# Case Report Rapport de cas

# Commercial diet recommendations and follow-up for a large breed puppy with an intrahepatic portosystemic shunt

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**Abstract** – A 6-month-old, intact male Great Dane dog fed a veterinary therapeutic liver diet was evaluated after diagnosis of an intrahepatic portosystemic shunt and hind limb angular limb deformity to determine appropriateness of diet. Evaluation of the current diet revealed it to be inadequate to meet the nutrient requirements of a large breed puppy. The dog clinically improved following a change in diet. There was no longer any angular limb deformity and no reported neurological signs. This report highlights the importance of appropriate feeding management during growth and demonstrates that although veterinary therapeutic diets may appear to be an appropriate choice initially, they may not be ideal for growing puppies as a long-term feeding option.

#### Key clinical message:

An individual approach is key for nutritional management of complicated canine veterinary medical cases and includes consideration of the patient's life stage requirements when modifying nutrient intake to manage clinical disease.

**Résumé – Recommandations alimentaires commerciales et suivi d'un chiot de grande race avec un shunt porto-systémique intrahépatique.** Un chien grand danois mâle intact âgé de 6 mois nourri avec une diète thérapeutique vétérinaire à base de foie a été évalué après le diagnostic d'un shunt porto-systémique intrahépatique et d'une déformation angulaire des membres postérieurs afin de déterminer la pertinence du régime alimentaire. L'évaluation du régime actuel a révélé qu'il était insuffisant pour répondre aux besoins nutritionnels d'un chiot de grande race. Le chien s'est amélioré cliniquement suite à un changement de régime. Il n'y avait plus de déformation angulaire des membres et aucun signe neurologique signalé. Ce rapport souligne l'importance d'une gestion appropriée de l'alimentation pendant la croissance et démontre que bien que les régimes thérapeutiques vétérinaires puissent sembler être un choix approprié au départ, ils peuvent ne pas être idéaux pour la croissance des chiots en tant qu'option d'alimentation à long terme.

#### Message clinique clé :

Une approche individuelle est essentielle pour la gestion nutritionnelle des cas médicaux vétérinaires canins compliqués et comprend la prise en compte des besoins du patient au stade de la vie lors de la modification de l'apport en nutriments pour gérer la maladie clinique.

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## **Case description**

A 6-month-old, intact male Great Dane dog was presented to the Ontario Veterinary College-Health Sciences Centre (OVC-HSC), Companion Animal Surgery Service for discussion of surgical correction of a previously diagnosed intrahepatic portosystemic shunt (PSS).

The dog had been surrendered by the breeder to a veterinarian in Michigan, USA at 8 wk of age for failure to thrive. The veterinarian elected to pursue further testing including a complete blood (cell) count (CBC), serum biochemistry, and measurement of bile acids. The dog was anemic with decreased hemoglobin. There were abnormalities with mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and reticulocyte hemoglobin. Other abnormal findings included leukocytosis, monocytosis, hypernatremia, hypoproteinemia, hypoalbuminemia, hypoglobulinemia, hypocholesterolemia, decreased amylase and lipase, increased creatine kinase (CK), and elevated pre-prandial bile acids (Tables 1, 2).

(Traduit par D<sup>r</sup> Serge Messier)

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**Table 1.** Complete blood (cell) count at time of diagnosis (8 wk of age) and following medical and nutritional intervention (15 wk and 12 mo of age) in a Great Dane puppy with an intrahepatic portosystemic shunt.

Parameter	8 wk	15 wk	12 mo
Complete blood (cell) count			
$\dot{WBC}$ ( $\times 10^9/L$ )	<b>H</b> 18.7 (12.7 to 17.3) <sup>a</sup>	17.2 (4.9 to 17.6)	H 17.59 (5.05 to 16.76)
RBC ( $\times 10^{9}/L$ )	L 2.89 (4.5 to 5.9) <sup>a</sup>	L 4.7 (5.4 to 8.7)	7.07 (5.65 to 8.87)
Hemoglobin (g/L)	<b>L</b> 51 (103 to 125) <sup>a</sup>	L 84 (134 to 207)	146 (131 to 205)
Hematocrit (L/L)	L 0.18 (0.38 to 0.57) <sup>a</sup>	L 0.27 (0.38 to 0.57)	0.43 (0.37 to 0.62)
MCV (fL)	62 (59 to 76)	L 56 (59 to 76)	L 61.5 (61.6 to 73.5)
MCH (pg)	L 17.6 (21.9 to 26.1)	L 17.8 (21.9 to 26.1)	L 20.7 (21.2 to 25.9)
MCHC (g/L)	L 283 (326 to 392)	L 317 (326 to 392)	336 (320 to 379)
RDW (% CV)		<b>H</b> 21.4 (10.0 to 19.0)	17.1 (13.6 to 21.7)
Platelets ( $\times 10^{9}/L$ )	259 (240 to 435) <sup>a</sup>	292 (143 to 448)	L 126 (148 to 484)
Retic-Hemoglobin (pg)	L 17.9 (22.3 to 29.6)	L 21.2 (22.3 to 29.6)	23.1 (22.3 to 29.6)
% Reticulocyte	3.20%	3.90%	0.40%
Reticulocyte ( $\times 10^{9}/L$ )	92 (10 to 110)	<b>H</b> 183.3 (10 to 110)	26.9 (10 to 110)
Neutrophils ( $\times 10^{9}/L$ )	10.996 (6.2 to 11.8) <sup>a</sup>	10.1 (2.9 to 12.7)	H 12.61 (2.94 to 12.67)
Lymphocytes ( $\times 10^{9}/L$ )	4.189 (3.1 to 6.9) <sup>a</sup>	<b>H</b> 5.8 (1.1 to 5.0)	3.66 (1.06 to 4.95)
Monocytes ( $\times$ 10 <sup>9</sup> /L)	<b>H</b> 3.31 (0.4 to 1.7) <sup>a</sup>	1.2 (0.0 to 1.2)	<b>H</b> 1.25 (0.13 to 1.15)
Eosinophils ( $\times 10^{9}/L$ )	$0.15 (0.0 \text{ to } 1.2)^{a}$	0 (0.0 to 1.5)	<b>L</b> 0 (0.07 to 1.49)
Basophils ( $\times$ 10 <sup>9</sup> /L)	0.056 (0 to 0.1)	0 (0.0 to 0.1)	0.07 (0 to 0.1)

<sup>a</sup> Reference values taken from von Dehn 2014 (37).

H — High (above reference range); L — Low (below reference range); WBC — white blood cells; RBC — red blood cells; MCV — mean corpuscular volume; MCH — mean corpuscular hemoglobin; MCHC — mean corpuscular hemoglobin concentration; RDW — red cell distribution width.

A second bile acid panel was performed, and pre- and postprandial bile acids were elevated (Table 2). It was reported in the medical record that the dog had demonstrated neurological signs, consistent with hepatic encephalopathy, but these signs were controlled with medical management. No details regarding a description of the neurological signs observed or the medications prescribed were recorded in the medical history provided. The dog was referred to the Animal Surgical Center of Michigan for a contrast computed tomography (CT) scan, which showed a large intrahepatic shunt entering the right lateral liver lobe. A diagnosis of congenital portosystemic shunt was made, and surgical correction was recommended. At this time, responsibility of the case was transferred from the primary care veterinarian to a Great Dane rescue service in Ontario, Canada. At 15 wk of age, the dog was taken to a primary care veterinarian in Ontario, Canada and blood analysis was performed to assess response to medical management. Findings included improvement in several parameters (Tables 1, 2). New findings included decreased urea and an increase in reticulocytes, which indicated a regenerative response to the anemia (Tables 1, 2). Bile acids were assessed and were increased compared to previous results (Table 2).

At 6 mo of age, the dog was presented to the OVC-HSC Surgery Service for evaluation of surgical corrective options for the diagnosed intrahepatic shunt. Physical examination was unremarkable except for a valgus angular limb deformity of both pelvic limbs noted on orthopedic examination. No clinical signs of hepatic encephalopathy were noted. Medical management included metronidazole [7.5 mg/kg body weight (BW), PO, q12h] and lactulose (dose not listed in medical history). Surgical options were discussed; in particular, transvenous coil embolization. This procedure is performed when dogs are close to mature size to ensure that the stent is not too small (1) and involves the placement of a vascular stent in the vena cava at the level of the shunt (2). Embolic coils are then introduced to promote gradual occlusion. This can sometimes require multiple procedures to achieve adequate occlusion of the vessel (2). For some patients, the embolization procedure is enough to resolve clinical signs but in others, continued medical and dietary management are required (2).

Nutritional management of intrahepatic PSS was essential to consider in this case given the dog's young age. The OVC-HSC Clinical Nutrition Service performed a nutritional assessment and identified risk factors using the WSAVA Nutritional Assessment Checklist (3). A comprehensive diet history was taken using a standard diet history form. After diagnosis of the intrahepatic PSS at 8 wk of age and until 19 wk of age, the dog was fed a veterinary therapeutic liver diet (Diet A; Hill's Prescription Diet L/d Canine (Dry), Hill's Pet Nutrition, Topeka, Kansas, USA). Details about amount and feeding regimen were not reported and diet history before that time was not known. From 19 wk of age until 6 mo of age, the puppy was fed a different veterinary therapeutic liver diet (Diet B; Royal Canin Veterinary Exclusive Hepatic (Dry), Royal Canin Canada, Guelph, Ontario). He was fed a total of 2.5 cups 3 times per day at the time the diet history was taken, and any adjustments of amounts fed before that were not reported. For treats, he received a few small pieces of cheddar cheese, a veterinary therapeutic multi-purpose diet (Diet C; Hill's Prescription Diet w/d Multi-Benefit Canine dry, Hill's Pet Nutrition), and 2 tablespoons of Kraft smooth peanut butter delivered in a Kong toy each day. The dog weighed 27 kg and he had a body condition score (BCS) of 4 on a 9-point scale (4). The dog was also noted to have bilateral angular limb deformity in the hind limbs.

According to the Association of American Feed Control Officials (AAFCO) Nutritional Adequacy Statement on the product label, Diet B is formulated to meet the nutritional requirements for adult maintenance (5). Diet A has an AAFCO nutritional adequacy statement for growing puppies based on feeding trials, even though the nutrient content does not fit with the AAFCO puppy growth profile. Puppy feeding trials do not typically use large breed puppies; therefore, Diet A was **Table 2.** Serum biochemistry and pre- and post-prandial bile acids at time of diagnosis (8 wk of age) and following medical and nutritional intervention (15 wk and 12 mo of age) in a Great Dane puppy with an intrahepatic portosystemic shunt.

Parameter	8 wk	15 wk	12 mo
Serum biochemistry			
Glucose (mmol/L)	L 5.83 (6.8 to 8.8) <sup>a</sup>	8.6 (5.4 to 9.2) <sup>a</sup>	5.79 (4.2 to 6.6) <sup>a</sup>
Urea (BUN) (mmol/L)	8.57 (6.43 to 22.13) <sup>a</sup>	L 2.3 (3.2 to 11)	2.7 (2.5 to 9.6)
Creatinine (µmol/L)	26.5 (23 to 58) <sup>a</sup>	L 23 (24 to 78) <sup>a</sup>	<b>H</b> 83 (19 to 79) <sup>a</sup>
P (mmol/L)	3.39 (2.7 to 3.6) <sup>a</sup>	2.9 $(1.8 \text{ to } 3.1)^{a}$	1.57 (1.1 to 2.5) <sup>a</sup>
Ca (mmol/L)	L 2.25 (2.7 to 2.2) <sup>a</sup>	L 2.4 (2.5 to 3.3) <sup>a</sup>	2.37 (2.6 to 3.00) <sup>a</sup>
Sodium (mmol/L)	H 158 (142 to 152)	148 (139 to 159) <sup>a</sup>	152 (138 to 158) <sup>a</sup>
Potassium (mmol/L)	4.5 (4 to 5.4)	4.9 $(3.9 \text{ to } 6.1)^{a}$	4.9 (4.2 to 5.6) <sup>a</sup>
Na:K	35	30	31
Chloride (mmol/L)	<b>H</b> 124 (108 to 119)	114 (108 to 119)	112 (109 to 122)
Total protein (g/L)	<b>L</b> 2.6 (4.0 to 5.3) <sup>a</sup>	40 (45 to 73) <sup>a</sup>	60 (49 to 67) <sup>a</sup>
Albumin (g/L)	L 12 (27 to 39)	L 17 (27 to 39)	25 (23 to 40)
Globulin (g/L)	L 14 (24 to 40)	23 (22 to 35) <sup>a</sup>	35 (22 to 45) <sup>a</sup>
A/G Ratio	0.9	0.7	0.7
ALT (IU/L)	16 (10.3 to 24.3) <sup>a</sup>	$9 (< 32)^{a}$	<b>H</b> 54 (5 to 45) <sup>a</sup>
AST (IU/L)	30 (16 to 55)	<b>H</b> 24 (3 to 23) <sup>a</sup>	_
ALP (IU/L)	485 (153 to 527)	291 (126 to 438) <sup>a</sup>	252 (4 to 252) <sup>a</sup>
T. Bili (Total) (µmol/L)	1.7 (0.0 to 5.13)	2.1 (0 to 5.13)	< 2 (0  to  15)
D. Bil (Conj.) (µmol/L)	< 1.7 (0.0  to  3.42)	0.6 (0 to 3.42)	_
Cholesterol (mmol/L)	<b>L</b> 1.5 (3.8 to 9.0) <sup>a</sup>	4.1 (2.6 to 12.9) <sup>a</sup>	L 2.41 (3.5 to 7.2)
Amylase (IU/L)	L 221 (337 to 1469)	391 (337 to 1469)	690 (500 to 1500)
Lipase (IU/L)	L 123 (138 to 755)	$128 (< 139)^{a}$	<b>H</b> 426 (< 154) <sup>a</sup>
Creatinine kinase (IU/L)	H 304 (10 to 200)	H 280 (40 to 192) <sup>a</sup>	_
Bile Acids			
Bile acids — pre-prandial (µmol/L)	<b>H</b> 41.3 (0 to 6.9)	<b>H</b> 115 (0 to 6.9)	H 312 (0 to 6.9)
Bile acids — post-prandial (µmol/L)	H 75.9 (0 to 14.9)		_ `

<sup>a</sup> Reference range from von Dehn 2014 (37).

H — High (above reference range); L — Low (below reference range); ALT — alanine aminotransferase; AST — aspartate aminotransferase;

ALP — alkaline phosphatase.

also not an ideal choice for this dog. Requirements for essential nutrients for growth according to AAFCO and the United States National Research Council (US NRC) (6) are listed in Table 3 and compared to the nutrient content of the diets as provided by the manufacturers. Due to inadequate protein, calcium (Ca), phosphorous (P), and copper (Cu), neither Diet A nor B met the requirements for growth. Thus, through evaluation of the current diet and assessment of the dog's nutritional needs, the diet was deemed to be inappropriate.

Based on the diet history provided, it was estimated that the puppy was receiving approximately 2700 kcal metabolizable energy (ME) per day from his daily allotment of 7.5 cups of food. This did not include any food used as treats or fed in the Kong toy. The total calories from these sources was unknown because the amount of Diet C used in the Kong toy was not measured. However, 2 tablespoons of peanut butter would equal approximately 192 kcal ME. A range of estimated energy requirement was calculated using the equation  $70 \times \text{body}$ weight in kg<sup>0.75</sup> multiplied by a factor of 2 or 3 (2 for puppies over 4 mo of age and 3 for puppies younger than 4 mo of age) (7). The dog in this case was over 4 mo of age at the time of the nutritional assessment and, using a daily energy requirement (DER) factor of 2, yielded 1658 kcal/d (over 1000 kcal lower than the current estimated calorie intake). It was discussed with the owner that this energy intake seemed high and would likely need to be decreased to prevent rapid growth. Still, given the lack of diet history during the early months of puppyhood and since the dog had an ideal body fat percentage based on BCS assessment (8), the initial plan was to meet the dog's current energy intake and change the food type first. Close follow-up and re-assessment of food intake, body weight (BW), and BCS were recommended to inform adjustment of the food amount if needed.

A veterinary therapeutic diet indicated for liver dysfunction [Diet D; Royal Canin Veterinary Exclusive Vegetarian (Dry), Royal Canin Canada] was selected (Table 3). At the time of recommendation, this diet had undergone feeding trials for growth, although it did not meet the AAFCO nutrient profile for growth. To meet a calorie intake of 2700 kcal ME, a daily food amount of 143 g was prescribed. Gradual transition from Diet B to Diet D was recommended over 15 d to monitor for any neurological symptoms with a higher amount of dietary protein. To minimize the amount of protein delivered in one meal, a feeding management strategy of smaller portions fed in a greater number of meals per day was recommended. In Table 4, the US NRC recommended allowance (RA) for protein is compared to the total protein intake when the dog was fed to maintain body weight using Diet B compared to Diet D. The dog was not able to meet the US NRC RA for protein when consuming Diet B but was above the US NRC RA when fed Diet D. Furthermore, intake of nutrients essential for skeletal growth (Ca, P, and Cu) were much improved with Diet D (Table 4).

An additional nutrient that was considered was soluble fiber. Dietary fiber can reduce the availability and production of nitrogenous wastes in the GI tract (9,10). The dog was already prescribed lactulose; however, the owner was informed that if the dog's ammonia levels could not be well-controlled, an additional source of soluble fiber such as psyllium husk could be considered.

**Table 3.** Comparison of 3 veterinary exclusive therapeutic diets fed to a Great Dane puppy with a portosystemic shunt, to the US NRC 2006 RA and 2019 AAFCO growth requirements.

	US NRC 2006 RA (6)	AAFCO Growth 2019 (5)	Diet A	Diet B	Diet D
Energy (kcal ME/kg)	_	_	405	395.5	359.4
Per 1000 kcal ME					
Protein (g)	43.8ª	56.3	41	40.5	52.9
Ca (g)	3.0	3.0 to 4.5 <sup>b</sup>	1.8	1.9	2.3
P (g)	2.5	2.5 to 4.0	1.4	1.3	1.5
Copper (mg)	2.7	3.1	1.1	1.0	4.2
Zinc (mg)	25	25	69	62	53.4
Ca:P ratio		1:1 to 1.8:1 <sup>b</sup>	1.3	1.5	1.5
Vitamin D (IU)	300	125 to 750	227	253	278
EPA + DHA (g)	0.13	0.1	0.134	0.5	0

US NRC — United States National Research Council; RA — Recommended allowance; AAFCO — American Association of Feed Control Officials; Ca — Calcium; P — Phosphorus; DHA — Docosahexaenoic acid; EPA — Eicosapentaenoic acid.

<sup>a</sup> For puppies > 14 wk of age.

<sup>b</sup> For puppies with adult weight > 70 lbs.

Diet A — Hill's Prescription Diet L/d Canine (Dry).

Diet B — Royal Canin Veterinary Exclusive Hepatic (Dry).

Diet D — Royal Canin Veterinary Exclusive Vegetarian (Dry).

Follow-up contact was available for 7.5 mo during which the patient had been fed the prescribed diet. After transition, he was weighed frequently to establish a growth curve. The dog had gained 6 kg in less than 1 mo from the initial nutrition consultation at 6 mo of age, so his daily caloric intake was reduced by 10%. This weight gain was larger than expected, although it is important to note that the second weight was obtained by the owner, using a different scale and might have been recorded at a different time during the day. Nevertheless, such a growth spurt should be avoided because rapid growth can harm skeletal development and close follow-up, especially after starting a diet plan, is important. From then on, the dog's owner felt comfortable monitoring his BW and BCS and would adjust daily food amounts as needed. The owner followed up monthly with a BW to include in a growth curve (Figure 1). At 12 mo of age, the dog weighed 54.5 kg and had a BCS of 4/9. His angular limb deformity had completely corrected as noted on orthopedic examination. Blood analysis was performed by the family veterinarian (Table 1); anemia had completely resolved, and total protein, albumin, and globulin were within normal ranges. Bile acids were still markedly elevated (Table 2); however, the dog showed no clinical symptoms associated with decreased liver function and was deemed to be thriving on medical and nutritional management. Surgical correction of the PSS was completed at 15 mo of age, and the dog made an uneventful recovery. At the time of surgery, the dog's body weight was 57 kg.

#### Discussion

Nutritional management for growing animals with liver shunts can be challenging. A key nutrient of concern for both growth and liver disease is protein. If the liver is not functioning well, its ability to metabolize protein and amino acids can be compromised (11). Improper amino acid metabolism can result in a build-up of waste products (ammonia) in the blood (12). Ammonia can cross the blood brain barrier and hyperammonemia can then cause neurologic signs such as lethargy, ataxia, hypersalivation, head pressing, and seizures (12). If animals are showing these signs, this is an indication to modify dietary pro-

tein intake (13). One approach is to switch the patient directly to a restricted-protein diet. An individualized method in which protein intake is estimated and reduced is preferred. Growing animals provide a specific challenge because protein requirements for growth are higher than in adult animals. A second approach is to consider the sources of dietary protein (10,14,15). The liver is the site for degradation of aromatic amino acids but not branched chain amino acids; thus, using protein ingredients with a higher proportion of branched chain amino acids compared to aromatic amino acids could be beneficial (14). These ingredients are usually vegetarian (non-animal tissue) protein sources such as egg or soy, which was also the case for all 3 diets (Diets A, B, and D) considered for this dog. Although the source of protein has been suggested as a consideration for dogs with liver disease, research determined no difference in improvement of neurologic signs when a low protein vegetarian diet was compared to an equally low protein diet with chicken (15). This suggests that a lower protein level is more important than the source of protein for patients with hepatic encephalopathy. It is important to note that dogs have requirements for several indispensable amino acids and not just an absolute requirement for protein. A side effect of decreasing protein intake is that intake of the indispensable amino acids will also be decreased. The consequence of deficient amino acid intake depends on the amino acid, but in general deficiency can cause depressed growth (6). This is another reason why it is essential to consider the protein intake of growing puppies and to avoid restriction of protein if possible. If restriction is necessary, then the profile of amino acids must be carefully considered. Furthermore, selecting a low protein diet formulated for adult dogs may create a problem for growing puppies not only because of the lower protein content, but because concentrations of other nutrients important for skeletal development may be lower. This was the case with the dog described.

Calcium and phosphorus are essential for skeletal development. The literature in this area focuses on consequences of excess intake, although in this case the dog likely had a deficient intake of both Ca and P. Growing puppies require higher levels

**Table 4.** Comparison of nutrient intake at 2700 kcal ME for 3 veterinary exclusive therapeutic diets fed to a 27 kg Great Dane puppy with a portosystemic shunt, to US NRC 2006 RA growth requirements.

Amount per kg BW <sup>0.75</sup>	US NRC 2006 RA (6)	Intake Diet A	Intake Diet B	Intake Diet D
Protein (g)	12.2ª	9.35	9.23	12.06
Ca (g)	0.68	0.41	0.43	0.52
P (g)	0.68	0.32	0.30	0.34
Copper (mg)	0.76	0.25	0.23	0.96
Zinc (mg)	6.84	15.73	14.13	12.17
Vitamin D (IU)	38.4	51.74	57.67	63.37
EPA + DHA (g)	0.0036	0.03	0.11	0

US NRC — United States National Research Council; RA — Recommended allowance; Ca — Calcium; P — Phosphorus; DHA — Docosahexaenoic acid; EPA — Eicosapentaenoic acid.

<sup>a</sup> For puppies > 14 wk of age.

Diet À — Hill's Prescription Diet L/d Canine (Dry).

Diet B — Royal Canin Veterinary Exclusive Hepatic (Dry).

Diet D — Royal Canin Veterinary Exclusive Vegetarian (Dry).

**Table 5.** Protein intake in a Great Dane puppy with a portosystemic shunt using 2 veterinary therapeutic foods when fed 1, 3, 4, or 6 meals.

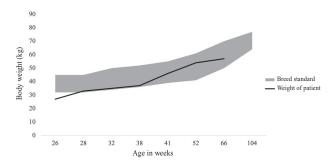
Manufacturer/ Brand	Protein requirement per day (g)	Total protein per day <sup>c</sup> (g)	Total protein per meal (g, 3 meals)	Total protein per meal (g, 4 meals)	Total protein per meal (g, 6 meals)
Diet B Diet D	118ª	109 143	36 48	36	24

<sup>a</sup> Based on US NRC RA of 43.8 g/1000 kcal ME.

<sup>b</sup> Based on 2700 kcal ME.

Diet B — Royal Canin Veterinary Exclusive Hepatic (Dry).

Diet D — Royal Canin Veterinary Exclusive Vegetarian (Dry).



**Figure 1.** Growth curve in a Great Dane puppy with an intrahepatic portosystemic shunt following medical and nutritional intervention starting at 26 wk of age weighing 27 kg ending at 66 wk of age (15 mo) weighing 57 kg.

of dietary Ca and P compared to adult dogs; however, large breed puppies do better when dietary Ca intake is kept below the maximum level accepted for small- and medium-sized breed puppies (5,16–19). The range of dietary Ca acceptable for growth in puppies is 3.0 to 6.25 g/1000 kcal ME, whereas the range for large breed puppies is 3.0 to 4.5 g/1000 kcal ME (6,16). Phosphorus deficiency has been reported in puppies with clinical signs ranging from reduced growth (6,20) to poor appetite, emaciation, and bowing and swelling of forelimbs and carpi (6,21). Phosphorous is required in amounts between 2.5 and 4 g/1000 kcal ME for growing puppies (5) and recommendations should be made with consideration of the calcium level (16). On a body weight basis, US NRC recommends a Ca and P intake of 0.68 g/kg BW<sup>0.75</sup> and in this case, intake was much lower for Ca and P (Table 4).

A narrower range of dietary Ca and the Ca:P ratio (1.1:1 to 1.8:1 rather than 1.1:1 to 2:1), have been shown to decrease

the risk of bone deformities in large breed puppies (18,22,23). A Ca:P ratio that is too low can lead to nutritional secondary hyperparathyroidism, although this is more related to Ca deficiency rather than an excess of phosphorus (18). When there is low circulating Ca, this signals parathyroid hormone to upregulate the metabolism of vitamin D to its active metabolite 1,25-dihydroxyvitamin D [1,25(OH)2D]. This increase in 1,25(OH)2D stimulates increased intestinal absorption and decreased renal excretion of both Ca and P. Also, 1,25(OH)2D stimulates increased osteoclast activity and releases Ca and P from bone (24). This keeps circulating levels of Ca within a tight biological range (24).

Copper is required in the diet of growing puppies and is recommended in the amount of 0.76 mg/kg BW<sup>0.75</sup> daily (Table 4) (6). Copper intake in the dog described herein was below this amount and at 0.23 mg/kg BW<sup>0.75</sup> when fed Diet B. Low dietary copper intake for 3 months' duration in growing puppies affects pigmentation of hair and skin (25). In this same study, dogs showed evidence of skeletal injury as noted by hyperextension of distal phalanges after only 1 additional month of low dietary copper intake (25).

Accelerated growth rates cause a rapid change in body size during the growth period and increase the risk of bone deformities in large breed puppies (1,9,16). High energy intake negatively affects the musculoskeletal system development during growth including development of angular limb deformities (8,16,17,26). Thus, to reduce the risk of bone deformities in young, large breed dogs, control of energy intake to prevent rapid weight gain is key. This can be achieved by accurately measuring food portions, meal feeding instead of *ad libitum* feeding, and not overfeeding treats and snacks (16). In this case, energy intake was calculated to be 2700 kcal ME/d from the diet alone. This energy intake is high when compared to requirements using various energy equations (27,28). More than 25 y ago researchers reported that Great Danes between the ages of 2 and 6 mo have an energy requirement equal to 0.74 to 0.81 MJ/body weight in kg<sup>0.75</sup> per day (29). Using that equation for this patient would yield between 2100 and 2300 kcal ME/d. According to the US NRC, the daily metabolizable energy requirements for growth of puppies after weaning is equal to

$$130 \times BW_{0.75} \times 3.2 \times [e^{-0.87p} - 0.1]$$

where: p is BW<sub>2</sub>/BW<sub>m</sub>, BW<sub>2</sub> represents actual body weight, BW<sub>m</sub> represents expected mature weight, and e is the base of natural  $\log(\sim 2.718)$  (6). A more recent study investigated energy intake and growth in privately owned dogs (30). The ME intake was determined to be considerably lower than the US NRC recommendations and researchers developed a linear equation to predict energy requirements (30). Using this equation, energy intake for the dog in this case should be close to 2200 kcal ME. The equation used in this case study was 70  $\times$   $BW^{0.75}$  multiplied by a factor of 2 or 3 to give an estimated range (27). Although these equations are important for estimating energy requirements, a review of energy requirements of adult dogs determined that estimations based on body weight alone may not be accurate and that other factors such as husbandry, neuter status, and activity level may be more important (31). Thus, energy requirements based on body weight could be considered starting points since individual animals differ in activity level and husbandry.

The use of BCS and expected adult weight have been the most common methods for assessing optimal growth in puppies. Body condition scoring as a tool to assess growth should be used with caution, however, as puppies can have a normal BCS but weigh too much for their age. A more appropriate assessment is to use a growth curve (32,33). Growth curves are useful tools for determining if a puppy is following an expected pattern of growth; dog standards charts have been developed for dogs of different sizes (33). These charts have been established for dogs with an adult body weight up to 40 kg but have not yet been established for giant breed dogs with adult body weights > 40 kg. A study in 2004 investigated growth curves for 12 different sized dog breeds, including Great Danes, and it was determined that their average mature weight was 51.1 kg (32). The sample size for this study was small (11 Great Danes; 6 males and 5 females) and the averages were not reported for each sex. More recently, researchers reported that by using the adult body weight of a patient, the target BW during growth could be calculated as a percentage of adult body weight (34). A limitation with this method is that adult body weight must be known and if a patient was below or above average as an adult; the targets for growth may not be as accurate.

A growth curve was made for this dog using body weights provided by the owner as shown in Figure 1; however, there were several limitations. These included infrequent weight updates from the owner and lack of body weight data before 6 mo of age. Under ideal conditions, body weight data would be available from birth and would be monitored weekly or biweekly until mature weight was reached.

Nutrient comparisons for this case study were made between AAFCO and US NRC recommendations and nutrient profiles of the diets. There are some differences between AAFCO requirements and US NRC requirements, particularly for protein. The protein requirement differs because the AAFCO minimum is for puppies of all ages, whereas the US NRC has separate requirements for puppies younger and older than 14 wk. Also, the US NRC reports nutrient content in the food as well as individual animal requirements, whereas AAFCO only recommends nutrient content in the food. Most nutrient requirements according to AAFCO are higher than the US NRC requirements, due to consideration of digestibility and bioavailability. Another consideration is to compare the actual nutrient intake based on energy intake relative to US NRC requirements on a per kg BW<sup>0.75</sup> basis. This dog's energy intake was high, and it could be assumed that intake of key nutrients would be greater than expected if the animal were eating more calories. As illustrated in Table 4, even though the dog was consuming a high number of calories, the intake of protein, Ca, P, and Cu was still below the US NRC RA.

Dietary options for this dog included supplementation of the current diet, formulation of a balanced homemade diet, or selection of a more appropriate therapeutic diet. Each of these options was considered for this dog and discussed (or presented) to the owner. Although key nutrients were still less than the US NRC RA for a 27 kg growing dog, consuming Diet D would result in intakes of protein, Ca, P, and Cu better than Diet A or Diet B. The owner thought that a homemade diet would be too labor-intensive and elected to feed a single commercial diet; therefore, the authors felt Diet D was the better option.

It is important to consider feeding management strategies that could have a positive effect on disease treatment or management. A feeding management strategy used in this case was feeding more frequent, smaller meals throughout the day (Table 5). When protein cannot be restricted to the level in the therapeutic liver diets, titrating postprandial blood ammonia peak through multiple small meals, with the addition of soluble fiber if needed, can be another approach. This strategy of feeding multiple small meals will help to optimize blood nitrogen concentration in the liver and minimize episodes of hepatic encephalopathy (35). Furthermore, multiple feedings will reduce the volume of ingested food entering the colon, the site of bacterial fermentation, at a given time (10). Studies in humans with liver failure have shown that multiple small meals can improve nitrogen balance (36); therefore, there is good reason to suspect that the same might be true in dogs with liver disease.

In conclusion, it is of utmost importance to provide adequate nutrition during the nutrient sensitive growth period to support development of puppies. Many commercial foods have been formulated to meet the nutritional requirements for growth or have undergone feeding trials to demonstrate adequacy when fed to puppies. Unfortunately, growing animals are not immune to development of clinical conditions for which nutrient intake should be considered and modified. This poses a problem that can be challenging for pet owners and veterinarians when determining the best food to feed a growing dog that also has a medical condition necessitating the restriction of a nutrient essential for growth.

This case report featured a large breed puppy diagnosed with a PSS and requiring modification of dietary protein intake. It also highlights the importance of individualized nutritional management. Through careful consideration of key nutrients of concern and through feeding management strategies, a strategy was developed to meet the needs for optimal growth and correct a bone deformity from inappropriate nutrition. The diet was selected in this specific case to provide improved nutrition, balancing various nutritional goals, although this diet may not be considered appropriate for a healthy puppy. It is also important to note that since this time, changes to the diet formulation have been made and the growth claim no longer applies. Veterinary professionals must be aware that diet composition can change and a diet that seems appropriate today may not be appropriate under the same circumstances in the future. This solution also assisted in management of a PSS through elimination of all neurological signs until surgical correction was performed.

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### References

- 1. Case JB, Marvel SJ, Stiles MC, et al. Outcomes of cellophane banding or percutaneous transvenous coil embolization of canine intrahepatic portosystemic shunts. Vet Surg 2018;47:59-66.
- 2. Weisse C, Berent AC, Todd K, Solomon JA, Cope C. Endovascular evaluation and treatment of intrahepatic portosystemic shunts in dogs: 100 cases (2001-2011). J Am Vet Med Assoc 2014;244:78-94.
- 3. Nutritional Assessment Checklist. WSAVA Global Nutritional Toolkit. [homepage on the Internet] World Small Animal Veterinary Association c2013. Available from: https://www.wsava.org/WSAVA/ media/Arpita-and-Emma-editorial/Nutritional-Assessment-Checklist. pdf Last accessed April 12, 2021.
- 4. Body condition scoring charts. WSAVA Global Nutrition Toolkit. [homepage on the Internet] World Small Animal Veterinary Association c2013. Available from: https://www.wsava.org/nutrition-toolkit Last accessed April 12, 2021.
- 5. Association of American Feed Control Officials (AAFCO). Nutritional Adequacy and Substantiation. In: Pet Food Labelling Guide. Harrisburg, Pennsylvania: Association of American Feed Control Officials, 2016: 55-61.
- 6. United States National Research Council (US NRC). Energy. In: Nutrient Requirements of Dogs and Cats. Washington, DC: National Academies Press, 2006:28-35.
- 7. Debraekeleer J, Gross KL, Zicker SC. Feeding growing puppies: Postweaning to adulthood. In: Hand M, Thatcher C, Remillard R, Roudebush P, Novotny, eds. Small Animal Clinical Nutrition. 5th ed. Topeka, Kansas: Mark Morris Institute, 2010:311-319.
- 8. Laflamme DP. Development and validation of a body condition score system for dogs. Canine Pract 1997;22:10-15.
- 9. Howard MD, Kerley MS, Sunvold GD, Reinhart GA. Sources of dietary fiber fed to dogs affects nitrogen and energy balance and intestinal microflora populations. Nutr Res 2000;20:1473-1484.
- 10. Meyer HP, Twedt DC, Roudebush P, Dill-Macky E. Hepatobiliary disease. In: Hand M, Thatcher C, Remillard R, Roudebush P, Novotny, eds. Small Animal Clinical Nutrition. 5th ed. Topeka, Kansas: Mark Morris Institute, 2010:3-21.
- 11. Blei AT, Cordoba J. Hepatic encephalopathy. Am J Gastroenterol 2001;96:1968 - 1976.
- 12. Butterworth RF, Giguère JF, Michaud JF, Lavoie J, Lavrargues GP. Ammonia: Key factor in the pathogenesis of hepatic encephalopathy. Neurochem Pathol 1987;6:1-12.

- 13. Laflamme DP, Allen SW, Huber TL. Apparent dietary protein requirement of dogs with portosystemic shunt. Am J Vet Res 1993;54: 719-723.
- 14. Meyer HP, Chamuleau RA, Legemate DA, Mol JA, Rothuizen J. Effects of a branched-chain amino acid-enriched diet on chronic hepatic encephalopathy in dogs. Metab Brain Dis 1999;14:103-115.
- 15. Proot S, Biourge V, Teske E, Rothuizen J. Soy protein isolate versus meat-based low-protein diet for dogs with congenital portosystemic shunts. J Vet Intern Med 2009;23:794-800.
- 16. Richardson D, Zentek J. Nutrition and osteochondrosis. Vet Clin North Am Small Anim Pract 1998;28:115-135.
- 17. Daemmrich K. Relationship between nutrition and bone growth in large and giant dogs. J Nutr 1991;121:114-121.
- 18. Hazewinkel HAW, Vandenbrom WE, Van't Klooster AT, Voorhout G, Van Wees A. Calcium metabolism in Great Dane dogs fed diets with various calcium and phosphorous levels. J Nutr 1991;121:99-106.
- 19. Hazewinkel HAW, Goedegebuure SA, Poulos PW, Wolvekamp WTC. Influences of chronic calcium excess on the skeletal development of growing Great Danes. J Am Anim Hosp Assoc 1985;21:377-391.
- 20. Jenkins K, Phillips P.The mineral requirements of the dog. 2.The relation of calcium, phosphorus and fat levels to minimal calcium and phosphorus requirements. J Nutr 1960;70:241-246. 21. Jenkins K, Phillips P. The mineral requirements of the dog.
- 1. Phosphorus requirement and availability. J. Nutr 1960;70:235-240.
- 22. Lauten SD, Cox NR, Brawner WR, et al. Influence of dietary calcium and phosphorus content in a fixed ratio on growth and development in Great Danes. Am J Vet Res 2002;63:1036-1047.
- 23. Dobernecker B. Factors that modify the effect of excess calcium on skeletal development in puppies. Br J Nutr 2011;106:142-145.
- 24. Hazewinkel H, Tryfonidou M. Vitamin D3 metabolism in dogs. Mol Cell Endocrinol 2002;197:23-33.
- 25. Zentek J, Meyer H. Investigations on copper deficiency in growing dogs. J Nutr 1991;121:S83-S84.
- 26. Hedhammar A, Wu F, Krook L, et al. Overnutrition and skeletal disease. An experimental study in growing Great Dane dogs. Cornell Vet 1974;64:1-160.
- 27. Thatcher CD, Hand MS, Remillard RL. Small animal clinical nutrition: An iterative process. In: Hand M, Thatcher C, Remillard R, Roudebush P, Novotny, eds. Small Animal Clinical Nutrition. 5th ed. Topeka, Kansas: Mark Morris Institute, 2010:3-21.
- 28. Meyer H, Zentek J. Influence of various levels of energy-intake on development of body-weight and skeleton in growing Great Danes. 1. Growth-rate and energy requirement. J Vet Med A-Zentralblatt Veterinarmedizin 1992;39:130-141.
- 29. Meyer H, Zentek J. Energy requirements of growing Great Danes. J Nutr 1991;121:35-36.
- 30. Klein C, Thes M, Boswald LF, Kienzle E. Metabolisable energy intake and growth of privately owned growing dogs in comparison with official recommendations on the growth curve and energy supply. J Anim Physiol Anim Nutr 2019;103:1952-1958.
- 31. Bermingham EN, Thomas DG, Cave NJ, Morris PJ, Butterwick RF, German AJ. Energy requirements of adult dogs: A meta-analysis. PLoS ONE 2014;9:e109681.
- 32. Hawthorne AJ, Booles D, Nugent PA, Gettinby G, Wilkinson J. Body-weight changes during growth in puppies of different breeds. J Nutr 2004;134:2027-2030.
- 33. Salt C, Morris PJ, German AJ, et al. Growth standard charts for monitoring bodyweight in dogs of different sizes. PLoS ONE. 2017;12: e0182064.
- 34. Zentek J. Erkrankungen des Bewegungsapparates. Im: Ernährung des Hundes: Grundlagen-Fütterung-Diätetik. 8. Aufl., Enke, Stuttgart, 2016:259
- 35. Remillard RL, Saker KE. Nutritional management of hepatic conditions. In: Ettinger SJ, Feldman EC, eds. Textbook of Veterinary Internal Medicine. 6th ed. Vol 1. St. Louis, Missouri: Elsevier Saunders, 2005:574-576.
- 36. Swart GR, Zillikens MC, van Vuure JK, van den Berg JW. Effect of a late evening meal on nitrogen balance in patients with cirrhosis of the liver. BMJ 1989;299:1202.
- 37. von Dehn B. Pediatric clinical pathology. Vet Clin North Am Small Animal Pract 2014;44:205-219.