6 years of age, amounts of lean body mass, body fat mass, and bone mass were estimated annually by use of **dual-energy x-ray absorptiometry (DEXA)**.[b]

Serum glucose, cholesterol, and triglycerides concentrations were measured annually.[c] Beginning at 4 years of age, serum T_3 concentration was measured annually with a radioimmunoassay.[d] Samples were obtained by means of jugular venipuncture after food had been withheld overnight. Beginning at 9 years of age, **IV glucose tolerance tests (IVGTT)** were performed annually. For this test, a 50% solution of glucose (2 ml/kg [0.9 ml/lb]) was administered IV; venous blood samples were collected before and 5, 30, 45, 60, and 120 minutes after glucose administration. Plasma insulin concentration was estimated with a radioimmunoassay.[d]

The dogs were monitored daily throughout life for signs of illness and abnormalities. When necessary, appropriate therapeutic measures consistent with established colony protocols were taken under the supervision of the attending veterinarian. Health management and euthanasia protocols were preestablished for the entire facility. Similar conditions were managed as uniformly as possible among dogs. Dietary treatments were not adjusted because of illness, and the choice of therapeutic measures was not influenced by dietary treatment. Forty-six of the 48 dogs eventually were euthanatized for humane reasons. Euthanasia was carried out only after extensive diagnostic evaluation, careful monitoring and assessment of response to treatment, serial evaluation of clinical condition, and consideration of prognosis, according to practices established for the entire colony.

Response variables were examined with a mixed-effects ANOVA model for a repeated-measures design.[11] Dietary treatment, age, and their interaction were considered to be the fixed effects of interest. Random effects accounted for variation among litters, pairs within litters, and their interaction with age. The repeated-measures aspect of the design was addressed by assigning blocks to individual dogs. The Wilcoxon signed rank test for paired data was used to evaluate differences in median life span.[12] The paired Prentice-Wilcoxon test was used to evaluate differences in median time to treatment for osteoarthritis and other chronic conditions.[13]

Results

Median life span for each dietary treatment group was calculated as the age when 50% of the dogs were deceased. Median life span for controlled-feeding dogs (11.2 years) was significantly ($P < 0.01$) less than median life span for restricted-feeding dogs (13.0 years; **Fig 1**). Maximum life span (ie, the time when 90% of the dogs were deceased) for controlled-feeding dogs (12.9 years) was not significantly different from maximum life span for the restricted-feeding dogs (14.0 years), although precise estimates of extreme percentiles are difficult to establish when sample sizes for the last surviving deciles are small.

Nutrient analyses of the adult formula diet fed after dogs were 3.25 years old indicated that mean protein content was 21.6%, mean fat content was 11.1%, and mean calculated ME was 3,530 Kcal/kg of diet. Serial analyses of the diet indicated that the nutrient content exceeded National Research Council recommendations for those nutrients analyzed[14] and did not deviate from expectations based on original formulation. No signs of nutritional deficiency (eg, progressive weight loss and general or specific clinical signs of a nutrient deficit) occurred during the study.

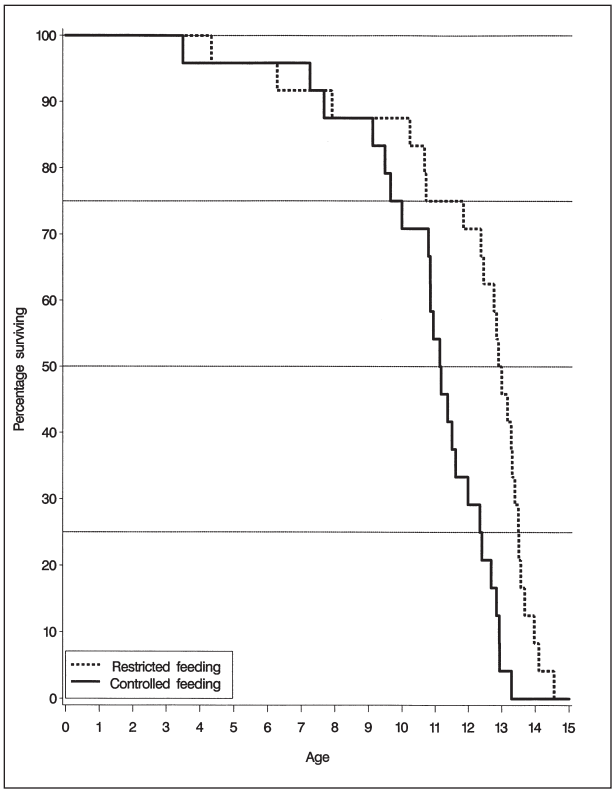


Figure 1—Survival curves for 24 Labrador Retrievers fed a nutritionally complete and balanced diet (controlled-feeding group) and a second group of 24 Labrador Retrievers, consisting of sex- and weight-matched siblings of the first group, that was fed 75% of the same food (restricted-feeding group).

Until 12 years of age, mean (± SEM) daily caloric intake for controlled-feeding dogs (1,745 ± 46 Kcal of ME) was significantly ($P < 0.01$) higher than mean daily caloric intake for restricted-feeding dogs (1,352 ± 34 Kcal of ME). After 12 years of age, daily caloric intake was more variable because of the increased incidence of illnesses, primarily among dogs in the controlled-feeding group.

For both groups, mean body weight increased until 3.25 years of age **(Fig 2)**. Mean body weight decreased initially in both groups after adjustments were made to the feeding regimen at 3.25 years of age, but then weights stabilized. Before and after implementation of these adjustments in the feeding regimen, the relationship between the 2 groups in regard to feed intake and body weight remained similar. Mean body weight of restricted-feeding dogs was, on average, 26% lower than mean body weight of pair-mates in the controlled-feeding group ($P < 0.01$). Mean (± SEM) body condition score during the period from 6 to 12 years of age was significantly ($P < 0.01$) higher for dogs in the controlled-feeding group (6.7 ± 0.19) than for dogs in the restricted-feeding group (4.6 ± 0.19; **Fig 3**).

Mean lean body mass remained constant from 6 through 9 years of age for controlled-feeding dogs and from 6 through 11 years of age for restricted-feeding dogs **(Fig 4)**. From 6 through 9 years of age, mean lean body mass was significantly ($P < 0.01$) greater for dogs in the controlled-feeding group than for dogs in the restricted-feeding group. A progressive decrease in lean

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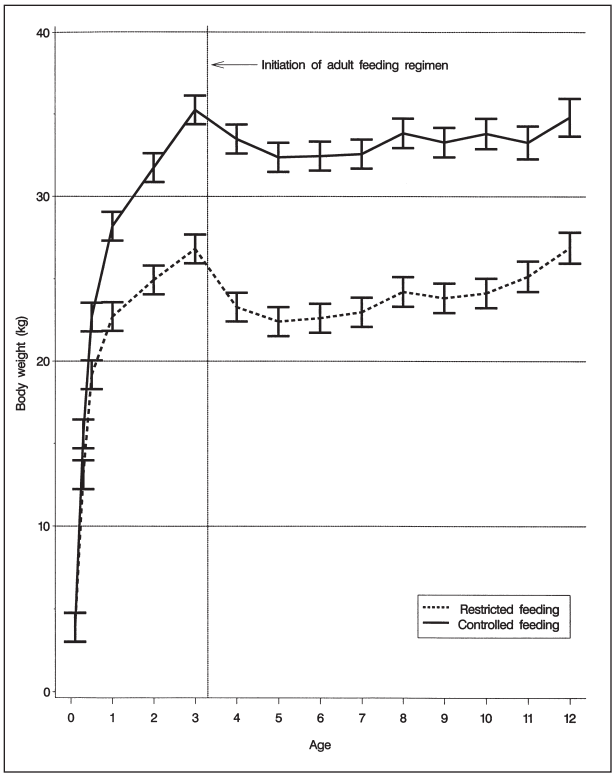


Figure 2—Least-squares mean body weights of the dogs in Figure 1. Error bars represent SE.

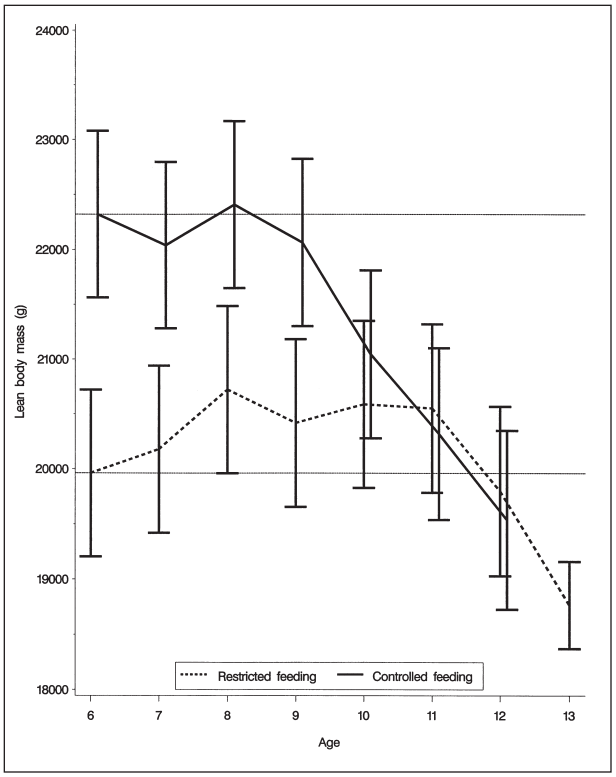


Figure 4—Least-squares mean lean body mass, estimated by use of dual-energy x-ray absorptiometry, of the dogs in Figure 1. Error bars represent SE; mean values are offset to allow SE to be seen.

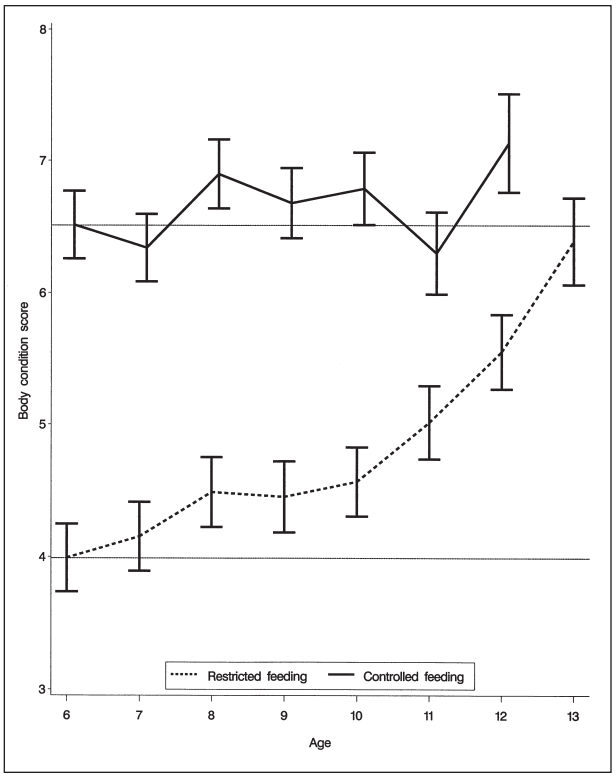


Figure 3—Mean body condition scores of the dogs in Figure 1. Potential scores ranged from 1 (emaciated) to 9 (severely obese). Error bars represent SE.

body mass was detected among dogs in the controlled-feeding group after 9 years of age, but a similar decrease was not detected among dogs in the restricted-feeding group until after 11 years of age. Mean percentage lean body mass decreased significantly ($P < 0.05$) in both groups from 6 through 12 years of age **(Fig 5)**; however, dogs in the restricted-feeding group always had a significantly ($P < 0.01$) greater mean percentage lean body mass.

Mean absolute and percentage body fat mass increased significantly ($P < 0.05$) in both groups from 6 through 12 years of age **(Fig 6 and 7)**. Body fat mass, expressed as an absolute (ie, grams of fat tissue) or as a percentage of body mass, always was significantly ($P < 0.01$) higher among dogs in the controlled-feeding group than among dogs in the restricted-feeding group. Mean percentage body fat mass for the entire period from 6 through 12 years of age was significantly ($P < 0.01$) higher for the controlled-feeding dogs (29.9%) than for the restricted-feeding dogs (16.8%).

Results for bone mass were similar to results for lean body mass **(Fig 8)**. Dogs in the controlled-feeding group had significantly ($P < 0.05$) higher bone mass than did dogs in the restricted-feeding group, from 6 through 9 years of age. After 9 years of age, bone mass among dogs in the controlled-feeding group decreased significantly ($P < 0.05$), whereas bone mass among dogs in the restricted-feeding group remained constant.

Mean serum triglycerides and glucose concentrations from 2 through 12 years of age, mean serum T_3 concentration from 4 through 12 years of age, and

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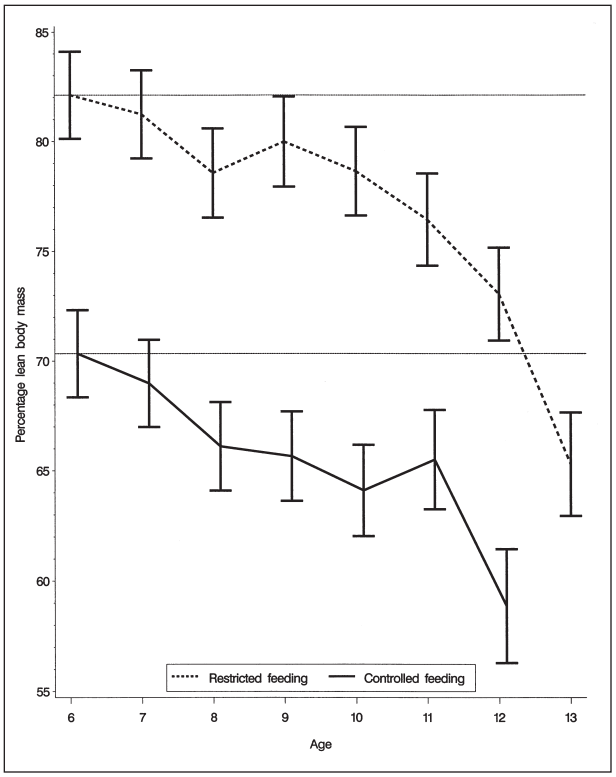


Figure 5—Mean percentage lean body mass of the dogs in Figure 1. Error bars represent SE.

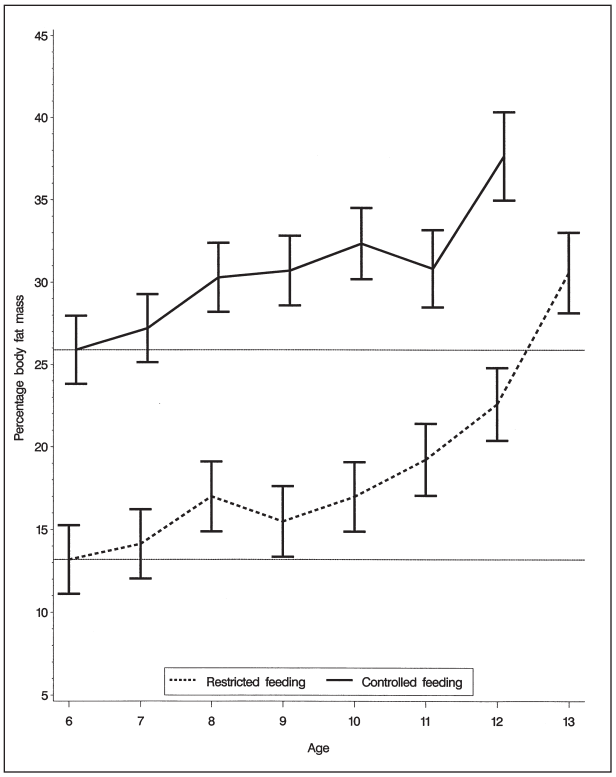


Figure 7—Mean percentage body fat mass of the dogs in Figure 1. Error bars represent SE.

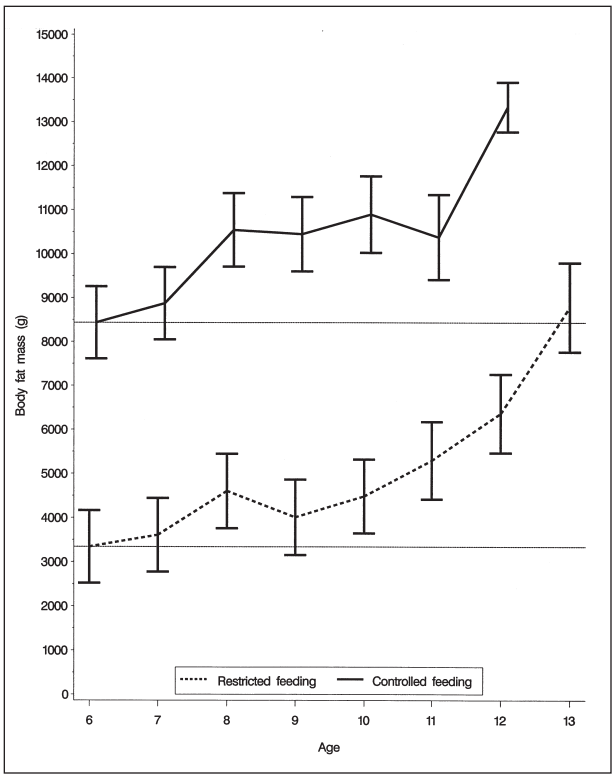


Figure 6—Least-squares mean body fat mass, estimated by use of dual-energy x-ray absorptiometry, of the dogs in Figure 1. Error bars represent SE.

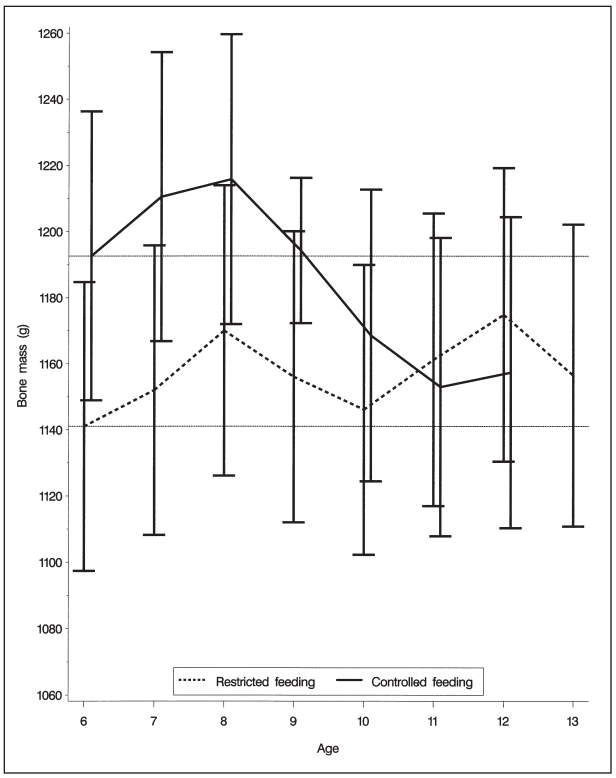


Figure 8—Least-squares mean bone mass, estimated by use of dual-energy x-ray absorptiometry, of the dogs in Figure 1. Error bars represent SE; mean values are offset to allow SE to be seen.

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Table 1—Effects of a 25% food restriction from 8 weeks of age to death on blood chemistry values in Labrador Retrievers

Variable	Group		Percentage difference
	Controlled-feeding	Restricted-feeding	
Triglyceride (mg/dl)*	49.9 (3.4)	41.5 (3.3)†	17
Cholesterol (mg/dl)*	209 (10)	202 (10)	3
Triiodothyronine (nmol/L)‡	1.16 (0.03)	0.98 (0.03)†	16
IV glucose tolerance test			
Baseline insulin (pmol/L)§	70.8 (9.2)	48.4 (8.7)†	32
Baseline glucose (mg/dl)*	100.7 (1.2)	93.5 (1.2)†	7
Peak glucose (mg/dl)§	578 (15)	493 (13)†	15
Delta G (mg/dl)§	478 (15)	401 (13)†	16
Rate of glucose decline (mg/dl/min)§	6.5 (0.77)	11.3 (0.75)†	72
Time to baseline (min)§	91.2 (2.7)	41.4 (2.7)†	55

Twenty-four dogs were fed a nutritionally complete and balanced diet (controlled-feeding group), and a second group of 24 dogs, consisting of sex- and weight-matched siblings of the first group, was fed 75% of the same food (restricted-feeding group).

*Measured annually from 2 through 12 years of age. †Significantly ($P < 0.05$) different from value for controlled-feeding group. ‡Measured annually from 4 through 12 years of age. §Measured annually from 9 through 12 years of age.

Peak glucose = Peak serum glucose concentration following IV administration of a 50% solution of glucose (2 ml/kg [0.9 ml/lb]). Delta G = Difference between baseline and peak glucose concentration.

Data are given as mean (SE).

mean fasted plasma insulin concentration from 9 through 12 years of age were significantly ($P < 0.05$) lower for dogs in the restricted-feeding group than for dogs in the controlled-feeding group (**Table 1**). Mean serum cholesterol concentration from 2 through 12 years of age was not significantly different between groups. Evaluation of results of IVGTT performed at 9, 10, 11, and 12 years of age revealed significantly ($P < 0.01$) higher mean peak glucose concentration and mean delta G values (difference between baseline and peak glucose concentration) for controlled-feeding dogs than for restricted-feeding dogs. Mean time for glucose concentration to return to baseline was significantly ($P < 0.01$) longer and rate of return to baseline was significantly ($P < 0.01$) lower in controlled-feeding dogs than in restricted-feeding dogs. Mean serum glucose, cholesterol, and T_3 concentrations decreased during the evaluation period in both groups, whereas mean serum triglycerides concentration did not change over time. Mean values for these variables were within reference intervals.

A variety of chronic diseases developed as the dogs aged. The chronic diseases diagnosed most commonly were osteoarthritis (43 dogs; the diagnosis was made radiographically); malignant neoplasia, including malignant mammary gland neoplasia (21 tumors in 17 dogs); benign neoplasia of the mammary glands (35 tumors in 12 dogs); benign neoplasia other than benign mammary gland neoplasia (7 tumors in 6 dogs); recurring skin disease (19 dogs); hepatic disease (11 dogs); cystic endometrial hyperplasia, pyometra, or recurring severe pseudopregnancy (11 dogs); hypothyroidism (4 dogs); and seizures (4 dogs).

Thirty-five of the 43 dogs that developed osteoarthritis (19 in the controlled-feeding group and 16 in the restricted-feeding group) eventually required treatment. Age at the time of first treatment for osteoarthritis ranged from 6.8 to 12.9 years for dogs in the controlled-feeding group and from 7.9 to 14.1 years for dogs in the restricted-feeding group. Mean age to which 50% of the dogs in each group survived without requiring long-term treatment for osteoarthritis was significantly ($P < 0.01$) lower for the controlled-feeding group (10.3 years) than for the restricted-feeding group (13.3 years).

Thirty-nine dogs (20 in the controlled-feeding group and 19 in the restricted-feeding group) eventually were treated for 1 or more chronic conditions. Age at the time of first treatment for any chronic condition ranged from 4.6 to 12.9 years for dogs in the controlled-feeding group and from 4.0 to 14.1 years for dogs in the restricted-feeding group. Mean age to which 50% of the dogs in each group survived without requiring treatment for a chronic condition was significantly ($P = 0.016$) lower for the controlled-feeding group (9.9 years) than for the restricted-feeding group (12.0 years).

Discussion

Results of this study indicate that diet restriction significantly increased median life span in this group of dogs. To our knowledge, this is the first study to document that diet restriction increases survival time in mammals larger than rodents. In studies of rodents, diet restriction consistently increased median and maximum life span. In the present study, median life span was increased by diet restriction, but maximum life span was not significantly different between groups.[1] The smaller number of subjects in the present study, compared with the numbers in previous rodent studies, may explain the lack of statistical significance between groups in regard to maximum life span, since the 90th percentile estimates from our study involve outcome of just 3 dogs/group. In the present study, diet restriction also was associated with a longer median time to first treatment of osteoarthritis (the most common chronic disease among dogs in this study) and a longer median time to first treatment of any chronic condition.

Lean body mass was significantly higher among dogs in the controlled-feeding group than among dogs in the restricted-feeding group. Reasons for this finding are not resolved by our data, but the difference might relate at least partly to metabolic needs of a greater body mass, as well as to the higher food intake. Decreases in lean body mass late in life (after 9 years of age among controlled-feeding dogs and after 11 years of age in restricted-feeding dogs) might have been a consequence of deteriorating physiologic function associated with aging or disease, with delayed expression among dogs in the restricted-feeding group. Similar findings with respect to changes in lean body mass have been found in studies of rodents.[15]

A consistent observation in diet restriction studies, including the present study, has been excessive fat deposition in animals in which diet was not restricted. Even though obesity typically occurs with overfeeding, investigators have demonstrated that longevity of rodents is more closely related to amount of food consumption than to degree of adiposity.[16,17] Genetically obese and nonobese mice of the same strain were stud-

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ied to separate the effects of food restriction from the effects of adiposity. Genetically obese food-restricted mice had a mean body weight similar to that of control mice but had 50% more adipose tissue, even though the obese mice were fed a third less. However, the obese food-restricted mice lived longer, indicating that longevity effects were related primarily to food consumption.[16]

In the present study, body fat content of dogs in the restricted-feeding group ranged from 12 to 20% of body mass. Mean body condition score for these dogs ranged from 4 to 5, and median time to onset of treatment for osteoarthritis or any chronic condition was significantly longer than for dogs in the controlled-feeding group. An association between high body fat content and increases in incidence and severity of chronic diseases has been reported in other studies.[5,18,19] Lower morbidity rates also have been reported for food-restricted primates with body fat content ranging from 10 to 22%,[20] which closely parallels our observations.

Mean serum triglycerides concentration among dogs in the restricted-feeding group was approximately 15% lower than mean concentration among dogs in the controlled-feeding group, which was similar to data reported for rodents and primates.[1,3] However, mean serum cholesterol concentration was not significantly different between groups. A decrease in serum cholesterol concentration in response to diet restriction has been demonstrated in primates,[3] but responses in rodents have been inconsistent.[1] The lack of difference between groups in the present study might be explained by the amount of food restriction imposed by the design of our study or by the diet formulation, or it may represent a true species difference. Higher serum total T_3 concentration, as found in controlled-feeding dogs in the present study, has been observed in rodents and humans in which food intake was not restricted.[7] Overfeeding increases deiodination of thyroxine to T_3, whereas carbohydrate restriction and weight reduction reduce serum T_3 concentration.[7] The observation that baseline serum glucose and insulin concentrations were significantly lower among dogs in the restricted-feeding group parallels findings of studies[3,6] involving rodents and primates and suggests commonality in glucose metabolism among rodents, primates, and canines.

The actual caloric intake needed to achieve a desired extension of life span and improved health varies among individual dogs because of high intrinsic variation in caloric requirements both within breeds and within the species as a whole. Use of DEXA to estimate lean body mass and body fat mass is not practical in private veterinary practice, and as an alternative, we recommend that for purposes of health and longevity, dogs be fed to maintain a body condition score less than 5.

[a]Body condition score chart, Ralston Purina Company, St Louis, Mo.
[b]Model DPX alpha dual energy x-ray absorptiometer, Lunar Corp, Madison, Wis.
[c]Model 550 express blood chemistry analyzer, Ciba-Corning Corp, Boston, Mass.
[d]Michigan State University, East Lansing, Mich.

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