Linda FLEEMAN
BVSc, MACVSc

Jacquie RAND
BVSc (hons), DVSc,
Dipl ACVIM

Diabetes mellitus: nutricional strategies

Diabetes mellitus: nutritional strategies

Linda FLEEMAN
BVSc, MACVSc

Linda Fleeman graduated with honors from the University of Queensland and completed Clinical Residency training programs in Small Animal Medicine at both Murdoch University and the University of Melbourne in Australia. She is currently participating in a clinical PhD research project investigating the therapy and nutritional management of diabetes in dogs. She is currently Lecturer in Small Animal Medicine at the University of Queensland. Dr Fleeman is first author of a number of publications focusing on canine diabetes, and has lectured at many national and international conferences on this topic.

Jacquie RAND
BVSc (Hons), DVSc, Dipl ACVIM

Professor Rand graduated from the University of Melbourne (Australia) in 1975 and worked in private practice for 8 years before completing a residency and doctorate at the University of Guelph (Canada). She is currently Professor of Companion Animal Health at the University of Queensland and Director of the Centre for Companion Animal Health. Jacquie is recognized internationally as a leader in feline diabetes and nutrition research. She has authored over 100 articles, seventy abstracts and six textbook chapters. She currently has a team of 10 postgraduate students working in diabetes, obesity and nutrition research in companion animals.

Diabetes mellitus is a common endocrine disease of dogs and requires life-long therapy. Nutritional management is an important part of the treatment regimen and feeding guidelines based on evidence from well-designed clinical studies are essential. The first part of this chapter provides an understanding of the pathogenesis of diabetes in dogs, which is required before evaluation of issues relating to nutritional management. This allows comparison of the current, evidence-based, nutritional recommendations for human patients with types of diabetes analogous to canine diabetes. The second part reviews the available evidence from feeding studies in dogs and provides detailed analysis of the recommendations for dietary fiber, carbohydrate, fat, protein, and selected micronutrients in diabetic dogs. The final summary uses the American Diabetes Association grading system to rank the scientific basis of the nutritional recommendations for canine diabetes.

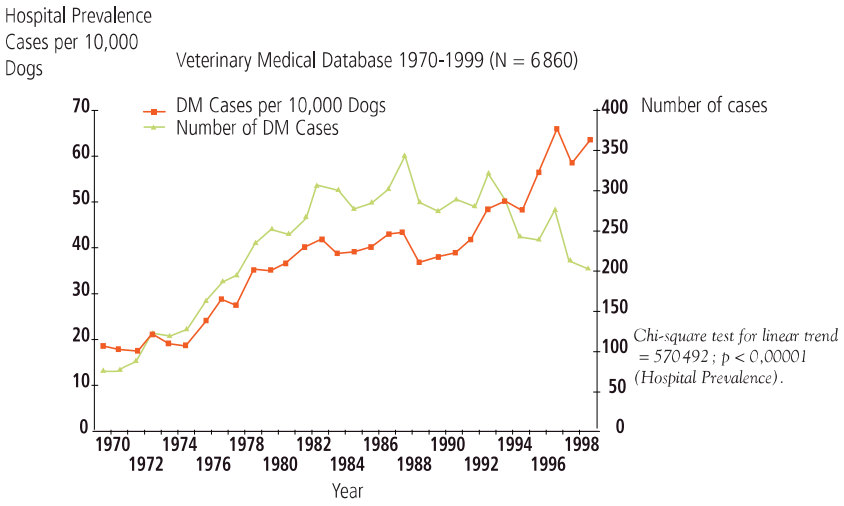
1 - Diabetes in dogs

► Prevalence of diabetes mellitus in dogs

Diabetes mellitus is one of the most frequent endocrine diseases affecting middle-aged and older dogs, and the prevalence is increasing. Thirty years ago, 19 in 10,000 dogs visiting veterinary hospitals were diagnosed with diabetes mellitus *(Marmor et al, 1982; Guptill et al, 2003)*. By 1999, the prevalence in the same veterinary hospitals had increased three-fold to 58 per 10,000 dogs **(Figure 1)** *(Guptill et al, 2003)*.

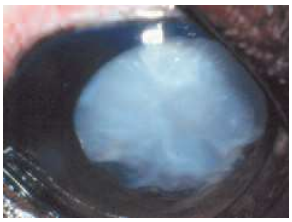
FIGURE 1 - INCREASING PREVALENCE OF CANINE DIABETES MELLITUS

Reprinted from Guptill et al, 2003, with permission from Elsevier.



Prevalence of DM increased over the study period. The number of institutions for which data are recorded is lower from 1995 to 1999 (16 institutions in 1994, 13 in 1995, 12 each in 1996-1997, 11 each in 1998-1999), therefore the number of cases per year is lower in these years.

FIGURE 2 - DIABETIC CATARACT ASSOCIATED WITH UVEITIS IN A DOG



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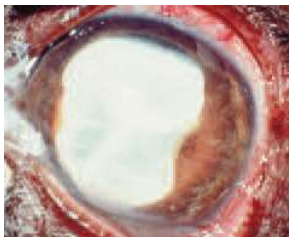
a: Advanced cataract in an aging dog. *Hyperemia is present in the sclera, indicating moderate uveitis.*



b: Severe uveitis in a diabetic dog. *The eye is red and painful, with the presence of mucopurulent ocular discharge and posterior synechia.*

► Clinical sequelae of diabetes in dogs

Insulin deficiency results in altered carbohydrate, fat, and protein metabolism. Abnormal carbohydrate metabolism manifests as hyperglycemia and glycosuria and is responsible for the polyuria, polydipsia, and cataract formation seen in diabetic dogs. The hyperlipidemia, ketone production, and hepatic changes seen in these dogs primarily results from altered fat metabolism. Decreased tissue utilization of glucose, amino acids, and fatty acids causes lethargy, weight loss, reduced stimulation of the satiety center, poor coat, and reduced immunity that is characteristic of untreated diabetic dogs.

> Cataract formation

Cataract formation is the most common, and one of the most important, long-term complications associated with diabetes in dogs *(Beam et al, 1999)* **(Figure 2)**. Cataracts are irreversible and can progress quite rapidly **(Figure 3)**. About 30% of diabetic dogs already have reduced vision at presentation *(Graham & Nash, 1997a)*. Cataracts will develop within 5-6 months of diagnosis in the majority of diabetic dogs and, by 16 months, approximately 80% will have significant cataract formation *(Beam et al, 1999)*. Importantly, the risk of cataract development seems to be unrelated to the level of hyperglycemia but increases with age *(Salgado et al, 2000)*. Thus, dietary manipulation is not likely to influence the rate or severity of cataract development in diabetic dogs.

FIGURE 3 - DEVELOPMENT OF DIABETIC CATARACTS IN A DOG
(From Fleeman & Rand 2000)

a: An eleven-year-old crossbred dog photographed shortly after diagnosis of diabetes mellitus.

b: The same dog three months after initial diagnosis of diabetes mellitus. Diabetic cataracts have rapidly developed and the dog's owner reported sudden vision loss.

c: The same dog following phacoemulsification surgery to remove the cataract from the right eye.

> Concurrent disease

Treated diabetic dogs have a similar chance of survival as compared to non-diabetic dogs of the same age and gender, although the hazard of death occurring is greatest during the first 6 months of therapy *(Graham & Nash, 1997b)*. Most diabetic dogs are middle-aged and older and are prone to diseases that commonly affect this age group. Consequently, many suffer concurrent problems that need to be managed in combination with the diabetes. For diabetic dogs receiving insulin therapy, the nutritional requirements of any concurrent disease may need to take precedence over the dietary therapy for diabetes. Regardless of the diet fed, glycemic control can still usually be maintained with exogenous insulin therapy.

If concurrent illness causes transient inappetence, it is generally advisable to administer half the usual insulin dose to reduce the risk of hypoglycemia. Diabetic dogs with a reduced appetite will often eat if they are hand-fed highly palatable food by their owner. If there is a more severe concurrent illness causing prolonged inappetence, diabetic dogs should be hospitalized for blood glucose concentration monitoring and treatment with a rapid-acting insulin preparation and intravenous fluids supplemented with glucose and potassium *(Feldman et al, 2004a)*.

► Insulin-induced hypoglycemia

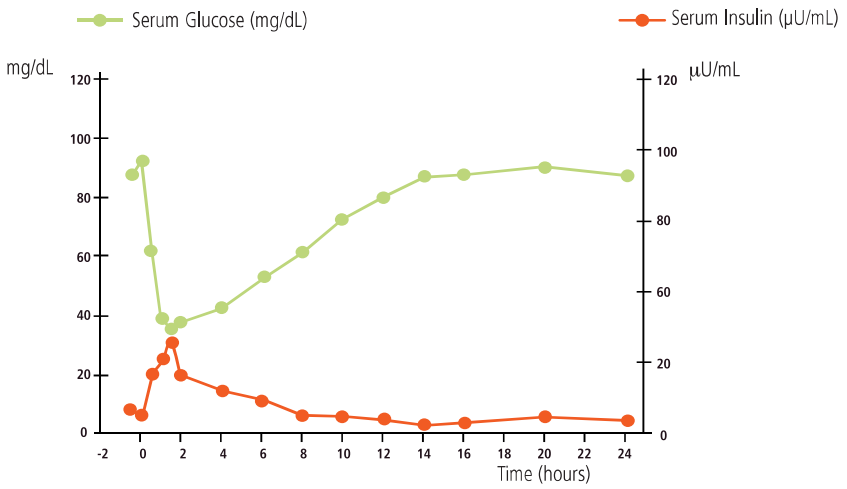
Severe hypoglycemia resulting from insulin overdose can cause irreversible brain damage and death, and avoidance of insulin-induced hypoglycemia is one of the primary aims of therapy in diabetic dogs. Dietary manipulation that reduces the risk of insulin-induced hypoglycemia affords important clinical benefit for diabetic dogs. Severe hypoglycemia has been reported in a diabetic dog that was fed ad libitum and received insulin at grossly irregular intervals *(Whitley et al, 1997)*. Commercial dog foods usually result in postprandial elevation of plasma glucose for less than 90 minutes following consumption by dogs *(Nguyen et al, 1998a)* and meals should ideally be timed so that maximal exogenous insulin activity occurs during the postprandial period *(Church, 1982)*. Thus, dogs should be fed within 2 hours of administration of lente insulin or within 6 hours of protamine zinc insulin *(Stenner et al, 2004)* **(Figure 4)**. In practice, a feasible compromise is to feed the dog immediately following the insulin injection. This considerably simplifies the home treatment regimen for most dog owners while still allowing good glycemic control to be readily achieved. In addition, many owners prefer this regimen because they feel their pet is rewarded for submitting to the injection.

Because the daily insulin-dosing regimen tends to be fixed for diabetic dogs, it is important that a predictable glycemic response is achieved following each meal. Ideally, every meal should contain the same ingredients and calorie content, and should be fed at the same time each day. It is crucial that the diet fed is palatable so that food intake is predictable. The major determinant of the postprandial glycemic response in dogs is the starch content of the meal *(Nguyen et al, 1998b)* so particular care should be applied to ensure consistent source and content of dietary starch.

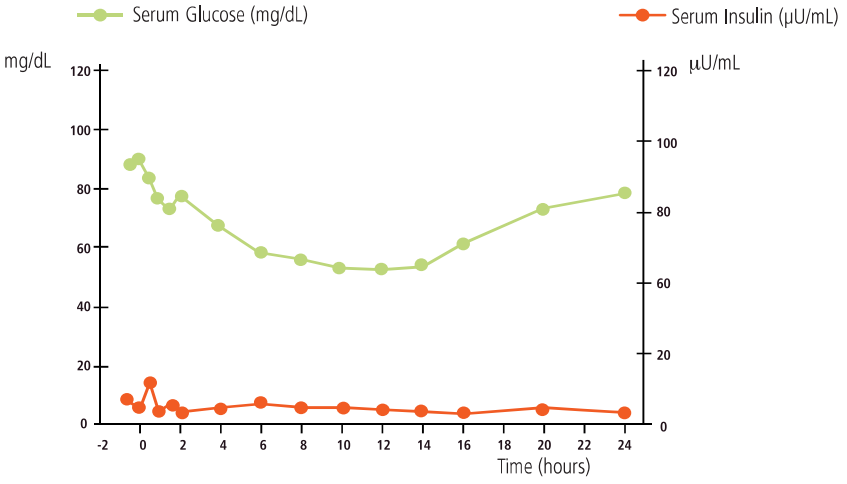
FIGURE 4 - PHARMACODYNAMICS AND PHARMACOKINETICS IN 9 HEALTHY, NON-DIABETIC DOGS FOLLOWING SUBCUTANEOUS INJECTION OF LENTE (CANINSULIN®, INTERVET) AND PROTAMINE ZINC INSULIN (PZI VET®, IDEXX) PREPARATIONS

(From Stenner et al, 2004)

Mean Serum Glucose and Insulin Concentrations vs Time in Lente Treated Dogs



Mean Serum Glucose and Insulin Concentrations vs Time in PZI Treated Dogs



For insulin-treated diabetic dogs, meals should ideally be timed so that maximal exogenous insulin activity occurs during the postprandial period. The pharmacodynamics and pharmacokinetics of two commercial veterinary insulin preparations, lente (Caninsulin®, Intervet) and protamine zinc insulin (PZI VET®, IDEXX), indicate that the maximal glucose-lowering effect occurs during the first 2 hours following subcutaneous administration for lente insulin, and within 6 hours of subcutaneous protamine zinc insulin injection. Commercial dog foods usually result in postprandial elevation of plasma glucose for less than 90 minutes following consumption, thus dogs should be fed within 30 minutes of administration of lente insulin or within 4.5 hours of protamine zinc insulin. A feasible compromise is to feed the dog immediately following the insulin injection. This considerably simplifies the home treatment regimen for most dog owners while still allowing good glycemic control to be readily achieved.

The importance of avoiding an insulin overdose cannot be over-emphasized. Every person in the diabetic dog's household needs to be aware of this life-threatening complication, which can rapidly develop into a serious emergency. If some insulin is spilt during the injection it should never be 'topped up', even if it appears that the dog has received no insulin. If the owner is ever uncertain about whether or not to give an insulin dose, the safest option is to withhold the injection, as the consequences of missing a single insulin dose are negligible. If mild signs of hypoglycemia develop, the owner should feed a meal of the dog's usual food. If the dog is unwilling or unable to eat, syrup containing a high glucose concentration can be administered orally. Suitable syrups are marketed for use by human diabetics. When the dog recovers, food should be fed as soon as possible. No more insulin should be given to the dog and the owner should discuss the case with a veterinarian before the next injection is due. A 50% reduction in insulin dose is usually recommended in these circumstances.

Successful management of 94% of diabetic dogs is achieved with twice-daily insulin dosing *(Hess & Ward, 2000)*. High doses of insulin and episodes of hypoglycemia are more common in diabetic dogs that receive insulin only once-daily *(Hess & Ward, 2000)*. Although treatment regimens comprising once-daily insulin injections are considered by some to be simpler and more convenient, most of these regimens involve feeding two meals each day, one soon after the insulin injection and another at the time of peak insulin activity about 8 hours later. Given the length of the usual working day, it may actually be more convenient for people to feed the second meal 12 hours after the first. Experienced owners rarely report any difficulty with the administration of insulin injections and, if they are required to be at home to feed the dog, it is little more effort to give the dog an insulin injection at the same time. As a result, many clinicians favor treatment regimens that involve administration of the same dose of insulin along with feeding of the same sized meal every 12 hours.

The owners of diabetic dogs should be aware that a consistent insulin-dosing and feeding routine is optimal. Conservative, fixed-dose, twice-daily insulin therapy, in conjunction with a palatable diet containing a consistent content and source of dietary starch, which is fed at defined times in relation to insulin administration, is likely to be associated with reduced risk of hypoglycemia in diabetic dogs.

► Pathogenesis of diabetes in dogs

The current classification of human diabetes mellitus is based on pathogenesis, and thus provides a rational foundation for understanding treatment issues. Adoption of these criteria for canine diabetes will afford a similar benefit for veterinarians. Human diabetes is divided into type 1, type 2, other specific types of diabetes, and gestational diabetes *(The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997)*. At present, there are no internationally accepted criteria for the classification of canine diabetes. If the criteria established for human diabetes were applied to dogs, at least 50% of diabetic dogs would be classified as type 1. The remainder are likely to have 'other specific types of diabetes' resulting from pancreatic destruction or chronic insulin resistance, or they have diestrus-induced diabetes.

> Type 1 diabetes

Evidence is mounting for a genetic basis for canine diabetes. An association with major histocompatibility complex alleles on the dog leukocyte antigen gene strongly suggests that the immune response has a role in the pathogenesis of diabetes mellitus *(Kennedy et al, 2003; Davison et al, 2003a; Rand et al, 2004)*.

Type 1 diabetes appears to be the most common form of diabetes in dogs, and is characterized by pancreatic beta cell destruction leading to absolute insulin deficiency. In people, this usually occurs via cell-mediated, autoimmune processes and is associated with multiple genetic predispositions and poorly defined environmental factors *(The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997)*. The majority of diabetic dogs have absolute insulin deficiency *(Montgomery et al, 1996)*. The etiology of beta cell destruction is often unknown, although there is evidence that in approximately 50% of diabetic dogs it is caused by immune-mediated processes similar to human type 1 diabetes *(Alejandro et al, 1988; Hoenig & Dawe; 1992; Davison et al, 2003a, 2003b)*.

Although genetic susceptibility appears to be a prerequisite, multiple environmental factors likely initiate beta cell autoimmunity, which once begun, then proceed by common pathogenic pathways *(Kukreja & Maclaren, 1999)*. Similar to canine diabetes, the incidence rate of type 1 diabetes in people is rising *(Onkamo et al, 1999)*, a trend that has been explained on the basis of increased contacts with adverse environmental factors *(Kukreja & Maclaren, 1999)*. There is a highly

significant seasonal incidence of diagnosis of both human type 1 diabetes (*Gamble & Taylor, 1969; Fleegler et al, 1979*) and canine diabetes (*Atkins & MacDonald, 1987*), with the incidence peaking in winter, indicating that environmental influences may have a role in disease progression just prior to diagnosis.

The rate of progression to absolute insulin deficiency is quite variable in human patients. It can be rapid in young children and much slower in middle-aged and older people. This latter group has the latent autoimmune diabetes of adults (LADA) form of type 1 diabetes, which is characterized by gradual beta cell destruction over months or years and is not associated with obesity (*Zimmet et al, 1994*). Distinct autoantibody patterns are recognized in the acute onset and slowly progressive (LADA) forms of human type 1 diabetes (*Zimmet et al, 1994; Seissler et al, 1998*), indicating a different pathogenesis for the two forms of the disease.

The rate of progression to absolute insulin deficiency has not been studied in dogs, but epidemiological factors closely match those of human patients with the LADA form of type 1 diabetes, who are usually not obese and tend to be middle-aged and older. Most affected dogs are over 7 years of age and the onset of clinical signs is typically insidious, ranging from weeks to months in duration (*Ling et al, 1977*). This has prompted speculation that there may also be similarities between the pathogenesis of canine diabetes and human LADA.

> Other types of canine diabetes

• *Association between diabetes and pancreatitis in dogs*

Extensive pancreatic damage, which likely results from chronic pancreatitis, is responsible for the development of diabetes in approximately 28% of diabetic dogs (*Alejandro et al, 1988*) and thus is the most common 'other specific type' of diabetes in dogs. Beta cell loss is being investigated in non-diabetic dogs with chronic pancreatitis and preliminary findings indicate that some have reduced beta cell function and appear to be pre-diabetic (*Watson & Herrtage, 2004*). Serum canine pancreatic lipase immunoreactivity (cPLI) is a sensitive marker for pancreatic inflammation in dogs (*Steiner, 2003*). Increases in serum cPLI concentration have been reported in 5 of 30 (17%) newly diagnosed diabetic dogs, although none of these dogs had serum cPLI concentrations above the diagnostic cut-off value for pancreatitis (*Davison et al, 2003b*).

In long-term diabetic dogs with no clinical evidence of exocrine pancreatic disease, serum cPLI concentrations in the diagnostic range for pancreatitis were found in 2 of 12 (17%) dogs, with a further 4 (33%) dogs recording increases in cPLI that did not reach the diagnostic cut-off value for pancreatitis, and an additional 2 (17%) dogs having laboratory evidence of exocrine pancreatic insufficiency (unpublished data). This indicates that subclinical exocrine pancreatic disease is common in diabetic dogs.

The association between canine diabetes and pancreatitis warrants particular attention because beta cell autoimmunity, pancreatic inflammation, and regulation of gut immunity might be linked in disease pathogenesis. The gut immune system likely plays a central role in the pathogenesis of human type 1 diabetes because accumulating evidence suggests that affected persons have aberrant regulation of gut immunity (*Vaarala, 1999, Akerblom et al, 2002*). The gut and the pancreas are probably immunologically linked, as well as anatomically linked, and influenced by environmental factors such as intestinal microflora, infections, and dietary factors (*Vaarala, 1999*).

Hypertriglyceridemia has been proposed as a possible inciting cause of canine pancreatitis (*Williams, 1994*) and is commonly seen in diabetic dogs (*Ling et al, 1977*). Obesity affects one-quarter to one-third of dogs presented to veterinary practices (*Edney & Smith, 1986*), and is also associated with an increased risk of pancreatitis (*Hess et al, 1999*). Environmental factors such as feeding high-fat diets, lipemia and disturbances in lipid metabolism, have been implicated as potential etiological factors in dogs with obesity-associated pancreatitis (*Simpson, 1993*), and

Adult Dachshund presenting an excess of weight
No epidemiological data examining the relationship between canine diabetes and obesity have been published since 1960 (Krook et al), *and an association between obesity and diabetes in dogs is not currently recognized.*

likely play a role in the development of pancreatitis in diabetic dogs. More detailed discussion on canine pancreatitis and hyperlipidemia can be found in chapters 5 and 7 of this encyclopedia.

• *Role of insulin resistance in canine diabetes*

Diabetes induced by insulin resistance states are less common 'other specific types' of canine diabetes.

Disease conditions such as hyperadrenocorticism *(Peterson, 1984)* and acromegaly *(Selman et al, 1994)* result in insulin resistance, and may induce diabetes in dogs. Iatrogenic causes of insulin resistance that might lead to induced diabetes include chronic corticosteroid therapy *(Campbell & Latimer, 1984)*. As most dogs do not develop overt diabetes with chronic corticosteroid therapy or spontaneous hyperadrenocorticism, for overt diabetes to develop it might require underlying reduced beta cell function resulting from immunological processes or chronic pancreatitis.

Although obesity causes insulin resistance in dogs, there are no published data clearly indicating that obesity is a risk factor for canine diabetes.
Obesity is a well-established risk factor for type 2 diabetes in cats and people. In contrast, there are no well-documented studies demonstrating convincingly that type 2 diabetes is a significant disease entity in dogs. In dogs, obesity causes insulin resistance *(Rocchini et al, 1999; Villa et al, 1999, Mittelman et al, 2002)*, which leads to hyperinsulinemia and impaired glucose tolerance *(Mattheeuws et al, 1984, Henegar et al, 2001)*. These effects are particularly pronounced when obesity is induced by feeding a diet high in saturated fat *(Truett et al, 1998)*. Dogs fed a high-fat diet develop insulin resistance that is not compensated for by increased insulin secretion, resulting in more severe glucose intolerance *(Kaiyala et al, 1999)*. Despite the evidence that obesity causes impaired glucose tolerance, it appears that very few dogs develop overt diabetes as a consequence of obesity-induced insulin resistance.

Diestrus- and gestation-associated diabetes

Gestational diabetes is another classification of diabetes recognized in human patients. In women, it is defined as any degree of glucose intolerance with onset or first recognition during pregnancy *(The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997)*. If overt diabetes persists after the pregnancy ends, then it is reclassified as type 1, type 2, or another specific type of diabetes. Reduced insulin sensitivity occurs in healthy bitches by day 30-35 of gestation *(McCann, 1983)* and becomes more severe during late pregnancy *(Concannon, 1986)*. The luteal phase of the non-pregnant cycle of the bitch is similar in duration to the 9 weeks of pregnancy and it is generally agreed that the hormone profiles during diestrus and pregnancy, are essentially identical *(Concannon et al, 1989; Feldman et al, 2004b)*. Progesterone elevation causes glucose intolerance and overt diabetes during diestrus in bitches *(Eigenmann et al, 1983, Scaramal et al, 1997)*. Progesterone also stimulates the mammary gland of bitches to produce growth hormone, which is a potent inducer of insulin resistance *(Selman et al, 1994)*.

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If diabetes is diagnosed in a bitch during either pregnancy or diestrus, it probably should be classified as being comparable to human gestational diabetes. If diabetes persists after pregnancy or diestrus ends, then it should be reclassified as type 1 or another specific type of diabetes.

The periodic influence of diestrus-associated insulin resistance might contribute to the increased risk of female compared with male dogs for developing diabetes *(Marmor et al, 1982; Guptill et al, 2003)*.

Classification of canine diabetes based on the current understanding of pathogenesis is summarized in **Table 1**.

TABLE 1 - CLASSIFICATION OF CANINE DIABETES MELLITUS BASED ON CURRENT UNDERSTANDING OF PATHOGENESIS

Form of canine diabetes mellitus	Analogous form of human diabetes mellitus	Estimated proportion of diabetic dogs	Pathogenesis	Clinical features
Type 1 diabetes	Latent Autoimmune Diabetes of Adults (LADA) form of type 1 diabetes	50%	• Autoimmune destruction of pancreatic beta cells • Genetic susceptibility related to the major histocompatibility complex on the dog leukocyte antigen gene • Most likely initiated in susceptible individuals by environmental factors that interact with gut immunity	• Middle-aged and older dogs • Not associated with obesity • Permanent, absolute insulin deficiency
Extensive damage from chronic pancreatitis	Other specific types of diabetes	30%	• Chronic pancreatitis causing widespread destruction of both endocrine and exocrine pancreatic tissue	• Onset of diabetes typically occurs many months before onset of exocrine insufficiency • Permanent, absolute insulin deficiency
Diabetes associated with insulin-resistant states	Other specific types of diabetes	20%	• Concurrent disease or therapy causing insulin resistance • Some dogs developing diabetes in association with insulin-resistant states might have underlying reduced beta cell function because of autoimmune destruction or chronic pancreatitis	• Occurs in dogs with insulin resistance, e.g. hyperadrenocorticism, corticosteroid therapy • Absolute or relative insulin deficiency
Diestrus-associated diabetes	Gestational diabetes	Prevalence dependent on proportion of intact bitches in the population	• Progesterone causes insulin resistance • Progesterone also stimulates growth hormone production by the mammary gland, which further contributes to insulin resistance • Might have underlying reduced beta cell function due to autoimmune destruction or chronic pancreatitis	• Occurs in intact bitches during diestrus or pregnancy • Absolute or relative insulin deficiency • Remission of diabetes is possible when diestrus or pregnancy ends
Not reported in dogs	Type 2 diabetes	0%	• Impaired insulin secretion and insulin resistance • Obesity is a risk factor • Although overt type 2 diabetes is not reported in dogs, the insulin resistance of obesity might have the potential to precipitate signs of overt diabetes in dogs with beta cell destruction associated with other forms of diabetes, such as chronic pancreatitis	-

► Nutritional perspectives based on pathogenesis of diabetes in dogs

Understanding the pathogenesis of diabetes in dogs provides a logical foundation for understanding issues relating to nutritional management of this disease. Recently, the American Diabetes Association released a position statement comprising a large meta-analysis presenting evidence-based nutrition principles and recommendations for the treatment and prevention of human diabetes *(Franz et al, 2002a)*. Consideration of the evidence-based recommendations for human patients with types of diabetes comparable to canine diabetes provides a rational perspective for dietary recommendations for diabetic dogs.

> Dietary carbohydrate and type 1 diabetes

Perspective gained from the dietary carbohydrate recommendations for human type 1 diabetics provide relevant perspective for canine diabetics because at least 50% of diabetic dogs appear to have analogous disease. Most relevant is perhaps the current recommendation regarding consumption of dietary fiber by human type 1 diabetics. After decades spent researching the effects of dietary fiber on the glycemic and lipemic responses of diabetic people, it is interesting that the current recommendation is that consumption of fiber is to be encouraged in all people and that those with type 1 diabetes require no more dietary fiber than non-diabetic people *(Franz et al, 2002a)*. This suggests that there might also be no clinical benefit of feeding a diet with increased levels of fiber to diabetic dogs compared with feeding 'typical', moderate-fiber diets formulated for adult maintenance.

With regard to the glycemic effects of carbohydrates, there is strong evidence in human diabetics that the total amount of carbohydrate in meals and snacks is more important than the source or type *(Franz et al, 2002a)*. Additionally, there is a strong association between the pre-meal insulin dosage required and the postprandial glycemic response to the carbohydrate content of the meal, regardless of the glycemic index, fiber, fat, or caloric content of the meal *(Franz et al, 2002a)*. As a regimen of fixed daily insulin dosages is typically used to manage diabetic dogs, it is rational to provide a consistent amount of carbohydrate in the meals fed each day.

> Dietary fat and type 1 diabetes

The primary goal regarding dietary fat in human patients with diabetes is to decrease intake of saturated fat and cholesterol to reduce the risk of coronary heart disease *(Franz et al, 2002a)*. As coronary heart disease is not recognized as a significant clinical entity in dogs, it might not be relevant to extrapolate dietary fat recommendations for human patients to diabetic dogs. For most human type 1 diabetics, effective insulin therapy returns serum lipid levels to normal and usually lowers plasma triglyceride concentrations *(Franz et al, 2002a)*. However, for obese individuals with type 1 diabetes, there is strong evidence that restricted intake of saturated fats, incorporation of monounsaturated fats into the diet, modest weight loss, and increased physical activity may be beneficial *(Franz et al, 2002a)*. The same recommendations might afford clinical benefit for obese diabetic dogs.

> Dietary protein and type 1 diabetes

The protein composition of the recommended diet for people with diabetes is the same as that recommended for the non-diabetic population *(Franz et al, 2002a)*. However, if microalbuminuria or persistent proteinuria develop, then protein restriction might help slow the progression of diabetic nephropathy in these people *(EASD, 1995)*.

> Diabetes with exocrine pancreatic disease

Approximately 60% of human type 1 diabetics have reduced exocrine pancreatic function and it is now recognized that diabetes secondary to exocrine pancreatic disease might be more frequent in people than previously realized *(Hardt et al, 2000)*. Despite this, no specific dietary recommendations are given in the current American Diabetes Association position statement regarding diabetic patients with concurrent exocrine pancreatic disease. Human diabetics with hypertriglyceridemia have increased risk of acute pancreatitis and current management recommendations include a fat-restricted diet *(Athyros et al, 2002)*.

> Dietary recommendations for gestational diabetes

In the supplemental American Diabetes Association position statement focusing on gestational diabetes *(Franz et al, 2002b)*, it is noted that restriction of dietary carbohydrate has been shown to decrease maternal postprandial glucose levels *(Major et al, 1998)*. Similarly, bitches with diestrus-associated insulin resistance might benefit from a carbohydrate-restricted diet. This would likely reduce postprandial blood glucose fluctuations, helping to alleviate the hyperinsulinemia associated with diestrus, thus preserving beta cell function and reducing the risk of overt diabetes. There is some evidence that reduced intake of total fat, particularly saturated fat, in people might improve insulin sensitivity and reduce the risk for insulin resistance-associated diabetes *(Franz et al, 2002a)*. Potentially, feeding a fat-restricted diet to bitches with diestrus-associated insulin resistance might improve insulin sensitivity and reduce the risk of overt diabetes. As both fat and carbohydrate restriction may be recommended for these animals, a high-protein diet is a rational choice.

Importantly, nutrient-restricted diets should never be recommended for pregnant bitches unless there is strong scientific evidence for both maternal and fetal benefit.

> Dietary recommendations for older diabetics

There are no evidence-based nutritional recommendations for aging diabetic persons and they must be extrapolated from what is known for the general population *(Franz et al, 2002a)*. There is strong evidence that energy requirements for older adults are less than those for younger adults, however it is pointed out that under-nutrition is more likely than over-nutrition in elderly people. Therefore, caution should be exercised when prescribing weight-loss diets *(Franz et al, 2002a)*.

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There are no evidence-based nutritional recommendations for aging diabetic dogs. Caution should be exercised when prescribing low-calorie diets to older dogs because this might result in excessive loss of body condition.

TABLE 2 - WHAT TO FEED DIABETIC DOGS: EVIDENCE RANKING SYSTEM

System used to rank scientific evidence on feeding recommendations for diabetic dogs	
1. Highest ranking	Randomized, controlled, clinical trials in diabetic dogs
	Other clinical trials in diabetic dogs
	Randomized, controlled clinical trials in non-diabetic dogs
4. Lower ranking	Expert opinion, clinical experience, and pathophysiological rationale

2 - What to feed diabetic dogs

► Evidence-based approach

Recommendations for feeding diabetic dogs should ideally be based on evidence provided by results of randomized, controlled clinical trials that clearly document significant clinical value of the test diet. Whenever this is lacking, clinicians must assess the best evidence that is available and interpret this in the light of expert clinical experience and knowledge of current pathophysiological concepts.

To assist this process, evidence in the following review has been ranked into categories **(Table 2)**:

1. Randomized, controlled, clinical trials in diabetic dogs
2. Other clinical trials in diabetic dogs
3. Randomized, controlled, clinical trials in non-diabetic dogs
4. Expert opinion, clinical experience, and pathophysiological rationale

► General goals of nutritional therapy for diabetic dogs

- ***Evidence based on expert opinion, clinical experience, and pathophysiological rationale***

The diet of diabetic dogs should provide adequate calories to achieve and maintain optimal body condition. Dogs with poorly controlled diabetes have a decreased ability to metabolize the nutrients absorbed from their gastrointestinal tract and lose glucose in their urine and so may require more calories for maintenance than healthy dogs. The diet fed should be nutritionally balanced and needs to be palatable so that food intake is predictable. Meals should ideally be timed so that maximal exogenous insulin activity occurs during the postprandial period *(Church, 1982)*. Because the daily insulin-dosing regimen tends to be fixed for diabetic dogs, it is also important that a predictable glycemic response is achieved following each meal. Consequently, every meal should contain roughly the same ingredients and calorie content, and should be fed at the same time each day. **The owners of diabetic dogs should be aware that a consistent insulin-dosing and feeding routine is optimal.**

► Dietary fiber and canine diabetes

> Total dietary fiber

- ***Evidence based on various clinical trials in diabetic dogs***

Some studies in diabetic dogs have indicated that high-fiber diets might be associated with improved glycemic control. However, these studies have compared high-fiber (56-73 g/1000kcal and 15%DM) with lower-fiber (16-27 g/1000 kcal) diets without including comparison with a control diet formulated for typical canine adult maintenance. Thus, there has not been a clear demonstration of clinical benefit for diabetic dogs fed a high-fiber formulation compared with feeding a typical adult maintenance diet.

Additionally, low-fiber diets typically contain increased dietary starch content, which might be a confounding factor when comparing the glycemic responses of diabetic dogs to high- and low-fiber diets. Regardless of the composition of the high-fiber diet or the length of time over which the diabetic dogs were monitored, no significant difference in daily insulin requirement *(Nelson*

et al, 1991; Graham et al, 1994; Nelson et al, 1998, 2000; Kimmel et al, 2000; Graham et al, 2002) or fasting triglyceride levels *(Nelson et al, 1991, 1998; Graham et al, 2002)* between groups of diabetic dogs fed low-fiber and high-fiber diets has been found.

Importantly, there seems to be marked variation between the responses of individual diabetic dogs to dietary fiber. In one study *(Nelson et al, 1998)*, significant improvement of all indices of glycemic control, including lowered daily insulin requirement, was seen in 9 of 11 dogs when they were fed a high-fiber diet (64.4g/1000kcal). The remaining 2 dogs were found to have improved glycemic control on the lower-fiber diet (27.0g/1000kcal or 11% in 4000kcal/kg of food).

In another study of 12 diabetic dogs *(Nelson et al, 2000)*, glycemic control was best in 6 dogs when fed a soy-based, moderate-fiber diet (total dietary fiber 8% DMB), in 4 dogs when fed a cellulose-based, high-fiber diet (total dietary fiber 16% DMB), in 1 dog when fed a cellulose-based, moderate-fiber diet (total dietary fiber 8% DMB), and glycemic response to diet could not be ranked in the remaining dog. A similar situation exists for people because high-fiber diets do not have a uniform effect in all diabetic subjects *(EASD, 1988)*. This might be partly due to the side effects that are sometimes associated with high-fiber diets, which include poor palatability, poor weight gain, poor hair coat, vomiting, voluminous feces, flatulence, diarrhea, and constipation. Individual tolerance to dietary fiber is dependent on a large number of factors, including the quality and type of the fiber.

- ***Evidence based on a randomized, controlled, clinical trial in diabetic dogs***

A randomized, controlled, trial was performed to assess the influence of canned, high-fiber, moderate-starch diets on insulin requirement and glycemic control in dogs with stabilized diabetes *(Fleeman & Rand, 2003)*. The two trial diets had high-fiber (50g/1000kcal) and moderate-starch (26% ME) content, but varied in fat content (31% ME and 48% ME). The control diet was a commercial dog food formulated for adult maintenance with moderate-fiber (35g/1000kcal), low-starch (2.3% ME), and higher fat (61% ME) content.

Diabetic control evaluated every 2 weeks included history, physical examination, and 2-hourly blood glucose measurements over 12 hours. Insulin dose was adjusted based on standardized criteria to maintain control of glycemia. At the end of each 2 month feeding period, glycemic control was evaluated by plasma fructosamine, glycosylated hemoglobin, and 48 hour serial blood glucose measurements. No significant differences in insulin requirement or glycemic response among diets were found. It was concluded that, for stable diabetic dogs, high-fiber, moderate-starch diets offer no significant advantage for insulin requirement or glycemic control compared with a commercial diet formulated for adult maintenance with moderate-fiber and low-starch content.

> Different types of dietary fiber

- ***Evidence based on pathophysiological rationale***

Soluble fiber: Dietary fiber can be characterized by degree of solubility, which is a reflection of its properties in an aqueous media. Soluble fiber, as provided by guar gum and psyllium, has great water-holding capacity, and forms a viscous solution in the intestine.

Dogs fed diets with increased viscosity might have more rapid postprandial glucose absorption, resulting in higher total postprandial glucose absorption and are more likely to develop secretory diarrhea than dogs fed diets with lower viscosity *(Nelson & Sunvold, 1998b)*.

This suggests that only diets with an intermediate viscosity (solubility) level might be associated with a delay in gastrointestinal transit time and optimal glucose homeostasis in dogs.
Soluble fiber, with the exception of psyllium, is usually also fermentable fiber.

Psyllium grains
The outer husk is high in non-fermentable mucilage that is soluble in water.

Fermentable fiber: Dietary fiber can be characterized by degree of fermentability, as well as solubility. Fermentable fiber is readily degraded by colonic microflora in dogs to produce short-chain fatty acids that are absorbed across the intestinal mucosa.

Fermentable dietary fiber is associated with increased intestinal glucose transport capacity, increased glucagon-like-peptide-1, and increased insulin secretion in non-diabetic dogs *(Massimino et al, 1998)*. **The overall effect is a significant reduction of the area under the blood glucose concentration versus time curve during oral glucose tolerance testing. As diabetic dogs lack the capacity to increase insulin secretion and match increased intestinal glucose transport, it needs to be investigated whether they benefit from diets containing high levels of fermentable fiber or whether these diets may actually contribute to glucose intolerance.**

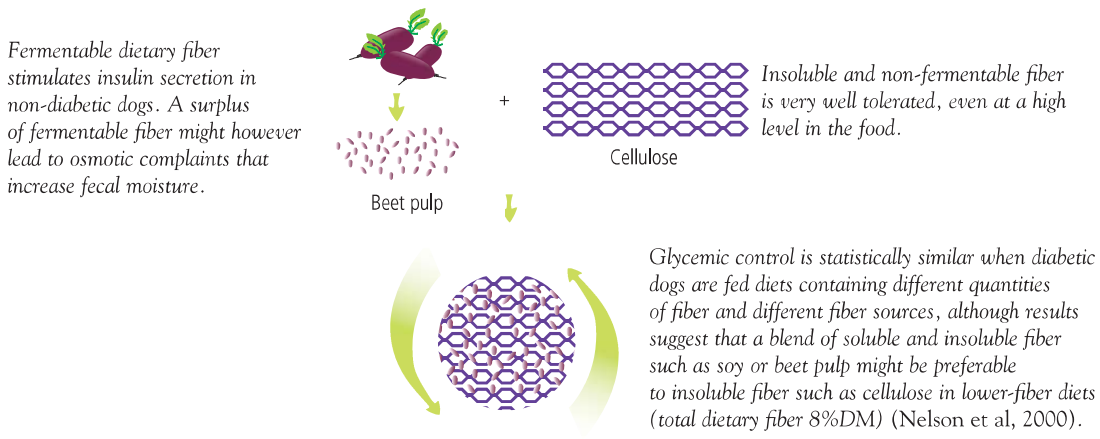
Insoluble, non-fermentable fiber: Dogs cannot digest the insoluble fiber component of their diet and it is excreted in the feces. In contrast to soluble fiber, **insoluble fiber such as purified cellulose seems to exert relatively little physiological effect in the canine gut and can be tolerated in fairly high dietary levels** *(Bauer & Maskell, 1995)*.

- ***Evidence based on a randomized, controlled, trial in non-diabetic dogs***

A randomized controlled evaluation in non-diabetic dogs of the effects of diets containing different fiber types (highly-soluble, highly-fermentable guar gum, poorly-soluble, poorly-fermentable cellulose, and mixed soluble-insoluble, moderately-fermentable sugar beet pulp fiber) at three different dietary concentrations has helped to clarify some of the issues relating to the putative glucoregulatory effects of dietary fiber in dogs *(Hoenig et al, 2001)* **(Figure 5)**. The different test diets were obtained by substituting 3.5%DM of cornstarch in the control diet with the fiber sources mentioned above. The total dietary fiber level varied between 4.9% and 17.2%DM *(Hoenig et al, 2001)*.

Compared with the control diets (total dietary fiber 3.5% and 4.4%DM), **there were no significant differences in physical findings, serum glucose and insulin concentrations during oral glucose tolerance testing, serum triglyceride concentrations, or cholesterol content of HDL, LDL, and VLDL associated with feeding any of the fiber-modified diets. The only significant findings were that total serum cholesterol concentrations were lower in dogs fed sugar beet fiber and higher in dogs fed cellulose fiber, compared with control diets. Although it was not objectively measured, it was noted that the dogs' coat hairs seemed to become dull and lusterless when they consumed the fiber-modified diets.**

FIGURE 5 - A MIXTURE OF BEET PULP AND CELLULOSE (BRAN)



The authors proposed that this might have been due to an inhibitory effect of fiber on the absorption of minerals and vitamins.

- ***Evidence based on various clinical trials in diabetic dogs***

When dogs were fed a single meal containing added soluble fiber or added insoluble fiber, a greater reduction of postprandial hyperglycemia was seen with the meal containing soluble fiber *(Blaxter et al, 1990)* although the dietary fiber composition of the diets was not reported and were probably not comparable *(Davis, 1990)*.

When comparisons were made following long-term feeding for 1 or 2 months of diets high in soluble fiber or insoluble fiber (34g/1000kcal soluble fiber versus 60g/1000kcal insoluble fiber) *(Nelson et al, 1991)*; 10g/1000kcal soluble fiber versus 73g/1000kcal insoluble fiber *(Kimmel et al, 2000)*), a tendency for improved glycemic control and fewer side effects was seen with the diets containing increased insoluble fiber. In particular, significantly lower glycosylated hemoglobin *(Nelson et al, 1991)* or fructosamine *(Kimmel et al, 2000)* levels were recorded. The current evidence regarding dietary fiber and canine diabetes mellitus is summarized in **Table 3**.

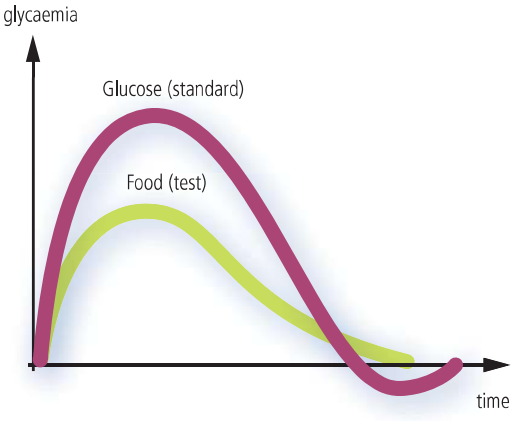
TABLE 3 - SUMMARY OF CURRENT EVIDENCE REGARDING DIETARY FIBER AND CANINE DIABETES MELLITUS

Perspective gained from current, evidence-based, dietary fiber recommendations for human type 1 diabetics	• Meta-analysis of all available evidence reveals that people with type 1 diabetes require no more dietary fiber than non-diabetic people
Evidence-based recommendations regarding canine diabetes and total dietary fiber	• There has been no clear demonstration of clinical benefit for diabetic dogs of feeding high-fiber formulations compared with feeding typical adult maintenance diets • Regardless of the composition of the high-fiber diet or the length of time over which the diabetic dogs were monitored, no significant difference in insulin requirement between groups of diabetic dogs fed low-fiber and high-fiber diets has been found • Some diabetic dogs might have improved glycemic control when fed diets with increased fiber content, although there is marked variation among the responses of individual dogs to dietary fiber
Evidence-based recommendations regarding the type of dietary fiber fed to diabetic dogs	• For non-diabetic dogs, there are no significant differences in physical findings, serum glucose and insulin concentrations during oral glucose tolerance testing, serum triglyceride concentrations, or cholesterol content of HDL, LDL, and VLDL associated with feeding diets containing different quantities of fiber and fiber sources • In diabetic dogs fed high-fiber diets, there is a tendency for improved glycemic control and fewer side effects when diabetic dogs are fed diets containing increased insoluble fiber, compared with increased soluble fiber • In diabetic dogs fed moderate-fiber diets, a blend of soluble and insoluble fiber such as soy or beet pulp might be preferable to insoluble fiber alone (such as cellulose)
Summary	• The most suitable dietary fiber recommendation for diabetic dogs might be moderate-fiber formulations (for example, 35 g/1000kcal) containing a blend of soluble and insoluble fiber, such as soy or sugar beet pulp • Further research is required to demonstrate clinical benefit of this formulation for diabetic dogs compared with typical commercial dog foods formulated for adult maintenance

FIGURE 6 - WHAT IS THE GLYCEMIC INDEX ?

Amount of food, equivalent to 50 g carbohydrate
-eaten within 13 minutes
Blood glucose levels are measured in the next 2 to 3 hours:
measurement of the Area Under the Curve (AUC)
Trial replicated with 8 - 10 individuals
Glycaemic Index (GI) = Ratio of curve integrals compared to a control (Glucose = 100%)

Classification:
< 55 : low GI
Between 55 and 70: medium GI
> 70 : high GI



In man, GI does not necessarily represent a practical guide for evaluating foods because data can be in conflict depending on the composition of the meal, the processing method, cooking, etc. Answers can also vary amongst individuals. In animals, results are more reliable because the diet can be better controlled.

► Dietary carbohydrate and canine diabetes

> Total dietary carbohydrate

- ***Evidence based on randomized trials in non-diabetic dogs***

The amount of starch in the diet has been shown to be the major determinant of the postprandial glycemic response of healthy dogs across 15 typical commercial dog foods (dietary starch 0.4-52.7% DMB), regardless of the carbohydrate source or type, or of the composition profile of other macronutrients *(Nguyen et al, 1998b)*. Although similar studies have not been performed in diabetic dogs, there is very good evidence in diabetic people for a strong association between the insulin dosage requirement and the carbohydrate content of the meal, regardless of the glycemic index **(Figure 6)**, the carbohydrate source or type, or the composition profile of other macronutrients *(Franz et al, 2002a)*. The same might be true for diabetic dogs.

> Different types of dietary carbohydrate

- ***Evidence based on physiological rationale***

The postprandial glycemic response to dietary carbohydrate might be potentially influenced by the type of carbohydrate and by the way it has been processed. Digestion of dietary carbohydrate occurs in the small intestine of dogs and results in the breakdown of starch to glucose, fructose, and galactose. The postprandial glycemic response is directly dependent on the absorption of glucose, because fructose and galactose require hepatic metabolism for conversion to glucose. Thus, the type of starch contained in the dietary carbohydrate fed might influence the postprandial glycemic response. Carbohydrate sources that predominantly breakdown to glucose during digestion are likely to result in the greatest postprandial glycemic response.

The digestibility of whole cereal grains (in this case rice) is lower than that of the same cereal ground into meal.

Studies assessing the digestibility in dogs of different dietary carbohydrate substrates *(Murray et al, 1999; Bednar et al, 2000; Twomey et al, 2002)*, have found that the processing method as well as the carbohydrate source significantly influences digestibility *(Bednar et al, 2000)*. For example, barley flour is approximately five times more digestible in dogs compared with barley grain, while rice flour is almost ten times more digestible than white rice grain *(Bednar et al, 2000)*. When commercial dog foods are formulated, the dietary starch is usually in the form of flours prepared using a combination of roller milling, sieving, and steam cooking *(Murray et al, 1999)*. The extrusion process then tends to gelatinize the starch and make it even more digestible *(Camire, 1998)*, so that starch digestibility is essentially 100% for most carbohydrate sources included in commercial dry dog foods *(Murray et al, 1999; Twomey et al, 2002)*. **There is some evidence that the gelling agents used in canned commercial dog foods may similarly increase digestibility** *(Karr-Lilienthal et al, 2002)***. Thus, for most commercial dog foods, processing effects likely have minimal influence on the postprandial glycemic response and the major potential influence on the postprandial glycemic response is likely the dietary carbohydrate source.**

- ***Evidence based on a randomized trial in non-diabetic dogs***

Little is known about the glycemic responses of diabetic dogs to different sources of dietary carbohydrate. However, a study in non-diabetic dogs that examined the postprandial effects of five diets with equivalent starch content (30% DMB) from different cereal sources found marked differences in the glucose and insulin responses (*Sunvold & Bouchard, 1998; Bouchard & Sunvold, 2001*). **The rice-based diet resulted in significantly higher postprandial glucose and insulin responses. Sorghum generally caused the lowest postprandial glucose response while barley produced the lowest insulin response.** These findings form an interesting basis for future study on the effects of diets containing sorghum in diabetic dogs, but more work is required before specific recommendations can be made. Caution is required when extrapolating the results of dietary carbohydrate studies in non-diabetic dogs to clinical recommendations for diabetic dogs. This is because all diabetic dogs require exogenous insulin therapy, which has an overwhelming effect on carbohydrate metabolism and the postprandial glycemic response. It is also worth noting that studies in people have found a marked variability in the glycemic response to different types of barley (*Liljeberg et al, 1996*) and rice (*Jarvi et al, 1995*). The same is likely true for dogs.

The current evidence regarding dietary carbohydrate and canine diabetes mellitus is summarized in **Table 4**.

TABLE 4 - SUMMARY OF CURRENT EVIDENCE REGARDING DIETARY CARBOHYDRATE AND CANINE DIABETES MELLITUS

Perspective gained from current, evidence-based, dietary carbohydrate recommendations for human type 1 diabetics	• Meta-analysis of all available evidence reveals a very strong association between the insulin dosage requirement and the carbohydrate content of the meal, regardless of the glycemic index, the carbohydrate source or type, or the composition profile of other macronutrients
Evidence-based recommendations regarding canine diabetes and total dietary carbohydrate	• For non-diabetic dogs, the amount of starch in the diet has been shown to be the major determinant of the postprandial glycemic response across a wide range of typical commercial dog foods (dietary starch 0.4-52.7% DMB), regardless of the carbohydrate source or type, or of the composition profile of other macronutrients
Evidence-based recommendations regarding the type of dietary carbohydrate fed to diabetic dogs	• For most commercial dog foods, processing effects likely have minimal influence on the postprandial glycemic response and the major potential influence is likely the dietary carbohydrate source • In non-diabetic dogs, a sorghum-based diet generally resulted in the lowest postprandial glucose response • In non-diabetic dogs, a barley-based diet produced the lowest postprandial insulin response • In non-diabetic dogs, a rice-based diet resulted in significantly higher postprandial glucose and insulin responses
Summary	• As a regimen of fixed daily insulin dosages is typically used to manage diabetic dogs, it is rational to provide a very consistent amount of carbohydrate in the meals fed each day • Rice should be avoided in diets for diabetic dogs, while sorghum and barley are likely more suitable carbohydrate sources • Further research is required to demonstrate clinical benefit of these formulations for diabetic dogs and bitches in diestrus, compared with typical commercial dog foods formulated for adult maintenance

► Dietary fat and canine diabetes

> Evidence based on expert opinion, clinical experience, and pathophysiological rationale

Altered lipid metabolism occurs with insulin deficiency in dogs, yet there are minimal published data on the influence of dietary fat on diabetic dogs. In human patients, the lipid disorders that occur in association with diabetes are atherogenic and predispose to coronary artery disease *(Stamler et al, 1993)*. Restricted-fat diets reduce cardiovascular morbidity and mortality in diabetic people. Although atherosclerosis and coronary artery disease are not usually a clinical concern in diabetic dogs, atherosclerosis does occur in association with spontaneous canine diabetes *(Sottiaux, 1999; Hess et al, 2003)*. Perhaps of greater clinical relevance is that diabetes secondary to exocrine pancreatic disease appears to be common in dogs, and the diabetic state might also be a risk factor for pancreatitis. High-fat diets and hypertriglyceridemia have been proposed as possible inciting causes of canine pancreatitis *(Simpson, 1993; Williams, 1994)*. Low-fat diets (for example fat < 20% ME) are recommended for dogs with chronic pancreatitis. As it can be difficult to identify those diabetic dogs with subclinical pancreatitis *(Wiberg et al, 1999)*, **it might be prudent to consider feeding a restricted-fat diet (for example fat< 30% ME) to all diabetic dogs**. This might have the added benefit of improving insulin sensitivity in animals with insulin resistance-associated diabetes and reducing the risk of overt diabetes in bitches during diestrus. However, greater levels of energy restriction might lead to undesirable weight loss

> Evidence based on a randomized, controlled, clinical trial in diabetic dogs

The same randomized, controlled trial that assessed the influence of canned, high-fiber, moderate-starch diets on insulin requirement and glycemic control of dogs with stabilized diabetes also assessed the influence of dietary fat *(Fleeman & Rand, 2003)*. Different amounts of dietary fat in the high-fiber (50 g/1000 kcal), moderate starch (26 % ME) diets had no significant influence on insulin requirement or glycemic control of the dogs. Lower dietary fat content (31% ME compared with 48% ME) was associated with significantly improved lipid profiles. The low fat, high fiber, moderate starch diet resulted in significantly lower mean total cholesterol concentration compared with either of the other diets, and significantly lower mean glycerol and free fatty acids than the commercial diet. It is unknown whether any health benefits for dogs might be attributed to these improvements in the lipid profile. Significant weight loss occurred when the dogs were fed the low-fat, high-fiber, moderate-starch diet, whereas maintenance of weight was achieved with both of the other diets. It was concluded that **diets with lower fat content may result in improved lipid profiles in diabetic dogs, but might contribute to undesirable weight loss.** Therefore, restricted-fat diets should not routinely be recommended for diabetic dogs with thin body condition.

The current evidence regarding dietary fat and canine diabetes mellitus is summarized in **Table 5**.

► Dietary protein and canine diabetes

> Evidence based on pathophysiological rationale

The optimal dietary protein for diabetic dogs has not been determined and **it is rational that recommendations would be no different than for non-diabetic dogs.** As restriction of dietary carbohydrate might reduce postprandial hyperglycemia in diabetic dogs and dietary fat restriction might be beneficial if there is concurrent pancreatitis, there will be a tendency for suitable diets to have higher protein levels (>30%ME).
Microalbuminuria and proteinuria do occur in diabetic dogs *(Struble et al, 1998)* and lower dietary protein intake may be indicated in diabetic dogs with microalbuminuria.

► Dietary L-carnitine and canine diabetes

> Evidence based on pathophysiological rationale

TABLE 5 - SUMMARY OF CURRENT EVIDENCE REGARDING DIETARY FAT AND CANINE DIABETES MELLITUS

Perspective gained from current, evidence-based, dietary fat recommendations for human type 1 diabetics	• The primary goal regarding dietary fat restriction in human diabetics is to reduce the risk of coronary heart disease • As coronary heart disease is not recognized as a significant clinical entity in dogs, it might not be relevant to extrapolate dietary fat recommendations for human patients to diabetic dogs
Evidence-based recommendations regarding canine diabetes and dietary fat	• Diabetes secondary to exocrine pancreatic disease appears to be common in dogs, and the diabetic state might also be a risk factor for pancreatitis. As low-fat diets (for example fat< 20% ME) are recommended for dogs with chronic pancreatitis, in addition, since it can be difficult to identify those diabetic dogs with subclinical pancreatitis, it might be prudent to consider feeding a fat-restricted diet (for example fat< 30% ME) to all diabetic dogs • However, results of a randomized, controlled clincial trial in diabetic dogs indicate that diets with lower fat content (31% ME compared with 48% ME) may result in improved lipid profiles but may contribute to undesirable weight loss
Summary	• Although evidence of clinical benefit of feeding fat-restricted diets (< 30% ME) to diabetic dogs is lacking, this option may be considered for diabetic dogs with concurrent pancreatitis • To avoid undesirable weight loss, restricted-fat diets (< 30% ME) should not routinely be recommended for diabetic dogs in poor body condition

L-Carnitine is a conditionally essential, vitamin-like nutrient that plays a pivotal role in fatty acid metabolism. Supplemental L-Carnitine suppresses acidosis and ketogenesis during starvation in dogs *(Rodriguez et al, 1986)*. L-Carnitine supplementation at 50 ppm of diets fed to dogs enhances energy conversion from fatty acid oxidation and protects muscles from catabolism during weight loss *(Gross et al, 1998; Sunvold et al, 1999; Center, 2001)*. Dogs with poorly controlled diabetes experience weight loss, altered fat metabolism, ketogenesis, and hepatic changes, and so are likely to benefit from dietary L-carnitine supplementation. The majority of diabetic dogs are middle-aged and older and can be expected to already have reduced lean body mass *(Kealy et al, 2002)* before the onset of diabetes-associated weight loss. Consequently, it is important to consider any dietary intervention, such as L-carnitine supplementation, that promotes maintenance of lean body mass in these animals.

► Dietary chromium and canine diabetes

> Evidence based on pathophysiological rationale and a controlled clinical trial in diabetic dogs

Chromium tripicolinate is a dietary mineral supplement that has been shown to increase the clearance rate of glucose from the blood by approximately 10% in healthy dogs *(Spears et al, 1998)*. However this potential benefit is only possible if there is chromium deficiency because chromium is a nutrient, not a drug. Thus, supplementation may only result in benefits if the individual is deficient or marginally deficient in chromium.

It is now clear that dietary chromium levels of people in industrialized countries are sub-optimal *(Anderson, 1998)*. Similar information is not available for dogs and further studies are warranted to try and establish the minimum recommended dietary chromium intake for healthy dogs.

Chromium is thought to potentiate insulin's ability to store glucose and would theoretically be useful in dogs with insulin resistance or as an adjunct to exogenous insulin therapy. It is also possible that inadequate dietary intake of chromium by dogs might increase their risk of developing

diabetes. It has been postulated that some insulin-dependent diabetic people might lose their ability to convert inorganic chromium to the biologically active form and might actually need to consume foods that contain active forms of chromium *(Anderson, 1992)*. At this stage, there is little information available on the effects of chromium supplementation in human patients requiring insulin therapy *(Ravina et al, 1995; Fox et al, 1998)*. Supplementation with chromium picolinate capsules has not been found to improve glycemic control in insulin-treated dogs *(Schachter et al, 2001)*. The influence of chromium supplementation on bitches with diestrus-induced insulin resistance is unknown.

Dietary chromium supplements usually contain low molecular weight chromium salts such as trivalent chromium [Cr(III)], which has a large safety margin but can be toxic at very high doses *(Jeejeebhoy, 1999)*. In contrast, oral hexavalent chromium [Cr(VI)] appears to be 10-100 times more toxic than trivalent chromium compounds and is an unsuitable dietary supplement *(Katz & Salam, 1993)*.

Summary of dietary recommendations for canine diabetics

The American Diabetes Association uses a grading system to rank the scientific principles of their nutritional recommendations.
- The highest ranking, Grade A, is assigned when there is supportive evidence from multiple, well-conducted studies
- Grade B is an intermediate rating
- Grade C is a lower ranking
- Grade E represents recommendations based on expert consensus.

If this grading system is used to rank the scientific basis of the nutritional recommendations for canine diabetes, current evidence can be summarized in the following fashion.

Grade B evidence
- Controlled evaluation in non-diabetic dogs of diets with different amounts and types of fiber indicate that increased fiber intake has no significant influence on glucose homeostasis, compared with typical diets formulated for canine adult maintenance.
- Several studies in diabetic dogs indicate that high-fiber diets, compared with low-fiber diets, might be associated with improved glycemic control. However, randomized, controlled comparison identified no measurable benefit for insulin requirement or glycemic control in diabetic dogs, compared with a conventional, moderate-fiber diet formulated for adult maintenance (Grade C evidence).
- There seems to be marked variation between the responses of individual diabetic dogs to dietary fiber.
- High-fiber diets do not significantly improve hypertriglyceridemia in diabetic dogs but might lower serum cholesterol concentrations.
- Supplementation with chromium capsules has not been found to improve glycemic control in insulin-treated dogs.

Grade C evidence
- When lower-fiber diets are fed to diabetic dogs, a blend of soluble and insoluble fibers (such as soy fiber or beet pulp) might be preferable to insoluble fiber alone.
- Comparison in non-diabetic dogs found that a rice-based diet resulted in significantly higher postprandial glucose and insulin responses, while a sorghum-based diet caused reduced glucose responses, and barley produced lower insulin responses.
- Diabetic dogs might benefit from dietary L-carnitine supplementation.
- Diets with lower fat content might result in improved lipid profiles in diabetic dogs, but might also contribute to undesirable weight loss.

Grade E evidence
- The diet fed to diabetic dogs should be palatable so that food intake is predictable
- The diet fed to diabetic dogs should be nutritionally balanced.
- The nutritional requirements of any concurrent disease may need to take precedence over the dietary therapy for diabetes.
- As a regimen of fixed daily insulin dosages is typically used to manage diabetic dogs, it is rational to provide a consistent amount of carbohydrate in the meals fed each day.
- The optimal dietary protein for diabetic dogs has not been determined. Lower dietary protein might be indicated only in diabetic dogs with microalbuminuria or proteinuria.

Frequently asked questions regarding diabetes

Q	A
Do diabetic dogs have significant postprandial hyperglycemia? If they do, how long does it last?	Yes. In non-diabetic dogs, commercial dog foods usually result in postprandial elevation of blood glucose concentration for less than 90 minutes. Diabetic dogs lack endogenous insulin secretion, resulting in failure of the major physiological mechanism for counter-regulation of increasing blood glucose concentration. Consequently, **postprandial hyperglycemia in diabetic dogs is of greater magnitude and duration compared with non-diabetic dogs.**
When should diabetic dogs be fed in relation to administration of insulin injections?	Therapy with exogenous insulin has a marked effect on postprandial hyperglycemia. Insulin administration and meal feeding should ideally be timed so that maximal exogenous insulin activity occurs during the postprandial period. Thus, dogs should be fed within 2 hours of subcutaneous administration of lente insulin or within 6 hours of protamine zinc insulin **(Figure 2). A feasible compromise is to feed the dog immediately following the insulin injection.** This considerably simplifies the home treatment regimen for most dog owners while still allowing good glycemic control to be readily achieved. In addition, many owners prefer this regimen because they feel their pet is rewarded for submitting to the injection.
What should be done if a diabetic dog will not eat?	It is crucial that the food fed to diabetic dogs is highly palatable so that food intake is predictable. If the diet is not palatable, it should be changed to a formulation that is more acceptable to the dog. Whenever an individual diabetic dog does not reliably consume meals when they are fed, it should be recommended that insulin injections are administered immediately after meal feeding. If the dog consumes the meal, the full insulin dose can be administered. **If the dog refuses to eat, then administration of half the usual insulin dose should be recommended to reduce the risk of hypoglycemia.** If a diabetic dog refuses to eat a meal that it usually finds palatable, the possibility of concurrent illness should be considered and veterinary examination is recommended.
Can diabetic dogs be fed ad libitum or should they all be meal fed?	**Diabetic dogs should ideally be fed a set number of meals per day.** The daily insulin-dosing regimen tends to be fixed for diabetic dogs, and the timing of meals should be matched to insulin administration so that a predictable glycemic response occurs at the time of maximal exogenous insulin activity. Thus, meals should be fed at the same times each day. Severe hypoglycemia has been reported in a diabetic dog that was fed ad libitum and received insulin at grossly irregular intervals (*Whitley et al, 1997*). The majority of diabetic dogs will readily consume meals twice-daily if the meals are highly palatable and contain half the daily caloric requirement. For finicky eaters, the meal should be fed at the time of insulin administration and remain available until the expected end of the period of maximal exogenous insulin activity.
Can the meals fed to a diabetic dog be varied from day to day?	Ideally, **every meal should contain the same ingredients and calorie content.** This is an important aspect of diabetes management in dogs and owner compliance should be encouraged. However, care should be taken to consider each case individually. It is usually possible to allow some changes in the feeding regimen without compromising the clinical response of the dog.

Q	A
What is the recommended fiber content of diets fed to diabetic dogs?	There is no evidence of clinical benefit for diabetic dogs of feeding a high-fiber formulation compared with feeding a typical adult maintenance diet. There is marked variation between the responses of individual diabetic dogs to dietary fiber. Some diabetic dogs will have improved glycemic control when fed diets with an increased amount of dietary fiber, while others will not. The response to dietary fiber must be individually assessed in each case. Increased dietary fiber intake is not recommended for diabetic dogs that are underweight, or for dogs for which fiber-supplemented formulations are unpalatable or associated with unacceptable gastrointestinal side-effects. **The most suitable general dietary fiber recommendation for diabetic dogs may be moderate-fiber formulations** (for example, 35 g/1000kcal), although further research is required to demonstrate clinical benefit of this formulation for diabetic dogs compared with typical commercial dog foods formulated for adult maintenance.
Is a low-carbohydrate, high-protein diet now recommended for diabetic dogs similar to the current recommendation for diabetic cats?	Dogs and cats are prone to different types of diabetes and also have different basic macronutrient requirements. Diabetic dogs have forms of diabetes analogous to both human type 1 diabetes and end-stage pancreatitis, while diabetic cats have a form analogous to human type 2 diabetes. There is no evidence that type 2 diabetes occurs in dogs, so it is not valid to extrapolate information on either this disease or feline diabetes to dogs. Unlike dogs, a large proportion of diabetic cats have sufficient beta cells to allow diabetic remission if glucose toxicity and its associated insulin resistance can be reversed, and there is evidence that remission rates are higher if diabetic cats are fed a low-carbohydrate diet. This does not apply to dogs. Diabetic dogs have absolute insulin deficiency and require life-long therapy with exogenous insulin. **As a regimen of fixed daily insulin dosages is typically used to manage diabetic dogs, it is rational to provide a very consistent amount of starch in the meals fed each day.**
What is the best method to achieve body weight gain in a thin diabetic dog, and weight loss in an overweight diabetic dog?	Caloric intake in diabetic dogs should be adjusted to achieve and maintain an ideal body condition. Dogs with poorly controlled diabetes have a decreased ability to metabolize the nutrients absorbed from their gastrointestinal tract and loose glucose in their urine, so require more calories for maintenance than healthy dogs. Most dogs have weight loss by the time diabetes is diagnosed. Many will be underweight while others might still be obese even though they will have experienced weight loss. Insulin therapy ends this state of catabolism and weight loss will soon be arrested. At this stage, a weight management program can be initiated. **Body weight and body condition should be monitored regularly in all diabetic dogs and caloric intake should be adjusted at each re-evaluation until the desired rate of gain or loss is achieved**. If a diabetic dog fails to gain weight when there is good glycemic control and adequate caloric intake, concurrent disease such as exocrine pancreatic insufficiency should be considered. Conversely, a possible cause of obesity in treated diabetic dogs is excessive insulin dose, because insulin has an anabolic action on adipose tissue.
What diet is recommended for diabetic dogs with recurring pancreatitis or exocrine pancreatic insufficiency?	**Dietary therapy for recurring pancreatitis or exocrine pancreatic insufficiency is usually a higher clinical priority than dietary therapy for diabetes.** The prognosis might be improved if these concurrent conditions are recognized early in diabetic dogs and specific nutritional and medical therapy instituted. The dietary recommendations for exocrine pancreatic diseases can be found in **Chapter 5** of this encyclopedia.

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EXAMPLES OF HOME-PREPARED THE TREATMENT OF

Example 1

COMPOSITION
(1000 g diet)

Mullet ..... 500 g
Pasta, wheat whole-meal ..... 270 g
Carrots (boiled, drained) ..... 155 g
Wheat bran ..... 50 g
Pectin ..... 10 g
Rapeseed oil ..... 15 g

Add a well-balanced mineral and vitamin supplement.

ANALYSIS		
The diet prepared in this way contains 46% dry matter and 54% water		
	% dry matter	g/1000 kcal
Protein	33	88
Fat	10	27
Available carbohydrate	41	109
Fiber	12	32

INDICATIVE RATIONING			
Energy value (metabolizable energy) 1710 kcal/1000 g diet prepared (3750 kcal/1000 g DM)			
Dog's weight (kg)	Daily amount (g)*	Dog's weight (kg)	Daily amount (g)*
2	130	45	1320
4	220	50	1430
6	290	55	1540
10	430	60	1640
15	580	65	1740
20	720	70	1840
25	850	75	1940
30	970	80	2030
35	1090	85	2130
40	1210	90	2220

Key Points

- **Incorporating cereals with a low glycemic index** to smooth out the postprandial hyperglycemic peak
- **Intake of soluble and insoluble fiber** to help regulate glycemia
- **Reducing the fat content** due to the risk of subclinical pancreatitis

* *The number of meals must be adapted to the insulin injection protocol. Ideally, each meal must be given in such a way that the postprandial period corresponds to the maximum period of activity of the insulin.*

DIETS ADAPTED TO DIABETES MELLITUS

Example 2

COMPOSITION
(1000 g diet)

Turkey, breast without skin ..... 280 g
Cottage cheese * ..... 330 g
Rolled oats ..... 250 g
Carrots (boiled, drained) ..... 60 g
Wheat bran ..... 60 g
Pectin ..... 10 g
Rapeseed oil ..... 10 g
** 35% of dry matter is fat*

Add a well-balanced mineral and vitamin supplement.

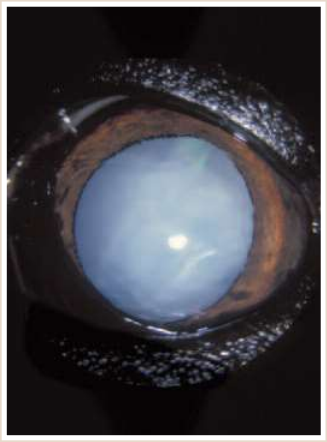
INDICATIVE RATIONING			
Energy value (metabolizable energy) 1675 kcal/1000 g diet prepared (3730 kcal/1000 g DM)			
Dog's weight (kg)	Daily amount (g)*	Dog's weight (kg)	Daily amount (g)*
2	130	45	1350
4	220	50	1460
6	300	55	1570
10	440	60	1670
15	590	65	1780
20	730	70	1880
25	870	75	1980
30	990	80	2080
35	1120	85	2170
40	1230	90	2270

ANALYSIS		
The diet prepared in this way contains 45% dry matter and 55% water		
	% dry matter	g/1000 kcal
Protein	34	91
Fat	11	28
Available carbohydrate	38	102
Fiber	14	38

Contra-indications

Gestation
Lactation
Growth

Examples of home-made diets are proposed by Pr Patrick Nguyen
(Nutrition and Endocrinology Unit; Biology and Pathology Department, National veterinary School of Nantes)



Cataracts are the most common complication among diabetic dogs. The risk increases as the dog grows older. The word comes from the Greek word kataraktès (rupture) where the crystalline lens loses its transparency and the eye has a gray-blue opalescence.

Key Points
with respect to:

The role of nutrition in the treatment of diabetes mellitus in dogs

Rather than a traditional maintenance diet for adult dogs, the diet recommended for diabetic dogs and bitches presenting with diestrus-associated insulin resistance must meet the following key criteria:

- **High palatability** to guarantee regular consumption.
- **Limited starch content** (<50% carbohydrate calories): there is a correlation between the starch content and the dog's glycemic response *(Nguyen et al, 1998)*. It is easy to lower the starch content below 30% even in dry foods. If the pancreas no longer functions (which is more often the case in dogs), it is important to adjust the insulin dose to the starch intake every time the diet is changed. When the starch content of a diet is reduced, the insulin dose must also be reduced.
- High glycemic index starches such as rice and bread should be avoided in diabetic dogs. It is preferable to fed **cereals with starch that is digested more slowly**, facilitating slower, prolonged absorption of glucose. Low glycemic index cereals include corn, wheat, barley and sorghum.
- A diet with a higher fiber content compared with a standard maintenance diet for adult dogs may not be particularly beneficial for diabetic dogs. **The optimal fiber content depends on the dog's physical condition**, the level and source of the starch and the nature of the fiber used.
- Every type of fiber has its own particular properties, therefore intake of **fiber from different sources** is important

- *Insoluble, non-fermentable fiber (e.g. cellulose)* is well tolerated, even in large quantities. Varying the content of this type of fiber permits the adaptation of the energy density of a food to the dog's physical condition.

- *Soluble, non-fermentable fiber (e.g. fructo-oligosaccharides)* improves glucose tolerance.

- *Insoluble, non-fermentable fiber (e.g. psyllium)* impacts the speed of transit through the intestine and the release of glucose.

NB. Beet pulp contains both insoluble and non-fermentable fiber, and soluble and non-fermentable fiber.

- **The ideal fat content depends on the physical condition of the dog**, but diets with a high fat content should be avoided in diabetic dogs, due to the associated risk of pancreatitis. An intake of 20-35% lipid calories appears to be sufficient, unless the dog is in poor body condition. There is an inverse correlation between the dietary fat content and the postprandial glycemic and insulinemic responses (*Prudhomme et al, 1999*). This effect is probably a consequence of deceleration of gastric emptying associated with high fat foods.

- If the food contains moderate starch, fiber and fat content, the protein will be the main source of energy. There are no negative effects associated with providing at least 30%-45% protein calories in the food. **High protein intake helps compensate for the catabolism of protein and increased gluconeogenesis in diabetic dogs**, especially when the diabetes has not been properly stabilized.

- An **L-carnitine supplement** helps maintain the lean body mass.

- Diets for diabetic dogs must contain mineral and trace-element levels similar to those for non-diabetic dogs. **Particular attention should be given to potassium** to avoid deficiencies.

- **The level of water soluble vitamins should be increased** to compensate for losses due to polyuria.

- Oxidative stress is involved in the pathophysiology of diabetes. Therefore, appropriate supplementation with a blend of antioxidants is recommended.

POINTS TO BE MONITORED BY THE OWNER OF A DIABETIC DOG	
The quantities of water and food consumed by the dog	polydipsia (accompanied by polyuria), anorexia or conversely polyphagia may be signs of poor diabetic control
The dog's body weight	changes in body weight may require modification of the insulin dosage. Obesity is a risk factor contributing to insulin resistance
The dog's level of activity	regular physical activity should be included in the list of preventative measures to reduce the incidence of canine diabetes mellitus (*Hedhammar et al, 2005*)
The timing of meals	this is essential for successful treatment. Dividing the ration into two meals a day helps minimize the hyperglycemic peaks, regardless of the type of diabetes. With insulin therapy, the meals should ideally be served just after the insulin peaks, which vary according to the individual and the type of insulin administered
The composition of the meal	the appropriate food should not be changed after selection, as both the quantity and the type of carbohydrate ingested have a direct impact on the postprandial glycemic and insulinemic responses. Supplements, especially sugary treats or food rich in carbohydrates should not be given to dogs with diabetes mellitus
A few simple rules help prevent complications with diabetes mellitus in dogs.	

Focus on:

THE EFFECT OF DIETARY FIBER ON GASTRO-INTESTINAL TRANSIT

Dietary fiber plays a major role in gastro-intestinal transit, although it should be noted that the action differs depending on whether it is soluble or insoluble fiber.

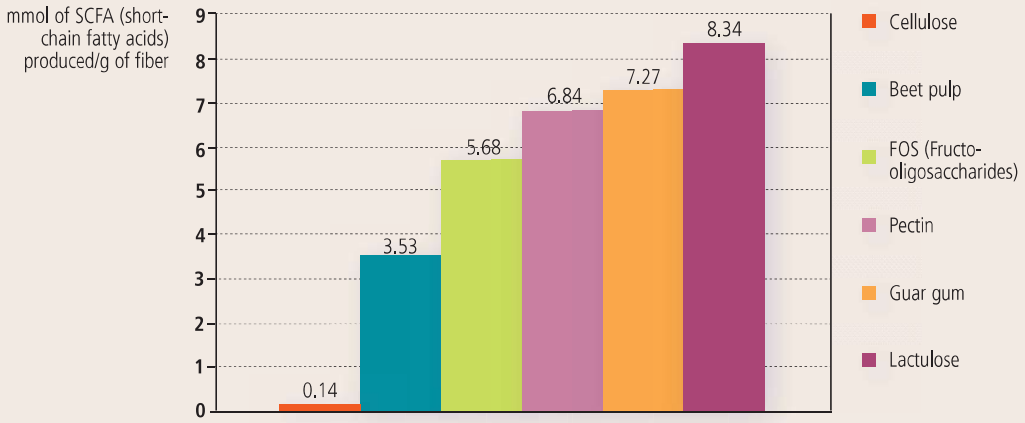
Soluble fiber

In contact with water, soluble fiber (pectins, gums, oligosaccharides, etc) forms a gel or a viscous solution. The viscosity of this type of fiber tends to slow down gastro-intestinal transit due to the simple increase in flow-through resistance *(Guilford, 1996)*.

The effect of fiber on the quality of stools varies according to its ability to be fermented by colonic bacteria. With the exception of psyllium, most types of soluble fiber are degraded by the microflora of the large intestine. The bacteria flora use the fermentable fiber as an energy source, and in the process, generate fermentation products such as short chain fatty acids and lactic acid which have a trophic effect on the colonic mucosa.

CAPACITY OF IN VITRO FERMENTATION OF SEVERAL DIETARY FIBERS

(From Sunvold et al, 1994)



The ratio that exists between fermentable and non fermentable fibers (F/nF) in the food influences the production of putrefaction by-products in the stools.
Example: if the F/nF increases from 0.15 to 0.48, the fecal concentration in amines is 50% lower, corresponding to a total dietary fiber content of 7.7% and 9.2%, respectively (Hernot et al, 2005).

However, a excess quantities of fermentable fiber in a diet is detrimental to digestive tolerance. A diet rich in fermentable fiber (pectins, guar gums) increases the water content and the volume of the feces *(Wiernusz, 1995; Silvio et al, 2000)*. Furthermore, the fermentation products may induce osmotic diarrhea by attracting free water into the intestinal lumen. These effects are mainly due to proliferation of the bacterial biomass produced.

Insoluble fiber

Insoluble fiber regulates transit, accelerating it during constipation and decelerating it during diarrhea *(Guilford, 1996)*.

Insoluble fiber is not generally degraded by the microflora of the colon. As a consequence, insoluble fiber is excreted almost fully intact in the stools. The capacity to increase the indigestible residue of feces contributes to fecal consistency as well as increasing the volume of stools *(Silvio et al, 2000)*. An excess quantity of insoluble fiber in a food is also detrimental to its good digestibility.

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