INTRODUCTION
The interactions of carbohydrate and lipid metabolism and their control by hormones comprise the basis for metabolic homeostasis in health and disease. Diagnosing and treating these disorders requires a working knowledge of cellular changes and the role of hormones in controlling nutrient flux. This chapter covers the nutritional aspects of diabetes mellitus, hyperthyroidism and hypothyroidism.

DIABETES MELLITUS
Diabetes mellitus describes an alteration in cellular transport and metabolism of glucose, lipids and amino acids wherein insulin-dependent tissues (e.g., skeletal and cardiac muscle, adipose tissue) either never receive the signal or fail to properly interpret the signal. Altered metabolism results in either an absolute or relative deficit in insulin secretion by pancreatic beta cells as perceived by insulin-dependent cells in the periphery of the body. Causative pathophysiologic mechanisms include: 1) insufficient insulin release from the pancreas (e.g., glucose toxicity, beta-cell degeneration or islet amyloid deposition), 2) decreased number of functional insulin receptors (down regulation) and 3) problems with transduction of the insulin signal following binding of insulin to insulin receptors (Table 29-1) (Feldman and Nelson, 2004, 2004a).

Classification
In people, diabetes mellitus is usually classified as: 1) type I, 2) type II, 3) secondary (type S), 4) impaired glucose tolerance (e.g., gestational diabetes) (type IGT) and 5) previous abnormality of glucose tolerance (type PrevAGT) based on the pathophysiologic mechanisms and pathogenic alterations affecting beta cells (Stogdale, 1986). Type I diabetes is characterized by a combination of genetic susceptibility and immunologic destruction of beta cells, with progressive and eventually complete insulin insufficiency. The presence of circulating autoantibodies against insulin, beta cells and/or glutamic acid decarboxylase usually precedes the development of hyperglycemia or clinical signs.

Type II diabetes mellitus is characterized by insulin resistance and “dysfunctional” beta cells; defects thought to be genetic in origin and which are evident for a decade or longer before hyperglycemia and clinical signs of diabetes develop. Deteriorous effects of type II diabetes mellitus can be accentuated by environmental factors such as obesity (Warram et al, 1990; Martin et al, 1992). Type II diabetes mellitus has been referred to as a relative insulin deficiency because the amount of insulin actually secreted by the beta cells may be increased, decreased or normal. The concentration of glucose in serum is thus determined by the relative response of peripheral tissues to the secreted insulin, which is usually blunted.

People with type I diabetes depend on insulin to control the disease (i.e., insulin-dependent diabetes mellitus [IDDM]),
whereas control of the diabetic state in people with type II diabetes is usually possible through diet, exercise and oral hypoglycemic drugs. Insulin treatment may be necessary in some type II diabetics if insulin resistance and beta-cell dysfunction are severe. As such, people with type II diabetes mellitus can have IDDM or non-insulin-dependent diabetes mellitus (NIDDM).

Classifying diabetic dogs and cats as type I or type II based on criteria established for people is difficult, in part, because: 1) familial history is rarely available for diabetic dogs and cats, 2) the clinical presentation is usually unhelpful in differentiating type I from type II diabetes, 3) insulin secretagogue tests are not routinely performed and their results may be misleading and 4) autoantibody tests for type I diabetes are not readily available (Nelson et al, 1993; Kirk et al, 1993). It is probably more clinically relevant to classify dogs and cats as insulin-dependent and non-insulin dependent based on their need for insulin.

The overwhelming majority of dogs have IDDM at the time diabetes is diagnosed. Cats are more confusing because islet pathology may be mild to severe and progressive or static; reversible suppression of beta-cell function occurs with chronic hyperglycemia (glucose toxicity), and responsiveness of tissues to insulin varies, often in conjunction with the presence or absence of concurrent inflammatory, infectious, neoplastic or hormonal disorders. These variables affect a cat's need for insulin, insulin dosage and ease of diabetic regulation. Furthermore, these variables may change with time. Cats may have IDDM or NIDDM at the time diabetes is diagnosed. Cats with NIDDM may progress to IDDM with time, cats with apparent IDDM may revert to a non-insulin requiring state after initiation of treatment and cats may have IDDM or NIDDM as severity of insulin resistance and impairment of beta-cell function waxes and wanes.

### Patient Assessment

**History**

Dogs and cats with diabetes mellitus are usually examined because of polydipsia, polyphagia, weight loss and diminished activity. Care should be taken to differentiate between polyphagia from underfeeding compared to polyphagia associated with disease (true polyphagia). Less commonly, complaints of blindness (dogs), rear-limb weakness (cats) and lethargy (dogs and cats) may be identified. If diabetic ketoacidosis (DKA) develops, affected animals are often examined for anorexia, vomiting, diarrhea, weakness and a moribund state. DKA may be precipitated by infection, severe stress, hypokalemia, hypomagnesemia, renal failure, drugs that decrease insulin secretion, drugs that cause insulin resistance or inadequate fluid intake (Nichols and Crenshaw, 1995). Concurrent disease such as pancreatitis and bacterial infection is common in dogs and cats developing DKA and often accentuates the clinical signs of DKA, prompting owners to seek veterinary care. A thorough assessment of the patient is critically important for developing an appropriate management protocol for dogs and cats diagnosed with DKA (Feldman and Nelson, 2004, 2004a; Plotnick and Greco, 1995).

### Physical Examination

Body condition scores (BCS) for diabetic dogs and cats range from emaciated (BCS 1/5) to obese (BCS 5/5) depending on the severity and duration of disease. Weight loss, which becomes obvious with time, is a hallmark sign of diabetes mellitus. Other physical findings may include lethargy, unkempt coat (cats), hepatomegaly, cataracts (dogs), rear-limb weakness (cats) and dehydration (Plotnick and Greco, 1995; Feldman and Nelson, 2004, 2004a).

### Diagnostic Testing

#### HÉMOGRAMS

Results of complete blood counts are usually within normal ranges in uncomplicated cases of diabetes mellitus. An increase in packed cell volume may be present in dogs and cats with DKA due to decreased extracellular water attributable to osmotic diuresis. Occasionally, increased numbers of Heinz bodies may be noticed in cats with diabetes mellitus. Leukocytosis or shifts of white cell morphology to more immature types may indicate an underlying infectious process that confounds the diagnosis of uncomplicated diabetes mellitus.

### SERUM BIOCHEMISTRY PROFILES

The most consistent and requisite feature of diabetes mellit-
tus is persistent fasting hyperglycemia and glucosuria in the absence of other disease processes. Hyperglycemia, however, may be caused by other disease or physiologic states and drugs (Table 29-2). A thorough assessment may help identify the underlying cause of hyperglycemia. Repetitive determination of serum glucose concentrations may be required in cats to differentiate diabetes mellitus from stress hyperglycemia. A diagnosis of DKA is established if ketonuria is present with systemic metabolic acidosis.

Other commonly identified abnormalities include increased serum concentrations of cholesterol and triglycerides. Increased serum concentrations of urea nitrogen and creatinine may be present when dehydration becomes severe enough to impair renal diffusion (prerenal azotemia). Electrolyte and acid-base alterations are more common in animals with DKA and include: 1) hyponatremia, 2) hypokalemia, 3) hypocalcemia, 4) hypomagnesemia, 5) hypophosphatemia and 6) hypochloremia. A shift in acid-base balance towards metabolic acidosis with a compensatory respiratory alkalosis may occur.

Increased activity of alanine aminotransferase in serum may be present in cases in which hepatic lipolysis has resulted in hepatocellular damage. Activity of serum alkaline phosphatase may also be increased. Increased serum alkaline phosphatase activity is primarily associated with hepatomegaly and biliary stasis; however, pancreatic inflammation resulting in extrahepatic biliary obstruction may also be present. Less commonly, serum concentrations of bile acids and total bilirubin may be elevated.

Dogs and cats with diabetes mellitus may present with concurrent exocrine pancreatic insufficiency or pancreatitis (Williams and Minnich, 1990). Increased activity of amylase and lipase in serum may indicate pancreatitis; however, the correlation of these two enzyme activities with pancreatitis is poor, especially in cats. Other disease processes may also result in increased activity of these enzymes in serum.

OTHER BIOCHEMICAL TESTS

Determination of insulin concentration in serum is not routinely performed in suspected cases of diabetes mellitus. A reliable radioimmunoassay must be used when measuring serum insulin, especially in cats. Insulin exhibits variance in the primary amino acid sequence between species; therefore, the test methodology must be validated for each species. Serum insulin concentrations, when they are determined, may be high, normal or low. Concentrations of insulin greater than 15 µU/ml in animals not receiving exogenous insulin indicate the presence of functional beta cells. Conversely, concentrations of insulin less than 10 µU/ml do not preclude the possibility of functional beta cells. Serum pancreatic lipase immunoreactivity (increased activity) and trypsin-like immunoreactivity (decreased activity) can help identify pancreatitis and exocrine pancreatic insufficiency, respectively (Chapters 66 and 67).

Serum thyroid-hormone concentrations are usually normal in diabetic dogs and cats. However, both hypothyroidism and hyperthyroidism may be associated with insulin resistance and can occur in conjunction with diabetes mellitus. As such, evaluation of thyroid function may be useful in patients with diabetes mellitus that are difficult to control with insulin and dietary intervention (Case 29-2). Care must be exercised in the interpretation of serum thyroxine (T4) concentrations in sick dogs and cats because concentrations of T4 may be falsely low in poorly regulated cases of diabetes mellitus. This alteration is presumed to be attributable to the euthyroid sick syndrome (Feldman and Nelson, 2004c).

URINALYSES

Urine specific gravity is typically greater than 1.025 in diabetic dogs and cats. Urine specific gravity less than 1.015 should increase suspicion for concurrent disorders, such as renal insufficiency or hyperadrenocorticism. Glucosuria is a hallmark finding in untreated diabetic dogs and cats. Lack of glucosuria rules out diabetes mellitus as the cause of polydipsia and polyuria. Other common urinalysis findings include ketonuria, proteinuria and changes consistent with urinary tract infection (i.e., bacteriuria and pyuria). Proteinuria may result from either bacterial infection or glomerulopathy secondary to basement membrane damage from the primary disease process.

Risk Factors

Risk factors for development of diabetes mellitus in dogs and cats include genetics, age, sex, obesity and concurrent problems causing insulin resistance. Although diabetes can occur in dogs and cats of any age, gender and breed, the disease is more common in older dogs and cats with a peak prevalence of seven to nine years of age in dogs and nine to 11 years in cats (Panciera et al, 1990; Goossens et al, 1998). Juvenile-onset diabetes occurs in dogs and cats less than one year of age, but is uncommon. In dogs, females are affected about twice as frequently as males, whereas in cats, diabetes occurs predominately in neutered males (Panciera et al, 1990; Goossens et al, 1998). Breeds of dogs at risk for diabetes mellitus include Australian terriers, standard and miniature schnauzers, bichons frises, spitz, fox terriers, miniature and toy poodles, Samoyeds, Cairn terriers, keeshonds, Maltese, Lhasa apsos and Yorkshire terriers (Guptill, 1999; Hess et al, 2000). There is no apparent breed predisposition in cats; however, Burmese cats may be overrepresented in Australia (Rand et al, 1997).

The presence and severity of insulin resistance is an important variable in the development and successful treatment of diabetes mellitus in dogs and cats. Insulin resistance increases the demand for insulin secretion. A sustained demand for insulin secretion in response to insulin resistance can lead to islet pathology and loss of beta cells. The more severe and chronic the insulin resistance and the more severe the loss of islets, the more likely hyperglycemia will develop. Persistent hyperglycemia can, in turn, suppress function of remaining beta cells, causing hypoinsulinemia, worsening hyperglycemia and further reducing the population of beta cells. Any chronic insulin-resistant disorder can have a deleterious effect on the population and function of beta cells and play a role in the development of NIDDM or IDD (Figure 29-1). Examples include obesity, chronic pancreatitis, acromegaly, hyperadreno-
**Etiopathogenesis**

Classic insulin-resistant disorder affiliated with development of progestagens. Obesity-induced carbohydrate intolerance is the corticism and long-term administration of glucocorticoids or fourfold (Scarlett, 1997).

**NIDDM in people and increases the risk for diabetes in cats by impermeable to glucose, all cells require carrier proteins to (Masharani and Karam, 2001). Because cell membranes are lipid synthesis and stimulation of other metabolic pathways lead to increased glucose transport, increased glycogen and is responsible for activating the signaling cascade that ultimately processes by a cleavage step that produces C-peptide and active insulin (Muench, 1986).

Active insulin released into the bloodstream normally interacts at target tissues via cell surface receptors specific for insulin. Most tissues have insulin receptors but some (e.g., skeletal and cardiac muscle and adipose tissue) depend more on insulin for the acquisition of glucose and amino acids than others, and are classified as insulin-dependent tissues (Harris, 1986; Granner, 1988). For example, brain tissue has insulin receptors, but is quite capable of transporting glucose intracellularly without the help of hormonal stimuli; therefore, it is considered an insulin-independent tissue.

Insulin receptors are membrane glycoproteins composed of two subunits; a larger alpha subunit that extends extracellularly, which is involved in binding the insulin molecule, and a smaller beta subunit that is predominately cytoplasmic, which is responsible for activating the signaling cascade that ultimately leads to increased glucose transport, increased glycogen and lipid synthesis and stimulation of other metabolic pathways (Masharani and Karam, 2001). Because cell membranes are impermeable to glucose, all cells require carrier proteins to transport glucose across the lipid bilayers into the cytosol. At least five glucose transporters have been described, to date, in people, each having a different affinity for glucose. GLUT 1 and GLUT 3 are present in all tissues and mediate basal glucose uptake and neuronal uptake of glucose, respectively. GLUT 2 is the major glucose transporter in beta and hepatic cells. It has a low affinity for glucose, and acts as a transporter during periods of hyperglycemia. GLUT 5 is found on the brush border of human small intestinal cells and is mainly a fructose transporter. GLUT 4 is found intracellularly in insulin-dependent tissues, most notably skeletal muscle and adipose tissue. Activation of the insulin signaling cascade results in movement of GLUT 4 transporters to the cell surface where the transporter facilitates glucose entry into cells (James et al, 1988; Thorens et al, 1990).

**DIABETES MELLITUS IN DOGS**

The most common clinically recognized form of diabetes mellitus in dogs is IDDM. In our hospital (School of Veterinary Medicine, University of California, Davis), virtually all dogs have IDDDM when diabetes mellitus is diagnosed. IDDM is characterized by permanent hypoinsulinemia and an absolute necessity for exogenous insulin to maintain glycemic control. The etiology of IDDM has been poorly characterized in dogs, but is undoubtedly multifactorial and may be similar to human type I diabetes. Genetic predispositions have been suggested by familial associations (Guptill, 1999; Hess et al, 2000). Common histologic abnormalities in dogs include a reduction in the number and size of pancreatic islets, a decrease in the number of beta cells within islets and beta-cell vacuolation and degeneration. In some dogs, an extreme form of the disease may occur, represented by a congenital absolute deficiency of beta cells and pancreatic islet hypoplasia or aplasia. Less severe pancreatic islets and beta-cell changes may predispose adult dogs to diabetes mellitus after exposure to environmental factors, such as insulin-antagonistic diseases and drugs, obesity or pancreatitis. Environmental factors may induce beta-cell degeneration secondary to chronic insulin resistance or may cause release of beta-cell proteins that induce immune-mediated destruction of the islets (Nerup et al, 1994). Studies designed to detect anti-beta-cell autoantibodies in diabetic dogs have been conflicting; they were identified in newly-diagnosed diabetic dogs with IDDM in one study (Hoenig and Dawe, 1992) but not in another (Haines, 1986). Immune-mediated insulinitis has also been described in diabetic dogs (Alejandro et al, 1988). Seemingly, autoimmune mechanisms, in conjunction with genetic and environmental factors, may play a role in the initiation and progression of diabetes in dogs.

**DIABETES MELLITUS IN CATS**

Common histologic abnormalities in cats with diabetes mellitus include islet-specific amyloidosis, beta-cell vacuolation and degeneration and chronic pancreatitis (Goossens et al, 1998). The cause of beta-cell degeneration is unknown. Still, other diabetic cats have reduced numbers of pancreatic islets and/or insulin-containing beta cells based on immunohisto-
Key nutritional factors for diabetic dogs and cats.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Dogs (increased-fiber/high-carbohydrate food)</th>
<th>Cats (increased-fiber/high-carbohydrate food)</th>
<th>Cats (low-carbohydrate/high-protein food)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>Fresh, clean water should be available at all times</td>
<td>Avoid simple sugars and starches</td>
<td>Avoid simple sugars and starches</td>
</tr>
<tr>
<td>Digestible carbohydrate</td>
<td>Provide foods with no more than 55% digestible carbohydrate</td>
<td>Provide foods with less than 40% digestible carbohydrate</td>
<td>Provide foods with less than 20% digestible carbohydrate</td>
</tr>
<tr>
<td>Fiber</td>
<td>7 to 18%</td>
<td>7 to 18%</td>
<td>-</td>
</tr>
<tr>
<td>Fat</td>
<td>&lt;25%</td>
<td>&lt;25%</td>
<td>&lt;25%</td>
</tr>
<tr>
<td>Protein</td>
<td>15 to 35%</td>
<td>28 to 55%</td>
<td>28 to 55%</td>
</tr>
<tr>
<td>Food form</td>
<td>Avoid semi-moist foods</td>
<td>Cats with renal failure should be fed protein at the low end of the range</td>
<td>Cats with renal failure should be fed protein at the low end of the range</td>
</tr>
</tbody>
</table>

*Nutrients expressed on a dry matter basis.

Key Nutritional Factors

Key nutritional factors consist of nutrients of concern and other factors such as food type. This section emphasizes key nutritional factors that vary significantly in commercial foods and markedly affect management of diabetes mellitus (Table 29-3). The degree to which any of these factors affects management of diabetes mellitus greatly depends on the efficacy of primary disease control through insulin or other pharmacologic treatment. However, it has been shown that appropriate nutritional support may allow for less medical intervention, and in some cases, precludes the need for medical intervention (Bennett et al, 2006; Farrow et al, 2002; Frank et al, 2001; Nelson et al, 1998, 2000; Rand et al, 2004; Thieß et al, 2004).

WATER

Increased water loss due to osmotic diuresis from glucose, and ketone bodies if DKA is present, must be compensated. Generally, a source of potable water is recommended in amounts sufficient to meet the increased water requirement. This is usually accomplished via free-choice access to water. Dehydrated patients and those with DKA may require parenteral fluid administration. Caution should be observed with type and rate of fluid replacement because of electrolyte perturbations. Rapid replacement of fluid loss with hypotonic solutions may lead to water intoxication and cerebral edema (Schaer, 1975).

DIGESTIBLE CARBOHYDRATE

Concerns have been raised about the composition of carbohydrate in cat foods because cats have a different capacity to metabolize carbohydrates than dogs (Maskell and Graham,
Table 29-4. Effect of feeding insoluble dietary fiber to dogs and cats with diabetes mellitus.*

<table>
<thead>
<tr>
<th>Dog food**</th>
<th>Mean daily insulin dose (U/kg/day)</th>
<th>Mean fasting blood glucose (mg/dl)</th>
<th>Mean blood glucose/24 hrs (mg/dl)</th>
<th>Mean urine glucose excretion (g/24 hrs)</th>
<th>Mean glycosylated hemoglobin (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-fiber food (1% DM)</td>
<td>1.9 ± 0.6</td>
<td>247 ± 99</td>
<td>246 ± 100</td>
<td>9.3 ± 14.0</td>
<td>6.9 ± 1.8</td>
</tr>
<tr>
<td>High-fiber food (13% DM)</td>
<td>1.7 ± 0.5</td>
<td>164 ± 69</td>
<td>184 ± 71</td>
<td>2.8 ± 3.3</td>
<td>5.9 ± 1.4</td>
</tr>
<tr>
<td>Cat food**</td>
<td>1.2 ± 0.7</td>
<td>328 ± 153</td>
<td>285 ± 131</td>
<td>Not done</td>
<td>2.7 ± 0.8</td>
</tr>
<tr>
<td>High-fiber food (12% DM)</td>
<td>1.0 ± 0.6</td>
<td>191 ± 118</td>
<td>182 ± 99</td>
<td>Not done</td>
<td>2.1 ± 0.4</td>
</tr>
</tbody>
</table>

Key: DM = dry matter.


**By the parameters shown here, dogs and cats eating the higher fiber food had better glycemic control than comparable animals eating the low-fiber food.

1994). The composition and quantity of carbohydrates in foods for management of diabetes mellitus differ between dogs and cats, in part, because dogs are omnivores and tolerate digestible (soluble) complex carbohydrates better than diabetic cats. In general, foods containing 55% or less digestible carbohydrate on a dry matter (DM) basis are acceptable for dogs with diabetes mellitus, especially when the food also contains an increased amount of dietary fiber (Nelson et al, 1991, 1998). In contrast, cats are carnivores and have higher dietary protein requirements than omnivores such as people and dogs. The activity of hepatic enzymes responsible for the phosphorylation of glucose for subsequent storage or oxidation (glucokinase, hexokinase) and the conversion of glucose to glycogen for storage in the liver (glycogen synthetase) are lower in cats, compared with that for carnivores with omnivorous dietary habits (Zoran, 2002). The low activity of these hepatic enzymes suggests that cats primarily use gluconeogenic amino acids and fat rather than starch in their diet for energy, and suggests that diabetic cats may be predisposed to developing higher postprandial blood glucose concentrations following consumption of foods containing a high carbohydrate load and vice versa.

The optimal level of digestible carbohydrates for foods for diabetic cats has not been determined. Currently there are two acceptable approaches: low-carbohydrate/high-protein foods and increased-fiber/high-carbohydrate foods. Limiting carbohydrate intake results in blood glucose being maintained primarily via hepatic gluconeogenesis. The advantage is that glucose resulting from gluconeogenesis is released into the circulation at a slow and steady rate. Wider fluctuations in postprandial blood glucose levels, such as would be expected from feeding higher-carbohydrate foods, are avoided (Kirk, 2006). The end result of feeding increased-fiber/high-carbohydrate foods is similar. Increased dietary fiber also reduces fluctuations in postprandial blood glucose levels (Chandalia et al, 2000; Nelson et al, 2000), even though such foods provide more carbohydrate. Both approaches (low-carbohydrate/high-protein and increased-fiber/high-carbohydrate) improve glycemic control in diabetic cats (Mazzaferro et al, 2001; Frank et al, 2001; Bennett et al, 2006; Nelson et al, 2000). In one of the studies comparing the two types of foods, diabetic cats from both groups were able to discontinue insulin and revert to a non-diabetic state; 41% of the cats fed an increased-fiber/high-carbohydrate food vs. 68% of the cats fed a low-carbohydrate/high-protein food (Bennett et al, 2006). Other studies have shown improved glycemic control in both healthy and diabetic cats fed low-carbohydrate/high-protein foods (Massaferro et al, 2003; Frank et al, 2001).

In general, digestible carbohydrates should be less than 20% DM in low-carbohydrate/high-protein foods for diabetic cats, and increased-fiber/high-carbohydrate foods for diabetic cats should contain less than 40% digestible carbohydrates DM (Nelson et al, 2000; Bennett et al, 2006). Digestible carbohydrate content of increased-fiber/high-carbohydrate foods for dogs should probably not exceed 55% DM.

Foods and snacks containing simple sugars rapidly increase blood glucose concentration and should be avoided for diabetic dogs and cats. Fructose should also be avoided in cats. Cats do not appear to metabolize fructose, which leads to fructose intolerance, polyuria and potential renal damage (Kienzle, 1994). Fructose may be found in commercial semi-moist foods, as a humectant in the form of sucrose, or high-fructose corn syrup. The potential effects of fructose in foods for dogs with diabetes mellitus have not been evaluated.

Fiber

As mentioned above, studies in diabetic cats have documented glycemic improvement in response to consumption of foods containing increased amounts of fiber (Nelson et al, 2000; Bennett et al, 2006). Foods containing increased fiber content also benefit glycemic control of diabetes in dogs (Table 29-4) (Nelson et al, 1991, 1998). The ability of fiber to form a viscous gel and thus impair convective transfer of glucose and water to the absorptive surface of the intestine appears to be the most important mechanism for slowing intestinal glucose absorption. The more viscous soluble fibers (e.g., gums, pectins) slow glucose diffusion to a greater degree than do the less viscous insoluble fibers (e.g., lignin, cellulose). Studies in diabetic dogs...

Although an ideal fiber content has not been established, it is evident that including moderate amounts (approximately 7 to 18% DM) of insoluble or mixed insoluble and soluble dietary fiber in high-carbohydrate foods aids nutritional management of type I and type II diabetes mellitus in dogs and cats. Low-carbohydrate/high-protein foods intended for diabetic cats typically contain lower levels of fiber; between 2 to 7% DM. Whether such levels are important in the efficacy of these type foods for the management of diabetes is unknown. Thus, at this time, dietary fiber is not considered to be a key nutritional factor in low-carbohydrate/high-protein foods for management of diabetes in cats.

Some soluble fibers and mixtures of soluble/insoluble fibers may decrease small intestinal digestion of certain nutrients without affecting total tract digestibility (Muir et al, 1996). Caution should be exercised with use of either fiber type in the management of diabetes mellitus because hyperglycemia inhibits the gastrocolic response, which may predispose to constipation (Sims et al, 1995). In addition, increased fiber levels may trap water in the gastrointestinal tract; therefore, water balance may need to be more closely monitored in patients with poorly controlled diabetes mellitus fed foods with moderate fiber levels.

**FAT**

Derangements in fat metabolism are common in diabetic dogs and cats and include increased serum concentrations of cholesterol, triglycerides, lipoproteins, chylomicrons and free fatty acids; hepatic lipodosis, atherosclerosis and a predisposition for development of pancreatitis may also occur (De-Bowes, 1987; Hess et al, 2003). Feeding high-fat food may also cause insulin resistance and promote hepatic glucose production (Massillon et al, 1997). Feeding a low-carbohydrate, high-protein, high-fat food also increases concentrations of fat metabolites in healthy male cats (Thiess et al, 2004). These findings strongly support feeding foods that are relatively low in fat content, i.e., less than 25% DM. Feeding lower fat foods will help minimize the risk of pancreatitis, control some aspects of hyperlipidemia and reduce overall caloric intake to favor weight loss or maintenance. Foods with a higher fat content may be needed for weight gain in thin or emaciated diabetic dogs and cats.

**PROTEIN**

Diabetic dogs and cats may have increased loss of amino acids in urine attributable to inappropriate or inadequate hormonal signals and renal glomerulopathy. It is important to provide protein quantity and quality that will meet the requirements of diabetic animals in the face of increased amino aciduria while avoiding excess protein content that may enhance renal damage or contribute to excessive insulin secretion.

As mentioned above, in cats, two basic nutritional approach-es are used for diabetes management (and weight loss, see Chapter 27). These include increased-fiber/high-carbohydrate foods and low-carbohydrate/high-protein foods. In one study, obese cats fed isocaloric amounts of a low-carbohydrate/high-protein food vs. obese cats fed a low-protein/high-carbohydrate food, researchers concluded that the low-carbohydrate/high-protein food was beneficial through maintenance of normal insulin sensitivity of fat metabolism, facilitating the loss of body fat during weight loss. Whether or not the beneficial effects were due to high protein, low carbohydrate, or both, was not determined (Hoenig et al, 2006).

Also, as mentioned above, as true carnivores, cats primarily use gluconeogenic amino acids rather than dietary carbohydrates for energy, which suggests that diabetic cats may be predisposed to developing higher postprandial blood glucose concentrations following consumption of high-carbohydrate/ lower-protein foods, and vice versa.

The protein content of foods for diabetic patients should be approximately 15 to 35% of the food DM for dogs and 28 to 55% of the food DM for cats.
Changes in trace mineral nutrition status associated with diabetes mellitus have been evaluated in multiple species. The role of zinc in diabetes mellitus is controversial; however, it may affect insulin release from the pancreas, glucose tolerance and insulin resistance through changes in insulin binding and activity. Zinc appears to have biphasic activity; low concentrations enhance insulin secretion and activity whereas higher levels reverse this effect. Whole body zinc stores are often low in patients with diabetes mellitus.

Chromium has been proven to be an essential trace element and is thought to have a role in glucose homeostasis. Chromium has no known enzymatic cofactor function, but it may exist as a complex with nicotinic acid and amino acids to form a “glucose tolerance factor” that may aid insulin action. Chromium supplementation may improve glucose tolerance in malnourished subjects and subjects with poor glucose tolerance. Chromium supplements given to diabetic people have mostly proven ineffective in improving glycemic control; however, efficacy may vary on a case-by-case basis and chromium may prove beneficial in some individuals. At present, there is no reliable method to detect marginal chromium deficiency. Cats may display some gastrointestinal side effects when supplemental chromium is administered.

Manganese deficiency has been associated with perturbations in insulin secretion and carbohydrate and lipid metabolism, including impaired glucose usage in laboratory animals; however, its importance in the etiopathogenesis of diabetes is controversial. Repletion of manganese in deficient animals restores normal glucose tolerance and improves insulin secretion. However, treatment of diabetic subjects with manganese supplements had no impact on glycemic control; therefore, it is inferred that manganese deficiency is not a major factor in the pathophysiology of diabetes mellitus.

Iron overload can cause glucose intolerance due to pancreatic damage secondary to hemochromatosis. Overall, iron status does not seem to play a role in diabetes mellitus. Other trace element deficiencies such as vanadium and selenium have been associated with changes in glucose tolerance or insulin-like activity. Vanadium administered to healthy cats caused vomiting and diarrhea but also lowered blood glucose levels in one diabetic cat. Selenium appears to play no role in the development or manifestation of diabetes mellitus.

Substantiation of trace mineral benefits in diabetic dogs and cats has been confounding. Improvement with supplementation appears to occur on a case-by-case basis. In general, until otherwise proven, providing a food with microminerals supplied according to Association of American Feed Control Officials (AAFCO) recommendations for the appropriate life stage should suffice for most animals with diabetes mellitus.

Diabetes mellitus may increase or decrease vitamin balance (Table 1). Conversely, vitamin status may affect the development and manifestations of diabetes mellitus. Much of the investigative work in this area is controversial and needs to be clarified. In general, foods that contain AAFCO recommended levels of vitamins for adult maintenance should meet most of the altered requirements induced by diabetes. In some cases of diabetes mellitus, it may be necessary to supplement the food with exogenous B vitamins.

Diabetic osteopenia is fairly well-documented in people and has a rational paradigm. Diabetes mellitus may lead to hypomagnesemia, which leads to decreased parathyroid hormone secretion and action, which then results in decreased formation of 1,25-dihydroxyvitamin D₃. Insulin deficiency further impairs formation of 1,25-dihydroxyvitamin D₃. The resultant impaired ability to enhance calcium absorption and retention in the face of hypercalcioria leads to calcium depletion.

Vitamin A homeostasis and status may influence development and control of diabetes mellitus. However, studies have yielded conflicting results; therefore, the effect of vitamin A on diabetes mellitus remains clouded. Most commercial pet foods provide abundant vitamin A.

**Box 29-1. Trace Minerals and Vitamins in Diabetes Mellitus.**

<table>
<thead>
<tr>
<th>Minerals</th>
<th>IDDM</th>
<th>NIDDM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromium</td>
<td>Normal to increased</td>
<td>Normal</td>
</tr>
<tr>
<td>Copper</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Iron</td>
<td>Normal to decreased</td>
<td>Increased</td>
</tr>
<tr>
<td>Manganese</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Selenium</td>
<td>Normal to decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Zinc</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vitamins</th>
<th>IDDM</th>
<th>NIDDM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiamin</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>Decreased?</td>
<td>Normal</td>
</tr>
<tr>
<td>Vitamin B₁₂</td>
<td>Normal to decreased</td>
<td>Normal</td>
</tr>
<tr>
<td>Vitamin B₆</td>
<td>Normal to decreased</td>
<td>Normal</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Normal to decreased</td>
<td>Normal</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Increased</td>
<td>Increased</td>
</tr>
</tbody>
</table>

Key: IDDM = insulin-dependent diabetes mellitus, NIDDM = non-insulin-dependent diabetes mellitus.

Table 1. Micronutrient status in people with diabetes mellitus.*

The Bibliography for Box 29-1 can be found at www.markmorris.org.

**FOOD FORM**

Semi-moist foods tend to have a hyperglycemic effect compared to dry foods because they contain increased levels of simple carbohydrates and other ingredients used as humectants (Figure 29-2). Semi-moist foods should be avoided in dogs and cats with diabetes mellitus (Table 29-3).

**Other Nutritional Factors**

**ELECTROLYTES**

The osmotic diuresis induced by glycosuria and ketonuria results in urinary loss of electrolytes such as sodium, potassium, chloride, calcium, phosphorus and magnesium. Total body deficits in electrolytes often exist in poorly-regulated and ketotic diabetic dogs and cats, even when serum concentrations are within the normal range (Feldman and Nelson, 2004b). In addition, treatment of DKA may result in shifts of serum electrolytes between the intracellular and extracellular compartments. Perhaps the most clinically relevant is the shift of potassium, phosphorus and magnesium into intracellular compartments following initiation of insulin treatment for DKA, which
can lead to severe reductions in serum concentrations of these cations. Frequent monitoring of serum electrolytes and adjustments in the electrolyte composition of the intravenous fluids helps prevent life-threatening deficiencies of these electrolytes from developing during treatment of DKA.

Feeding foods containing appropriate amounts of electrolytes is important to achieve and maintain normal homeostasis in diabetic dogs and cats. However, no studies have been performed to establish recommended levels of minerals in foods for animals with diabetes mellitus. Dogs and cats without renal impairment should be fed foods with adequate amounts of phosphorus to avoid and replace whole body phosphorus deficits. However, excess dietary phosphorus should be avoided in animals with renal impairment. Diabetic cats fed foods with low magnesium content should be monitored carefully to avoid magnesium depletion. In general, foods that meet Association of American Feed Control Officials (AAFCO) recommendations for adult maintenance should supply adequate amounts of cations and anions to compensate for the increased losses described above. Most, if not all, commercial veterinary therapeutic foods will provide adequate amounts of these minerals. Diabetes mellitus may also affect micromineral and vitamin status (Box 29-1).

**OMEGA-3 FATTY ACIDS**

Omega-3 (n-3) fatty acids have been used in people with diabetes mellitus to decrease the incidence of atherosclerotic disease (Nettleton, 1995). At present, the recommendation of fish oil (enhanced with omega-3 fatty acids) for management of type I diabetes mellitus is more accepted than for type II diabetes mellitus in people. The dose of fish oil, diet composition and type of diabetes have resulted in confounding results. Administration of supplemental omega-3 fatty acids to diabetic people generally increased high-density lipoprotein concentrations, improved blood viscosity, reduced triglyceride levels and reduced blood pressure. However, reports of reduced glycemic control, increased apolipoprotein B levels and increased low-density lipoprotein levels with concomitant increases in cholesterol concentrations have dampened enthusiasm for the use of omega-3 fatty acids in diabetic people (Nettleton, 1995). Administration of omega-3 fatty acids to diabetic dogs and cats has not been evaluated, but may prove to have benefits similar to those shown in other species.

**Feeding Plans**

Treatment for diabetes mellitus usually involves a combination of commonly available options. Treatment with injectable insulin or oral sulfonylurea agents has been the mainstay of pharmacologic intervention for uncomplicated diabetes mellitus (Feldman and Nelson, 2004, 2004a). Nutritional intervention is the major non-pharmacologic treatment modality for diabetes mellitus and plays an important role in the successful management of diabetic dogs and cats. Adjustments in food and feeding methods (amount fed and timing of feedings) should be considered when insulin therapy is initiated and should be directed at correcting or preventing obesity, maintaining consistency in the timing and caloric content of the meals and furnishing a food that helps minimize postprandial hyperglycemia.

The nutritional plan for cats with non-insulin-dependent type II diabetes is similar to that for type I diabetes mellitus. In many diabetic cats, clinical signs and hyperglycemia resolve with appropriate dietary treatment and proper case management (Figure 29-3) (Bennett et al, 2006; Reusch et al, 2006).

Exercise also plays an important role in improving and maintaining control of glycemia by helping promote weight loss, eliminating insulin resistance induced by obesity and promoting glucose usage by muscle (Nishida et al, 2001). The amount and timing of exercise should be consistent from day to day to avoid unpredictable fluctuations in blood glucose that may result in potentially severe hypoglycemia. Finally, changes in diet, body weight and exercise may alter insulin requirements and should be accompanied by concurrent monitoring to assess if glycemic control has been affected. For example, an increase in dietary fiber may decrease blood glucose concentrations and lead to hypoglycemia or the Somogyi response. Similarly, loss of body weight will improve insulin sensitivity and may lead to hypoglycemia unless the insulin treatment regimen is modified.

**Assess and Select the Food**

Levels of the key nutritional factors should be evaluated in foods currently being fed to diabetic patients. Semi-moist foods should be avoided. Amounts and levels of key nutritional factors should be compared to those established for diabetic dogs and cats (Table 29-3). Information from this aspect of assessment is essential for making any changes to foods currently provided. If key nutritional factors in the current food do not match the recommended levels, then changing to a more appropriate food is indicated. Tables 29-5 through 29-7 list the recommended key nutritional factors for diabetic dogs and cats.
and selected commercial veterinary therapeutic foods often fed to patients with either insulin-dependent type I, or non-insulin-dependent type II, diabetes mellitus.

There are two types of foods for diabetic cats: increased-fiber/high-carbohydrate foods and low-carbohydrate/high-protein foods (Tables 29-6 and 29-7, respectively). Both have been shown to improve glycemic control in diabetic cats (Mazzaferro et al, 2001; Frank et al, 2001; Bennett et al 2006; Nelson et al, 2000). In one of the studies comparing the two types of foods, diabetic cats from both groups were able to discontinue insulin and revert to a nondiabetic state. Forty-one percent of the cats fed an increased-fiber/high-carbohydrate food and 68% of the cats fed a low-carbohydrate food became nondiabetic (Bennett et al, 2006). On the basis of calculated odds ratios, cats fed a low-carbohydrate food are three times more likely to discontinue insulin therapy and revert to a nondiabetic state (Kirk, 2006). Other studies have shown improved glycemic control in both healthy and diabetic cats fed low-carbohydrate foods (Massaferro et al, 2003; Frank et al, 2001). When choosing a type of food to feed diabetic cats, besides considering the aforementioned study results, the clinician's personal experience with a given approach is also important.

Another criterion for selecting a food that may become increasingly important in the future is evidence-based clinical nutrition. Practitioners should know how to determine risks and benefits of nutritional regimens and counsel pet owners accordingly. Currently, veterinary medical education and continuing education are not always based on rigorous assessment of evidence for or against particular management options. Still, studies have been published to establish the nutritional benefits of certain pet foods. Chapter 2 describes evidence-based clinical nutrition in detail and applies its concepts to various veterinary therapeutic foods.

**Assess and Determine the Feeding Method**

Determining the amount to feed diabetic dogs and cats requires special consideration. Patients with diabetes mellitus display a classic clinical picture of polyphagia with weight loss. Before making recommendations for daily energy requirement (DER), it is important to emphasize that the clinical response of patients with diabetes mellitus to dietary manipulation depends on the level of control of the primary disease process and the presence or absence of concurrent disease. For example, if weight loss or weight gain is a continuing problem, it may be due to poorly controlled diabetes mellitus or concurrent disease such as thyroid disorders (dogs and cats), lymphoplasmacytic enteritis (cats) or hyperadrenocorticism (dogs), rather than inappropriate calculation of DER. Consistent reevaluation and owner education are important tools in adjusting food dose and managing diabetes mellitus. After a patient's DER is estimated, the amount of food to feed (cups and/or cans) can be determined by dividing the DER by the as fed energy density of the food which can be found in Tables 29-5 through 29-7.

The basal metabolic rate may actually be decreased in patients with poorly controlled diabetes mellitus because of the euthyroid sick syndrome. Caution should therefore be taken to
avoid over diagnosis of true hypothyroidism in light of the prevalence of euthyroid sick syndrome. Hyperthyroidism is rare in dogs but may occur in some cats with diabetes mellitus.

The energy intake of diabetic patients must be assessed in relation to body condition. For most patients (BCS 2/5 to 4/5), feeding at the daily energy requirement (DER) for ideal body weight in conjunction with adequate control of diabetes mellitus will achieve desired body weights. It is best to calculate a DER as a multiple of resting energy requirement (RER) based on the standard formulas for normal dogs and cats (Chapter 1). For neutered dogs, a factor of 1.6 x RER, and for intact dogs, a factor of 1.8 x RER are good initial estimates of DER. For inactive/obese-prone dogs (most dogs), a range of 1.2 to 1.4 x RER is suggested. Factors of 1.2 x RER and 1.4 x RER for neutered and intact cats, respectively, are appropriate starting points. For inactive/obese-prone cats (most cats), using 1.0 x RER is appropriate. All patients should be reevaluated regularly with food doses adjusted based on body condition.

Diabetic dogs and cats often present with an obese body condition. For overweight and obese diabetic patients, a conservative weight-loss protocol may need to be instituted after medical problems are stabilized. For controlled weight loss in overweight/obese dogs, a starting point for DER is 1.0 x RER and for overweight/obese cats 0.8 x RER. These calculations assume RER for ideal body weight and are a good initial estimate for calculation of food doses. Frequent monitoring and readjustment should be the norm rather than the exception in weight-loss programs for patients with concurrent disease such as diabetes mellitus. Note that in these patients, improvement in insulin resistance is often accomplished with weight loss. Because many cats with type II diabetes mellitus are obese, caloric restriction may be a requisite part of their dietary management. In cats, care must be taken to avoid rapid weight loss that may predispose to hepatic lipidosis. Loss of 0.5 to 1% of initial body weight per week is considered safe (Chapter 27). Hepatic lipidosis does not seem to be a weight-loss concern for dogs. See Box 29-2 for a feeding plan for DKA.

Feeding a food with moderate to high levels of fiber may pose problems for weight gain or even maintenance of current weight in diabetic patients that are too lean. These patients may need to be fed a food with less than 10% DM crude fiber and/or with slightly increased fat content to increase food energy density to a level where body weight is increased or maintained. Also, in these cases, feeding an increased quantity of food may prove useful. However, increasing the amount of food may not result in desired effects on body weight and condition if diabetes is poorly controlled.

Regarding when to feed, the feeding schedule should be designed to enhance the actions of insulin, maximize food usage and minimize postprandial hyperglycemia (Figure 29-4). The development of postprandial hyperglycemia depends, in part, on the amount of food consumed per meal, the rate at which glu-

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**Table 29-6.** Selected commercial fiber-enhanced veterinary therapeutic foods marketed for cats with diabetes mellitus compared to recommended levels of key nutritional factors.*

<table>
<thead>
<tr>
<th>Dry foods</th>
<th>Energy density (kcal/cup)**</th>
<th>Carbohydrate (%)</th>
<th>Fiber (%)</th>
<th>Fat (%)</th>
<th>Protein (%)***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommended levels</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hill’s Prescription Diet r/d Feline</td>
<td>263</td>
<td>33.5</td>
<td>13.6</td>
<td>9.3</td>
<td>36.9</td>
</tr>
<tr>
<td>Hill’s Prescription Diet r/d with Chicken Feline</td>
<td>266</td>
<td>32.2</td>
<td>13.8</td>
<td>9.8</td>
<td>37.7</td>
</tr>
<tr>
<td>Hill’s Prescription Diet w/d Feline</td>
<td>281</td>
<td>37.4</td>
<td>7.6</td>
<td>9.8</td>
<td>39.0</td>
</tr>
<tr>
<td>Hill’s Prescription Diet w/d with Chicken Feline</td>
<td>278</td>
<td>35.4</td>
<td>7.6</td>
<td>9.9</td>
<td>39.9</td>
</tr>
<tr>
<td>Iams Veterinary Formula Weight Control D/Optimum Weight Control</td>
<td>326</td>
<td>41.2</td>
<td>1.5</td>
<td>12.2</td>
<td>38.6</td>
</tr>
<tr>
<td>Iams Veterinary Formula Weight Loss/Restricted-Calorie</td>
<td>268</td>
<td>44.5</td>
<td>2.5</td>
<td>11.0</td>
<td>35.2</td>
</tr>
<tr>
<td>Purina Veterinary Diets OM Overweight Management</td>
<td>321</td>
<td>22.4</td>
<td>5.6</td>
<td>8.5</td>
<td>56.2</td>
</tr>
<tr>
<td>Moist foods</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recommended levels</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hill’s Prescription Diet r/d with Liver &amp; Chicken Feline</td>
<td>114/5.5 oz.</td>
<td>31.3</td>
<td>15.4</td>
<td>9.2</td>
<td>37.5</td>
</tr>
<tr>
<td>Hill’s Prescription Diet w/d with Chicken Feline</td>
<td>127/5.5 oz.</td>
<td>26.4</td>
<td>10.6</td>
<td>16.6</td>
<td>39.6</td>
</tr>
<tr>
<td>Iams Veterinary Formula Weight Loss/Restricted-Calorie</td>
<td>172/6 oz.</td>
<td>32.3</td>
<td>1.7</td>
<td>15.5</td>
<td>44.2</td>
</tr>
<tr>
<td>Purina Veterinary Diets OM Overweight Management</td>
<td>150/5.5 oz.</td>
<td>23.2</td>
<td>10.2</td>
<td>14.6</td>
<td>44.6</td>
</tr>
</tbody>
</table>

Note: Fresh water should be available at all times; semi-moist foods should be avoided.

*From manufacturers’ published information or calculated from manufacturers’ published as fed values; all values are on a dry matter basis unless otherwise stated.

**Energy density values are listed on an as fed basis and are useful for determining the amount to feed; cup = 8-oz. measuring cup. To convert to kJ, multiply kcal by 4.184.

***Cats with renal failure should be fed protein at the low end of the range.

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Endocrine Disorders
Table 29-7. Selected commercial low-carbohydrate/high-protein veterinary therapeutic foods marketed for cats with diabetes mellitus compared to recommended levels of key nutritional factors.*

<table>
<thead>
<tr>
<th>Moist foods</th>
<th>Energy density (kcal/can)** (%) (%) (%) ***</th>
<th>Carbohydrate (%)</th>
<th>Fat (%)</th>
<th>Protein (%)***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hill’s Prescription Diet m/d Feline</td>
<td>156/5.5 oz.</td>
<td>15.7</td>
<td>19.4</td>
<td>52.8</td>
</tr>
<tr>
<td>Iams Veterinary Formula Stress/Weight Gain Formula</td>
<td>333/6 oz.</td>
<td>12.2</td>
<td>37.2</td>
<td>41.8</td>
</tr>
<tr>
<td>Purina Veterinary Diets DM Dietetic Management</td>
<td>194/5.5 oz.</td>
<td>8.1</td>
<td>23.8</td>
<td>56.9</td>
</tr>
</tbody>
</table>

Recommended levels

<table>
<thead>
<tr>
<th>Dry foods</th>
<th>Energy density (kcal/cup)** (%) (%) (%) ***</th>
<th>Carbohydrate (%)</th>
<th>Fat (%)</th>
<th>Protein (%)***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hill’s Prescription Diet m/d Feline</td>
<td>480</td>
<td>14.7</td>
<td>22.0</td>
<td>51.5</td>
</tr>
<tr>
<td>Medi-Cal Diabetic DS 44</td>
<td>247</td>
<td>25.6</td>
<td>12.9</td>
<td>49.5</td>
</tr>
<tr>
<td>Purina Veterinary Diets DM Dietetic Management</td>
<td>592</td>
<td>15.0</td>
<td>17.9</td>
<td>57.8</td>
</tr>
<tr>
<td>Royal Canin Veterinary Diet Diabetic DS 44</td>
<td>239</td>
<td>25.6</td>
<td>12.9</td>
<td>49.5</td>
</tr>
</tbody>
</table>

Recommended levels

- From manufacturers’ published information or calculated from manufacturers’ published as fed values; all values are on a dry matter basis unless otherwise stated.
- Energy density values are listed on an as fed basis and are useful for determining the amount to feed; cup = 8-oz. measuring cup. To convert to kJ, multiply kcal by 4.184.
- Cats with renal failure should be fed protein at the low end of the range.

Body Weight and Condition

Achievement of weight goals can be measured through assessing body condition and weight. These measurements may also provide insight about the degree of glycemic control and the presence of other disease processes, especially in cases in which adjustments in food dose do not produce expected changes in body condition. Patients should be weighed every two weeks and have body condition assessed at least monthly. The owner should be encouraged to keep a chart of body weights and BCS. It may take several months to achieve weight-loss goals in obese patients. A loss of 10% body weight in already thin animals indicates a need for reassessment of the dietary and pharmacologic regimens.

Food Intake

Food intake, with maintenance of body weight, should decrease in patients with a favorable response to exogenous insulin administration. This response is caused by increased nutrient usage associated with hormonal treatment. If patients are...
anorectic or have depressed food intake, the relative palatability of the food may be poor and another food should be tried after ruling out medical causes. It is especially important to monitor food intake in cats because prolonged anorexia is a risk factor for hepatic lipidosis (Barsanti et al, 1977).

**Urine Glucose and Ketones**

Although most owners can monitor urine for glucose and ketones, urine testing for glucose is a crude indicator of glycemic control status. In the newly-diagnosed or ketogenic diabetic dog or cat, a decrease in urinary ketone bodies and glucose signals a favorable response to treatment. Well-controlled diabetic dogs and cats should not have ketone bodies in their urine. Occasional monitoring of urine for glycosuria and ketonuria in the home environment is helpful in those diabetic dogs and cats that have problems with recurring ketosis or hypoglycemia to determine if ketonuria or persistent negative glycosuria is present, respectively. In cats that have reverted to a non-insulin-requiring diabetic state, monitoring helps determine if glycosuria has recurred; in cats treated with oral hypoglycemic drugs, it helps determine if glycosuria has improved or worsened; and in cats with suspected stress-induced hyperglycemia, monitoring helps differentiate transient from persistent hyperglycemia. Owners should not adjust daily insulin dosages based on results of urine glucose testing, except to decrease the insulin dose in dogs or stop insulin treatment in cats with recurring hyperglycemia and persistent negative glycosuria.

**Biochemistry Profiles**

The biochemistry profile should return to normal with well-controlled diabetes and adequate nutritional intake. The primary exception is hyperglycemia that may or may not be present depending on when the blood sample is obtained in relation to insulin administration. Abnormalities of biochemical constituents in the face of controlled diabetes mellitus should be evaluated as separate disease entities.

**Serum Fructosamine**

Measurement of glycated proteins (e.g., glycosylated hemoglobin and serum proteins [fructosamine]) is a common method of monitoring glycemic control in diabetic people and animals. Glycosylated hemoglobin is the most common glycated protein measured in diabetic people, but assays are time-consuming, often of questionable accuracy and not routinely evaluated in diabetic dogs and cats. Serum fructosamine is the most common glycated protein measured in diabetic dogs and cats (Reusch et al, 1993; Crenshaw et al, 1996; Elliott et al, 1999). Fructosamines result from an irreversible, nonenzymatic, insulin-independent binding of glucose to serum proteins. Serum fructosamine concentrations are a marker of mean blood glucose concentration during the circulating lifespan of the protein, which varies from one to three weeks, depending on the protein. The extent of glycosylation of serum proteins is directly related to the blood glucose concentration; the higher the average blood glucose concentration during the preceding two to three weeks, the higher the serum fructosamine concentration, and vice versa. Serum fructosamine concentrations increase when glycemic control of diabetic dogs and cats worsens and decrease when glycemic control improves. Serum fructosamine concentration is unaffected by acute increases in blood glucose concentration, as occurs with stress or excitement-induced hyperglycemia, but can be affected by hypoalbuminemia (<2.5 g/dl), hyperlipidemia (triglycerides >150 mg/dl) and hyperthyroidism (Lutz et al, 1995; Crenshaw and Peterson, 1996; Reusch and Haberer, 2001). Interpretation of serum fructosamine in diabetic dogs and cats should consider the fact that hyper-
glycemia is common, even in well-controlled diabetics. Most owners are happy with their pet’s response to insulin treatment if serum fructosamine concentrations can be kept between 350 and 450 µmol/l. Values greater than 500 µmol/l indicate inadequate control of the diabetic state and values greater than 600 µmol/l indicate serious lack of glycemic control. Serum fructosamine concentrations in the lower half of the normal reference range (i.e., <300 µmol/l) or below the normal reference range should raise concern for significant periods of hypoglycemia in diabetic dogs and cats. Increased serum fructosamine concentrations (i.e., >500 µmol/l) suggest poor control of glycemia and the need for insulin adjustments, but do not identify the underlying problem.

Serial Blood Glucose Curves
Serial blood glucose curves are indicated during the initial regulation of newly-diagnosed diabetic dogs and cats and whenever an adjustment in insulin therapy is deemed necessary after reviewing the history, physical examination, changes in body weight and serum fructosamine concentration. Results of the serial blood glucose curve provide guidance when adjusting the insulin treatment regimen, unless blood glucose measurements are unreliable because of stress, aggression or excitement. Reliance on history, physical examination, body weight and serum fructosamine concentration to determine when a blood glucose curve is needed helps reduce the frequency of performing blood glucose curves, reduces the number of venipunctures and shortens the time the dog or cat spends in the hospital, thereby minimizing the patient’s aversion to these evaluations and improving the chances of obtaining meaningful results when a blood glucose curve is needed.

When assessing glycemic control, the insulin and feeding schedule used by the owner should be maintained. The dog or cat should be dropped off at the hospital early in the morning, and blood obtained every one to two hours throughout the day for glucose determination. The marginal ear vein prick technique for blood sampling can be used in diabetic cats to minimize problems with stress-induced hyperglycemia. Home monitoring of blood glucose concentrations using the marginal ear vein prick technique is also a viable option. Details on adjustment and in-depth analysis of serial glucose curves are provided elsewhere (Feldman and Nelson, 2004, 2004a).

FELINE HYPERTHYROIDISM
Hyperthyroidism is a clinical condition that results from excessive production and secretion of thyroxine (T4) and triiodothyronine (T3) by the thyroid gland. Hyperthyroidism is the most common endocrine disease affecting cats. The first clinical reports appeared in the late 1970s and early 1980s (Peterson et al, 1979; Holzworth et al, 1980). Disease prevalence has been estimated at one in 300 from necropsy findings (Ferguson, 1993). In a 1993 survey conducted at the Animal Medical Center in New York City, approximately 22 cats with hyperthyroidism were identified monthly (Broussard et al, 1995). It is unclear whether the prevalence of hyperthyroidism continues to escalate; however, there is no doubt that feline hyperthyroidism is now commonly recognized throughout the world and is one of the most frequently diagnosed diseases in small animal practice.

In contrast, hyperthyroidism is uncommon in dogs and is caused by functional thyroid adenomas and carcinomas, not adenomatous hyperplasia as typically occurs in cats (See below.) (Feldman and Nelson, 2004d). Thyroid carcinomas are highly malignant tumors that spread quickly in dogs. Thyroid carcinoma should always be assumed in any dog diagnosed with hyperthyroidism until histopathologic evaluation of the thyroid mass proves otherwise. Diagnosis is based on presence of clinical signs similar to those seen in hyperthyroid cats (See below.), identification of a thyroid mass with
digital palpation and cervical ultrasound and documentation of increased serum T4 and free T4 and non-detectable serum thyroid-stimulating hormone (TSH) concentration. Surgical removal of the thyroid mass is the treatment of choice whenever possible. Radiation therapy, chemotherapy, radioactive iodine-131, methimazole or a combination of these treatment modalities is usually indicated following removal of a thyroid carcinoma, especially if surgical debulking is incomplete or metastasis is suspected.

The remainder of this chapter will focus on feline hyperthyroidism.

**Patient Assessment**

**History and Physical Examination**

Hyperthyroidism is a disease of older cats. The average age at the time of diagnosis is 13 years with a range of four to 20 years. Fewer than 5% of cats with this disorder are younger than eight years (Feldman and Nelson, 2004e). There is no sex-related predisposition and domestic shorthair and long-hair cats are the most frequently affected breeds. Clinical signs result from excessive secretion of thyroid hormone by the thyroid mass and typically include weight loss (which may progress to cachexia), polyphagia and restlessness or hyperactivity (Table 29-8). Polyphagia is due to increased cellular metabolism. In some hyperthyroid cats, appetite may be decreased following a prolonged period of polyphagia. Decreased appetite is usually associated with weakness, muscle wasting and severe weight loss. The most common finding on physical examination is digital palpation of one or more discrete thyroid masses in the ventral neck. Because of the multisystemic effects of hyperthyroidism, the variable clinical signs and its resemblance to many other feline diseases (Table 29-9), hyperthyroidism should be suspected in any aged cat with medical problems.

**Laboratory and Other Diagnostic Testing**

The primary purpose of laboratory testing is to confirm the diagnosis of hyperthyroidism and screen the cat for concurrent disease, most notably renal insufficiency, which is common in geriatric cats and often present in conjunction with hyperthyroidism. Any number of abnormalities may be present in individual cats; however, clinical studies have elucidated common changes (Table 29-10). Specific diagnostics for thyroid dysfunction should be performed if thyroid disease is still consistent with and suspected from results of the initial screening of blood and urine tests.

**SERUM THYROID HORMONE TESTING**

The diagnosis of hyperthyroidism is based on identification of appropriate clinical signs, palpation of a thyroid nodule and documentation of an increased serum T4 concentration. Measurement of random baseline serum T4 concentrations has been extremely reliable in differentiating hyperthyroid cats from those without thyroid disease. Cats with early disease may have serum T4 concentrations within the upper portion of the reference range (i.e., 2.5 to 5.0 µg/dl). Serum T4 concentrations that fall within the upper portion of the reference range can create a diagnostic dilemma, especially when clinical signs suggest hyperthyroidism and a nodule is palpated in the ventral region of the neck. Cats with mild or occult hyperthyroidism and hyperthyroid cats with significant non-thyroidal illness can have normal serum T4 concentrations. The diagnosis of hyperthyroidism should not be excluded on the basis of one normal test result, especially in a cat with appropriate clinical signs and a palpable neck mass. Additional diagnostics to consider include measurement of the non-protein-bound fraction of T4 (i.e., free T4) in the circulation, the T3 suppression test, sodium pertechnetate thyroid scan or repeating the serum T4 test three to six months later. Measurement of serum free T4 using an equilibrium dialysis technique is the current recommendation of choice to confirm hyperthyroidism in cats with non-diagnostic serum T4 test results (Peterson et al, 2001). Measurement of serum free T4 is a more reliable means of assessing thyroid gland function than serum T4 concentration, in part, because non-thyroidal illness has less of a suppressive effect on serum free T4 than T4 and serum free T4 is increased in many cats with occult hyperthyroidism and normal T4 test results (Peterson et al, 2001). Occasionally, concurrent illness will cause an increase in serum free T4 concentration in cats; an increase that can exceed the reference range. For this reason, serum free T4 should always be interpreted in conjunction with T4 measured from the same blood sample.

**TRIOIODOTHYRONINE (T3) SUPPRESSION TEST**

The T3 suppression test is used to distinguish euthyroid from mildly hyperthyroid cats in cases in which T4 and free T4 test results are nebulous. The T3 suppression test is based on the theory that oral administration of T3 will suppress pituitary TSH secretion in euthyroid cats, resulting in a

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**Table 29-9. Differential diagnoses for hyperthyroidism.**

<table>
<thead>
<tr>
<th>Category</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-thyroid endocrine disease</strong></td>
<td>Acromegaly (rare)</td>
</tr>
<tr>
<td></td>
<td>Diabetes insipidus (rare)</td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td></td>
<td>Hyperadrenocorticism (rare)</td>
</tr>
<tr>
<td><strong>Renal disease</strong></td>
<td>Congestive cardiomyopathy</td>
</tr>
<tr>
<td></td>
<td>Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td><strong>Heart disease</strong></td>
<td>Idiopathic dysrhythm</td>
</tr>
<tr>
<td><strong>Gastrointestinal disease</strong></td>
<td>Cancer</td>
</tr>
<tr>
<td></td>
<td>Diffuse gastrointestinal disorders</td>
</tr>
<tr>
<td></td>
<td>Inflammatory</td>
</tr>
<tr>
<td><strong>Pulmonary disease</strong></td>
<td>Hepatopathy</td>
</tr>
</tbody>
</table>

---

decrease in circulating T4. In contrast, pituitary TSH secretion is already suppressed in cats with hyperthyroidism, oral administration of T3 will not cause further suppression and serum T4 will not decrease following T3 administration. In this test, T3 is administered orally three times daily for seven treatments and serum T4 concentration is determined before and eight hours after the last T3 administration (Feldman and Nelson, 2004c).

**SODIUM PERTECHNETATE THYROID SCAN**

The sodium pertechnetate thyroid scan is used to identify functional thyroid tissue. Radioactive sodium pertechnetate is administered intravenously and uptake by thyroid tissue is assessed by scintillation scan. Uptake of sodium pertechnetate will be greater and the distribution and size of functioning thyroid tissue will be abnormal in hyperthyroid cats, compared with scans obtained in euthyroid cats. Sodium pertechnetate uptake is useful for diagnosing unilateral vs. bilateral thyroid lobe involvement, identifying ectopic thyroid tissue and identifying sites of metastasis in cats with thyroid carcinoma.

**Etiopathogenesis**

**NORMAL THYROID FUNCTION**

The thyroid gland is the site of thyroid hormone synthesis and is regulated by integration of cortical and substrate feedback signals (Figure 29-5) (Feldman and Nelson, 2004c; Kaptein et al, 1994). The thyroid gland concentrates iodide under the influence of TSH for thyroid hormone synthesis. Iodide anions undergo peroxidation and linkage to tyrosine residues, which are components of larger acceptor proteins (i.e., primarily thyroglobulin). Excess absorbed iodine is eliminated primarily in urine; however, unabsorbed amounts may be found in feces (Kaptein et al, 1994).

Tyrosine residues attached to thyroglobulin may be either monoiodinated (monoiodotyrosine [MIT]) or diiodinated (diiodotyrosine [DIT]) and subsequent dimerization results in formation of the iodothyronines T3 and T4. Thyroglobulin is subsequently processed so that T4, and to a much lesser degree T3, are eventually released into the bloodstream. The thyroid gland directly produces all T4 and approximately 20% of T3 found in serum; 99% of these hormones are bound to serum proteins (Kaptein et al, 1994). The portion of T4 and T3 partitioned into serum, and not associated with protein, is often called free or fT4 and fT3. Some biologically inactive MIT and DIT and intact thyroglobulin may be released into the circulation. Reverse T3 (rT3) is another inactive thyroid metabolite found in serum and is formed from the deiodination of T4.

T3, the more active form of thyroid hormone, is primarily produced from thyroxine via deiodinase enzymes in target tissues. Deiodinase I, a selenoprotein, is located primarily in the kidneys and liver (Larsen and Berry, 1995). Deiodinase I prefers rT3 as a substrate, releasing DIT; therefore, it may be important in the deactivation process of thyroid hormone. Deiodinase I also has activity for T4, producing active T3; however, this is an order of magnitude less than the rT3 affinity. The T3 produced by the liver may be released into the general circulation to exert its biologic activity. The exact physiologic

**Table 29-10. Laboratory findings in animals with hypothyroidism and hyperthyroidism.**

<table>
<thead>
<tr>
<th>Laboratory tests</th>
<th>Feline hyperthyroidism</th>
<th>Canine and feline hypothyroidism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biochemical analysis</td>
<td>Increased ALT, ALP, creatinine, urea nitrogen, glucose, bilirubin and phosphate values</td>
<td>Increased cholesterol, triglyceride, ALT (mild), ALP (mild) and CK (mild, variable) values</td>
</tr>
<tr>
<td>Cardiac diagnostics</td>
<td>Tachycardia, PVCs, hypertrophic cardiomyopathy</td>
<td>Bradycardia, inverted T waves</td>
</tr>
<tr>
<td>Complete blood count</td>
<td>Erythrocytosis, leukocytosis, lymphopenia, eosinopenia, increased MCV</td>
<td>Normocytic, normochromic, nonregenerative anemia with leucocytes possible</td>
</tr>
<tr>
<td>Imaging</td>
<td>Normal or cardiac/respiratory abnormalities</td>
<td>Normal/thyroid mass, metastatic lesions, thoracic or abdominal effusion</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>Increased or decreased specific gravity, glucosuria, signs of inflammation</td>
<td>Normal to nonspecific increase in white blood cells</td>
</tr>
</tbody>
</table>

Key: MCV = mean corpuscular volume, ALT = alanine aminotransferase, ALP = alkaline phosphatase, PVC = premature ventricular contraction, CK = creatine kinase.

**Figure 29-5.** Schematic of the hypothalamic-pituitary-thyroid axis. Key: TRH = thyrotropin-releasing hormone, TSH = thyroid-stimulating hormone (thyrotropin), T4 = thyroxine, T3 = 3,5,3′-triiodothyronine, rT3 = reverse T3, + = stimulation, – = inhibition.
importance of deiodinase I in the liver has yet to be elucidated (Larsen and Berry, 1995).

The enzyme deiodinase II is specific for production of T3 from T4 and is found in low concentrations in most cells including those of the brain, skin, muscle and placenta (Larsen and Berry, 1995; Freake and Oppenheimer, 1995). Deiodinase II is responsible for the intracellular production of T3, which may subsequently be moved to the nucleus of these cells (Figure 29-6). Production of T3 and subsequent nuclear binding is probably the major physiologic route of thyroid action. Preliminary evidence suggests deiodinase II is a selenoprotein (Davey et al, 1995).

The major route of thyroid hormone action is thought to be via nuclear interaction at peripheral tissues. As a result, cells increase consumption and production of energy and exert hormonal effects for normal growth and development of skeletal muscle and neural tissues. The exact mode of this action has yet to be elucidated; however, it is thought to involve the key enzymatic controls of carbohydrate, fat and protein metabolism. In addition, investigators have proposed a possible uncoupling of oxidative phosphorylation and modulation of Na/K-ATPase activity at the cellular membrane (Kaptein et al, 1994).

**Risk Factors**

Although the clinical aspects of feline hyperthyroidism have been well characterized, the etiology of hyperthyroidism remains unknown. The presence of adenomatous hyperplasia rather than neoplasia in most affected cats, bilateral thyroid lobe involvement with differences in severity of involvement between the lobes and the initial involvement of one thyroid lobe progressing to involvement of both lobes suggests the presence of a goitrogenic factor that may influence development of thyrotoxicosis in a species that may be predisposed to the disease. It has been postulated that immunologic, infectious, nutritional, environmental or genetic factors may interact to cause pathologic changes (Scarlett, 1994; Gerber et al, 1994). Epidemiologic studies have identified consumption of commercial canned cat foods as a risk factor for development of hyperthyroidism, suggesting that a goitrogenic compound may be present in the diet (Table 29-11) (Scarlett et al, 1988; Kass et al, 1999; Martin et al, 2000; Edinboro et al, 2004). Environmental factors such as use of kitty litter may also be involved. The increase in the number of cats housed indoors and the corresponding change in quality of care and the types of cat food in the late 1960s and early 1970s followed by the sudden recognition of the disorder in the late 1970s supports a role for diet or the environment in the pathogenesis of hyperthyroidism. Iodine is one potential dietary goitrogen. Most commercially prepared cat foods contain adequate amounts of iodine, with measured levels ranging from three to 100 times recommended amounts (Mumma et al, 1986; Johnson et al, 1992). Variability in iodine intake has resulted in iodine-induced hyperthyroidism in people (Jodbasedow syndrome) (Skare and Frey, 1980; Fradkin and Wolff, 1983). In addition, deficient or excessive iodine intake in homemade or poorly formulated foods may also be goitrogenic (Scarlett, 1994). Soybean is another potential dietary goitrogen that is commonly used as a high quality vegetable protein in commercial cat foods (Court and Freeman, 2002; White et al, 2004). The goitrogenic effect of soybeans has been attributed to an inhibitory effect of the soy isoflavones genistein and daidzein on thyroid peroxidase, an enzyme essential to thyroid hormone synthesis (Divi et al, 1997). In a recent study, short-term administration of dietary soy to healthy cats resulted in a modest increase in serum T4 and free T4 concentrations relative to serum T3 concentrations (White et al, 2004). One epidemiologic study found consumption of pop-top canned (compared to dry) food was associated with a greater risk of developing hyperthyroidism and speculated that the chemicals lining the cans, specifically bisphenol A, may have migrated into the food and served as a goitrogen (Edinboro et al, 2004). Bisphenol A reduces binding of T3 to

**Figure 29-6.** Deiodinase II enzyme is found in low concentrations in most cells and is responsible for the intracellular production of T3 from T4. The production of T3 and subsequent nuclear binding is probably the major physiologic route of thyroid action.

<table>
<thead>
<tr>
<th>Nutrients or food types</th>
<th>Environmental</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cabbage (goitrin)</td>
<td>Polychlorinated biphenyls (fish-containing foods)</td>
</tr>
<tr>
<td>Canned foods</td>
<td>Pesticides</td>
</tr>
<tr>
<td>Cassava (linamarin)</td>
<td>Phthalates</td>
</tr>
<tr>
<td>Cyanides</td>
<td>Polyphenols (fish-containing foods)</td>
</tr>
<tr>
<td>Excess iodine</td>
<td>Propylthiouracil (drug)</td>
</tr>
<tr>
<td>Iodine deficiency</td>
<td>Resorcinols (fish-containing foods)</td>
</tr>
<tr>
<td>Millet</td>
<td>*Epidemiologic associations and risk factors.</td>
</tr>
<tr>
<td>Rutabagas</td>
<td></td>
</tr>
<tr>
<td>Sweet potatoes</td>
<td></td>
</tr>
<tr>
<td>Turnips</td>
<td></td>
</tr>
<tr>
<td>Seaweed</td>
<td></td>
</tr>
<tr>
<td>Various beans (including soybeans)</td>
<td></td>
</tr>
</tbody>
</table>

*Epidemiologic associations and risk factors.
thyroid receptors and interferes with signal transduction in rats (Moriyama et al, 2002) and has been detected in canned cat foods (Kang and Kondo, 2002).

Recent studies have also identified overexpression of the \( c\)-ras oncogene in areas of nodular follicular hyperplasia in feline thyroid glands, suggesting that mutations in this oncogene may play a role in the etiopathogenesis of hyperthyroidism in cats (Merryman et al, 1999). In normal cells, activation of the \( ras \) oncogene will result in desired body weight: Neutered cats: 1.2 x RER; Intact cats: 1.4 x RER.

Fat

Fat levels for normal cats are usually adequate until normal body condition is achieved (Tables 20-3 and 21-2). The following levels are adequate unless renal function is compromised: 28 to 45%.

Protein

The following dietary protein for underweight cats is recommended: Provide increased dietary protein for underweight animals. The following levels are adequate unless renal function is compromised: 28 to 45%. True protein digestibility should be greater than 85%.

Fiber

Avoid fiber levels greater than 8% in patients with poor body condition. Some references are made to the key nutritional factors for foods for normal weight young adult cats and mature adult cats, respectively.

Macrominerals

Ensure food meets AAFCO recommendations for adult maintenance to compensate for increased losses of magnesium, potassium, chloride, calcium and phosphorus vary greatly in trace mineral content. It may be necessary to contact product manufacturers to determine iodine and selenium levels.

Trace minerals

Generally, foods that meet AAFCO minimum allowances for trace minerals are adequate; however, commercial products may vary greatly in trace mineral content.

Table 29-12. Key nutritional factors for hyperthyroid cats.*

<table>
<thead>
<tr>
<th>Factors</th>
<th>Recommended food levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>Fresh, clean water should be available at all times</td>
</tr>
<tr>
<td>Energy</td>
<td>Feeding at the DER for ideal weight in conjunction with adequate control of hyperthyroidism will result in desired body weight: Neutered cats: 1.2 x RER; Intact cats: 1.4 x RER</td>
</tr>
<tr>
<td>Fat</td>
<td>Provide increased dietary fat for underweight cats</td>
</tr>
<tr>
<td>Protein</td>
<td>Provide increased dietary protein for underweight cats</td>
</tr>
<tr>
<td>Fiber</td>
<td>Avoid fiber levels &gt;8 in cats with poor body condition</td>
</tr>
<tr>
<td>Macrominerals</td>
<td>Ensure food meets AAFCO recommendations for adult maintenance to compensate for increased losses of magnesium, potassium, chloride, calcium and phosphorus</td>
</tr>
<tr>
<td>Trace minerals</td>
<td>Generally, foods that meet AAFCO minimum allowances for trace minerals are adequate; however, commercial products vary greatly in trace mineral content</td>
</tr>
</tbody>
</table>

Key: DER = daily energy requirement, RER = resting energy requirement, AAFCO = Association of American Feed Control Officials.

* Nutrients expressed on a % dry matter basis.

Hyperthyroid cats are in a hypercatabolic state and may exhibit signs of protein wasting and deficiency. Increased protein intake may be needed during the recovery period to replenish body protein. However, hyperthyroidism is frequently associated with renal failure, which should prompt a complete evaluation of renal function before feeding higher protein foods (Chapter 37).

Provide increased dietary protein for underweight animals. The following DM levels are adequate unless renal function is compromised: 28 to 45%. True protein digestibility should be greater than 85%.

FIBER

Avoid food with DM fiber levels greater than 8% in patients with poor body condition (Table 29-12).

MACROMINERALS

Because hyperthyroidism may result in macromineral abnor-
malities (i.e., phosphorus, potassium, sodium, calcium), it is best to avoid foods with excess (all-purpose foods) or deficient levels. Decreased sodium chloride intake may benefit some cases in which hypertension and cardiac disease are primary problems (Chapter 36). Foods that exceed AAFCO minimum nutrient allowances should suffice in most cases. Most commercial cat foods will provide adequate levels of these nutrients. A more refined recommendation would be the mineral key nutritional factor recommendations for normal weight young adult and mature adult cats (Tables 20-3 and 21-2).

**TRACE MINERALS**

Iodine may be excessive or deficient in different states of thyroid disease. Iodine intake should be thoroughly evaluated to determine adequacy. Generally, foods that meet AAFCO minimum allowances for trace minerals are adequate; however, some commercial products vary greatly in trace mineral content (Box 29-3).

**Feeding and Treatment Plan for Hyperthyroid Cats**

The success of nutritional management of hyperthyroidism depends to a great degree on the effectiveness of medical/surgical treatment for the primary disease. Three modes of treatment are generally accepted for hyperthyroidism in cats: 1) long-term antithyroid medication, 2) surgical thyroidectomy and 3) radioactive iodine (Kintzer, 1994).

**Assess and Select the Food**

Information obtained from assessing the food is essential for making changes to foods currently fed. Compare the current food’s key nutritional factor content with the recommendations in Table 29-12 and those in Tables 20-3 and 21-2 for healthy young adult and mature adult cats in the sections for normal body weight and condition. Identify any discrepancies between the recommended levels of key nutritional factors and current intake. If discrepancies exist, consider selecting a food that more closely matches the key nutritional factor targets from Tables 20-3 and 21-2. During the convalescent period, in those cases that require additional protein and energy to regain body weight, commercially prepared maintenance-type foods may be mixed with growth/reproduction-type formulas to achieve higher protein and fat intakes (Feldman and Nelson, 2004c). However, growth/reproduction-type foods may add excessive sodium and phosphorus possibly complicating concurrent renal disease or primary cardiac disease, if present.

**Assess and Determine the Feeding Method**

It may not always be necessary to change the feeding method when managing animals with hyperthyroidism. However, a thorough evaluation includes verification that an appropriate feeding method is being used. Any deviations from ideal feeding methods should be identified and changes made as required.

Patients will usually return to normal body weight if provided energy at the calculated DER for ideal body weight. Small amounts in several feedings may need to be fed during recovery. Two daily feedings are adequate after a patient resumes normal eating behavior.

**Reassessment**

Patient response to treatment is assessed by owner observation of clinical signs, bimonthly body weight charting and monitoring food intake, findings on physical examination and measurement of serum T4 concentrations. Return to normal activity, body condition and appearance, and normal serum T4 concentration indicate a successful response to treatment. Treatment is inadequate if clinical signs persist, body weight and body condition remain poor and serum T4 concentration remains increased. Adjustments in the treatment regimen and problems with owner compliance should be considered if the cat is being treated with oral methimazole. Remnants of hyperfunctioning thyroid tissue should be considered if thyroidectomy was performed or radioactive iodine-131 was administered.

**HYPOTHYROIDISM**

Adult-onset hypothyroidism may be the most common endocrine disease affecting dogs and results from destruction of the thyroid gland. Two histologic forms of primary hypothyroidism predominate in dogs: lymphocytic thyroiditis and idiopathic atrophy. Lymphocytic thyroiditis is an immune-mediated disorder that appears to have a genetic component based on breed predisposition for the disease (Nachreiner et al, 2002). Idiopathic atrophy of the thyroid gland may be a primary degenerative disorder or an endstage of lymphocytic thyroiditis (Gosselin et al, 1981; Conaway et al, 1985). In contrast, naturally-acquired adult-onset hypothyroidism occurs rarely in cats, but iatrogenic hypothyroidism may occur following treatment of hyperthyroidism. Congenital hypothyroidism is very uncommon in dogs and cats and usually results from thyroid dysgenesis or dyshormonogenesis (Feldman and Nelson, 2004c).

The diagnosis of hypothyroidism is based on the presence of appropriate clinical signs (Table 29-8), findings on physical examination, results of routine blood and urine tests and tests of thyroid gland function, including serum T4, free T4 and TSH (Table 29-10). Treatment involves oral administration of sodium levothyroxine once or twice daily. In adult dogs, all abnormalities caused by hypothyroidism will resolve with appropriate thyroid hormone replacement therapy. A tendency to gain weight and development of hyperlipidemia are two problems associated with untreated hypothyroidism that may require dietary intervention. Weight gain often occurs without a corresponding increase in appetite or food intake. In one study, energy expenditure, as measured by indirect calorimetry, was approximately 15% lower in hypothyroid dogs, compared with healthy dogs (Greco et al, 1998). Energy expenditure returned to normal after initiating levothyroxine sodium treatment. Initiating a weight-loss program in conjunction with thyroid hormone replacement therapy is warranted in obese cats.
Since the first clinical reports in 1979 and 1980, pathologic and epidemiologic studies of hyperthyroidism have indicated that the incidence of the disease has increased. A recent study showed that the prevalence of this disease increased 20% over a 20-year period and the estimated overall prevalence is 2%. The cause of this epizootic is important, particularly because this disease has become a leading cause of morbidity in middle-aged and older cats.

A number of epidemiologic studies indicate a greater incidence of hyperthyroidism in cats consuming canned foods (i.e., two- to fourfold higher incidence in cat populations consuming canned foods relative to cats consuming dry foods only). Figures 1 and 2 show that selenium concentrations are markedly higher in canned cat foods vs. dry cat foods, suggesting that selenium could be a factor in this disease. Selenium concentrations in cat foods are also higher than in dog foods. This selenium difference may explain why hyperthyroidism is prevalent in cats, but not dogs. There is also a known metabolic basis for selenium’s involvement in thyroid hormone metabolism. Iodothyronine deiodinase, the enzyme that converts thyroxine (T₄) to the metabolically active 3,3',5-triiodothyronine (T₃), is a selenium-containing enzyme.

Iodine is another nutrient that can profoundly affect thyroid gland function. Iodine concentrations in pet foods can vary widely from deficient to excess (100x the minimum recommended dietary allowance). This variation may be of importance; people living in iodine-deficient areas who later become exposed to normal or excessive amounts of iodine can present with signs of hyperthyroidism.

**Box 29-3. Role of Selenium and Iodine Excess in Hyperthyroid Disease.**

Since the first clinical reports in 1979 and 1980, pathologic and epidemiologic studies of hyperthyroidism have indicated that the incidence of the disease has increased. A recent study showed that the prevalence of this disease increased 20% over a 20-year period and the estimated overall prevalence is 2%. The cause of this epizootic is important, particularly because this disease has become a leading cause of morbidity in middle-aged and older cats.

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Iodine is another nutrient that can profoundly affect thyroid gland function. Iodine concentrations in pet foods can vary widely from deficient to excess (100x the minimum recommended dietary allowance). This variation may be of importance; people living in iodine-deficient areas who later become exposed to normal or excessive amounts of iodine can present with signs of hyperthyroidism.

**Figure 1.** Selenium (Se) concentrations in U.S. vs. New Zealand pet food. Bars represent average Se concentration (dry matter basis) for four categories: Wet (canned) cat food, dry cat food, wet dog food and dry dog food and compare U.S. products (left) vs. New Zealand products (right) (n = number of samples). Se concentrations in U.S. wet and dry cat food ranged from 0.81 to 5.0 and 0.43 to 1.9 mg/kg Se, respectively. Se ranges were not given for New Zealand products. Regardless of country, Se concentrations in wet cat food are generally two- to fourfold higher than those of dry cat food. Furthermore, Se concentrations in most wet cat foods exceed safe upper limits established for people, but vary widely among products of pet food companies. Key: LOAEL = lowest observable adverse effect level.

**Figure 2.** Selenium (Se) concentrations in U.S. feline canned foods. Companies are not identified, but noted as A to G; (n = number of samples). Bars represent average Se concentrations (dry matter [DM] basis). Se concentrations ranged from 0.81 to 5.0 mg/kg. The minimum Se requirement of adult cats is 0.13 mg/kg DM Se (Wedekind et al, 2003). According to sources, beneficial anti-cancer effects are observed when Se is fed at 5 to 10x the requirement (Combs, 2000; Neve, 2002). For cats, this optimal range is 0.65 to 1.3 mg/kg. However, the safe upper limit for Se for cats should probably be set at 1.3 mg/kg Se. There is probably little benefit of additional Se above this range and possibly harm. In people, the lowest observable adverse effect level (LOAEL) occurs at 913 µg/d and the no observable adverse effect level (NOAEL) occurs at 800 µg/d (DRI, 2001), which equates to 1.57 mg/kg Se (metabolic equivalent for cats) and 1.38 mg/kg Se, respectively. Overt signs of selenosis in people include hair loss and nail sloughing.
Figures 3 and 4 confirm the variability and excessive levels of iodine concentrations that exist in some commercial pet foods. There have been several theories regarding the role of diet and environment in hyperthyroid disease: 1) iodine excess, 2) immunoglobulins, 3) goitrogenic compounds and 4) environmental exposure to chemicals and infectious agents. However, none of these theories have conclusively identified the factor or factors involved in this disease.

The evidence presented below suggests selenium as a factor in the disease. One other study evaluated the role of selenium in hyperthyroid cats, but these researchers were unable to document a link between selenium status and hyperthyroid incidence.

Evidence of selenium’s role in feline hyperthyroidism:

1. Serum T3 increases with increasing selenium intake. There is a metabolic basis for selenium’s role in thyroid hormone metabolism.
2. Serum T3 is highly correlated with serum selenium concentration.
3. Serum selenium concentrations are higher in cats (approximately fivefold greater) than levels in other species. Cats fed foods containing similar selenium levels as dogs have significantly higher serum selenium concentrations (Table 1).
4. A dose-titration study in dogs showed excess selenium produces changes in thyroid hormone profiles directionally similar to those cited for hyperthyroid cats (Table 2).
5. Higher selenium concentrations are present in canned cat foods relative to dry cat foods and dry or canned dog foods (Figure 1).

**Figure 3.** Iodine (I) concentrations in U.S. pet foods vs. cat foods in Germany. Bars represent average I concentration (dry matter basis) for four categories: Wet (canned) cat food, dry cat food, wet dog food and dry dog food and compare U.S. products (left) vs. Germany products (right) (n = number of samples). I concentrations in U.S. cat foods ranged from 1.1 to 52.3 mg/kg; I concentrations in U.S. dog foods ranged from 0.8 to 196.8 mg/kg. Cat foods from Germany ranged from 0.22 to 6.4 mg/kg. Likewise, other investigators found highly variable and high I concentrations in U.S. pet foods (e.g., 1 to 36.8 mg/kg I) (Mumma et al, 1986). In the U.S., wet pet foods are typically higher in I than dry pet foods. Also, U.S. dog foods were generally higher in I than cat foods, but were highly variable. In people, the no observable adverse effect level (NOAEL) and lowest observable adverse effect level (LOAEL) for I are 1,000 and 1,700 µg/day, respectively (DRI, 2001). According to research, there is good agreement between people and cats with regards to measures of I status; thus, the human guidelines should be applicable to cats, and would equate to 3.5 and 6.0 mg/kg I, respectively (Wedekind et al, In press). Note that a number of pet foods exceed the safe upper limit established for people. High I intakes in people have been associated with thyroiditis, goiter, hypothyroidism, hyperthyroidism, thyroid papillary cancer and iodermia, a dermatologic reaction to iodine (DRI, 2001).

**Figure 4.** Iodine (I) concentrations in U.S. feline canned foods. Companies are denoted as A to F and not identified by name (n = number of samples). Bars represent average I concentrations (dry matter basis). I concentrations ranged from 1.1 to 52.3 mg/kg. The minimum I requirement of adult cats is 0.46 mg/kg (Wedekind et al, In press). For cats, the recommended optimal I range is between 0.60 to 3.5 mg/kg. The lower end is based on the experimentally derived requirement, plus 30% overage to allow for lower availability in certain foods, whereas the upper limit is extrapolated from people and is based on the no observable adverse effect level (NOAEL). In people, 10x the daily I requirement may lead to goiter and hypothyroidism (Pennington, 1990). Therefore, the upper limit should probably be less than 10x the cat requirement (i.e., 1,000 µg/day or 3.5 mg/kg I). Note that I concentrations vary widely by products from different companies and may greatly exceed safe upper limits established for people.
Fasting hypercholesterolemia, hypertriglyceridemia and lipemia are classic clinical chemistry findings in dogs with hypothyroidism. Hyperlipidemia can become severe with serum cholesterol and triglyceride concentrations exceeding 1,000 mg/dl. Thyroid hormones stimulate virtually all aspects of lipid metabolism, including synthesis, mobilization and degradation (Mahley et al, 2003). Both synthesis and degradation of lipids are depressed in hypothyroidism, with degradation affected more than synthesis. The net effect is an accumulation of plasma lipids and the potential for development of atherosclerosis (Hess et al, 2003). Fortunately, hyperlipidemia resolves fairly quickly after initiation of thyroid hormone replacement therapy. Regardless, feeding lower fat-containing foods to hyperlipidemic dogs diagnosed with hypothyroidism is warranted to help correct the hyperlipidemia, minimize problems associated with hyperlipidemia (e.g., atherosclerosis, abdominal discomfort, neurologic signs, pancreatitis) and reduce caloric intake to favor weight loss.

The references for Chapter 29 can be found at www.markmorris.org.
CASE 29-1

Polydipsia/Polyuria in a Cat
Richard W. Nelson, DVM, Dipl. ACVIM (Internal Medicine)
School of Veterinary Medicine
University of California, Davis
Davis, California, USA

Patient Assessment
A six-year-old, neutered female domestic shorthair cat was examined for polydipsia and polyuria of two weeks' duration, lethargy and anorexia. The cat remained indoors at all times and had been overweight for several years.

Physical examination revealed an alert, hydrated cat. Body weight was 4.8 kg with a body condition score (BCS) of 5/5. The optimal body weight was estimated to be 3.5 kg. The abdomen was tense when palpated but nonpainful. The borders of the liver were palpable beyond the margins of the rib cage and the bladder was distended. The coat had a greasy appearance with slight dander.

Results of a complete blood count were normal. Abnormal serum biochemistry profile results included increased glucose (398 mg/dl, reference interval = 70 to 110 mg/dl) and cholesterol (416 mg/dl, reference interval = 90 to 250 mg/dl) concentrations. Urinalysis revealed glucosuria and a urine specific gravity of 1.019. The tentative diagnoses were diabetes mellitus and obesity.

Assess the Food and Feeding Method
The cat was normally fed a commercial specialty brand dry cat food (Science Diet Feline Maintenance) free choice and one can of a commercial grocery brand “gourmet” cat food (Fancy Feast Chunk Chicken Feast) twice daily. Table 1 lists nutrient levels in these foods. The gourmet food contained approximately 85 kcal (356 kJ) per can. Water was available free choice. The cat’s appetite had always been very good until yesterday.

Questions
1. What factors may have predisposed this cat to developing diabetes mellitus?
2. What key nutritional factors should be considered for this patient?
3. Outline an appropriate feeding plan (foods and feeding method) for this cat.
4. How should this patient be monitored?

Answers and Discussion
1. Obesity is a known risk factor for development of non-insulin-dependent diabetes mellitus (type II), especially in cats. Type II diabetes mellitus may occur in obese animals subsequent to down regulation of peripheral insulin receptors, as occurs in people.

2. The key nutritional factors for patients with uncomplicated diabetes mellitus are water, digestible (soluble) carbohydrate, fiber, fat, protein and food form (avoid semi-moist foods). Dietary minerals and vitamins may also be important in patients with some forms of diabetes mellitus (ketoacidosis) and those with prolonged polydipsia and polyuria. Water should always be available free choice and in abundant amounts. The amount of energy and source of energy substrates (e.g., avoid simple sugars and fat) are also important. Complex carbohydrates and protein best supply energy for this patient. Excess dietary fat should also be avoided as part of a weight-reduction program. Increased dietary fiber helps reduce the caloric density of the food and helps maintain glycemic control in conjunction with medical management.

3. The goals of dietary management for this cat include: 1) reducing weight to improve or eliminate peripheral insulin resistance and other metabolic abnormalities, 2) providing consistent daily energy intake and 3) minimizing postprandial fluctuations in serum glucose concentrations. The cat should be fed a food that contains lower energy density, lower fat and higher crude fiber levels than the foods currently being offered. The amount of food should be divided and offered at least twice daily immediately after treatment with insulin or oral hypoglycemic agents. Daily food dosage should be calculated for optimal body weight. Many well-regulated overweight diabetic cats lose weight when fed at optimal body weight. An energy calculation of 1.2 x resting energy requirement (RER) for the estimated optimal body weight is a reasonable starting point.

4. Response to treatment can be assessed through careful owner observation. Favorable response to treatment is indicated by decreased water intake, decreased urination, decreased food intake (in animals that exhibit polyphagia), achievement of weight goals and a generalized increased thriftiness. Unfavorable responses include continuation of polydipsia, polyuria, polyphagia and inability to achieve weight goals. If the animal is stable and doing well then veterinary reassessment should take place every three to four months. If the animal is symptomatic then veterinary reassessment should take place every one to two weeks until stable.

Achievement of weight goals can be measured through BCS and body weight. Cats should be weighed and have body condition assessed at least once a month. The owner may keep a chart of body weight and BCS. Weight loss will usually take six to 12 months to occur. A loss of 10% body weight in already thin animals indicates a need for reassessment of the dietary regimen and
Maintenance of body weight with a reduction in food intake should occur in polyphagic animals responding favorably to exogenous insulin administration. This response occurs due to increased nutrient usage associated with hormonal treatment. If animals exhibit anorexia or depressed food intake then the relative palatability of the food may be poor and another food should be tried after ruling out medical causes. It is especially important to monitor food intake in cats because prolonged anorexia can lead to hepatic lipidosis.

Abnormalities in the serum biochemistry profile should return to normal with well-controlled diabetes and adequate nutritional intake. The major exception to this is hyperglycemia, which may or may not be present depending on when the blood sample is obtained in relation to when insulin is administered. Abnormalities of biochemical constituents in the face of controlled diabetes mellitus should be evaluated as separate disease entities.

**Progress Notes**

An oral hypoglycemic sulfonylurea drug (glipizide) was chosen (5 mg per os, twice daily) because the owners did not want to give insulin injections. The food was changed to a commercial moist veterinary therapeutic food (Prescription Diet w/d Felinea) that was lower in fat (16.6% dry matter [DM]) and higher in crude fiber (approximately 10% DM) than the previous foods. The digestible carbohydrate content of the new food was approximately 27% DM. The daily food amount was divided into two meals and offered 30 minutes after the drug treatment each morning and evening. Total daily energy intake was initially calculated at 1.2 x RER for a body weight of 3.5 kg (210 kcal/day, 880 kJ/day).

The cat lost weight over the next six months. It reached a body weight of 3.8 kg (BCS 3/5) and glipizide was eventually discontinued because normal glucose tolerance was maintained with dietary management alone. The lower fat, higher fiber food was continued but the amount fed was increased to maintain optimum body weight and condition.

**Endnotes**

a. Hill's Pet Nutrition, Inc., Topeka, KS, USA. This product is currently available as Science Diet Adult Original.
b. Friskies Petcare Co, Glendale, CA, USA.
c. Glucotrol. Roerig Division, Pfizer Inc., New York, NY, USA.

**Bibliography**


**Table 1. Nutrient levels in foods fed to a diabetic cat.**

<table>
<thead>
<tr>
<th>Nutrients (DM)</th>
<th>Dry specialty brand food*</th>
<th>Moist grocery brand food**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude fat (%)</td>
<td>23.0</td>
<td>34.0</td>
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<tr>
<td>Crude fiber (%)</td>
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<td>Energy (kcal/g)</td>
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<td>NFE (%)</td>
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<tr>
<td>Protein (%)</td>
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</table>

Key: DM = dry matter, NFE = nitrogen-free extract.

*aScience Diet Feline Maintenance, Hill’s Pet Nutrition, Inc., Topeka, KS, USA.

**Fancy Feast Chunk Chicken Feast, Friskies Petcare Co, Glendale, CA, USA.
CASE 29-2

Insulin Resistance in a Labrador Retriever
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University of California, Davis
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Patient Assessment
A five-year-old, 39-kg, castrated male Labrador retriever was admitted to a referral institution because of difficulty in controlling diabetes mellitus. Insulin-dependent diabetes mellitus (type I) had been diagnosed one year before referral. The dog had initially responded well to 25 IU of beef/pork NPH insulin administered once daily. During the two months before referral, the dog developed progressively worsening polydipsia and polyuria despite receiving 50 IU of insulin once daily. The owner and referring veterinarian reported no other abnormalities.

The dog was alert and responsive with normal temperature, pulse and respiratory rate. Abnormalities identified included obesity (body condition score 5/5), hepatomegaly and a dry lusterless coat. The estimated optimal body weight was approximately 32 kg.

Abnormalities of the serum biochemistry profile included hyperglycemia, preprandial lipemia, hypercholesterolemia and increased alanine aminotransferase activity. Urinalysis revealed glucosuria and bacteriuria and a urine culture isolated Escherichia coli. Abdominal ultrasonography and thoracic radiographs were unremarkable. An initial blood glucose curve revealed persistent hyperglycemia at all time points (greater than 300 mg/dl).

Assess the Food and Feeding Method
The dog was fed a mixture of commercial moist and dry food twice daily. One can of a grocery brand dog food (Cycle Adult®) mixed with one to two cups of a dry grocery brand dog food (Alpo Beef Flavored Dinner®) was offered at the time of the insulin injection in the morning. A second portion of the same dry and moist food mixture was offered eight hours later. Table 1 lists nutrient levels in these foods. The dog was eating approximately 1,600 to 1,800 kcal/day (6.69 to 7.53 MJ).

Questions
1. What factors may be contributing to the apparent insulin resistance in this dog?
2. What are the key nutritional factors that should be considered in this patient?
3. Outline an appropriate feeding plan (food and feeding method) for this dog.
4. What concurrent therapy should be used in this patient?

Answers and Discussion
1. Insulin resistance exists whenever normal concentrations of insulin produce a less than normal biologic response. Proposed mechanisms for insulin resistance include: 1) an abnormal insulin molecule, 2) increased insulin degradation, 3) insulin antibodies, 4) insulin-receptor antibodies, 5) high circulating levels of counter-regulatory hormones, 6) insulin-receptor defects (altered numbers or affinity) and 7) postreceptor defects. In diabetic dogs and cats, insulin resistance has been arbitrarily defined to exist when therapeutic doses of insulin exceed 2.0 to 2.5 units/kg body weight per day. Conditions that can contribute to insulin resistance include obesity, hyperadrenocorticism, acromegaly (excess growth hormone), hyperthyroidism (cats), hypothyroidism, renal failure, liver disease, bacterial infections, pregnancy and anti-insulin antibodies.

2. The key nutritional factors for patients with uncomplicated diabetes mellitus are water, digestible (soluble) carbohydrate, fiber, fat, protein and food form (avoid semi-moist foods). Water should always be available free choice and in abundant amounts. The source of energy substrates (e.g., avoid simple sugars) are also important. Excess dietary fat should be avoided as part of a weight-reduction program. Increased dietary fiber helps reduce the caloric density of the food and helps maintain glycemic control in conjunction with medical management.

3. The goals of dietary management in this dog include: 1) decrease obesity, which may improve or eliminate peripheral insulin resistance and other metabolic abnormalities, 2) provide consistent daily energy intake and 3) minimize postprandial fluctuations in serum glucose concentrations. The dog should be fed a food that contains lower energy density, lower fat and higher crude fiber levels than the foods currently being offered. The amount of food should be divided and offered at least twice daily immediately after treatment with insulin. Daily food dosage should be calculated; a starting energy calculation of 1.0 x resting energy requirement (RER) for the estimated optimal body weight is a reasonable starting point.

4. The bacterial urinary tract infection may be contributing to insulin resistance and should be eliminated with appropriate antimicrobial therapy. The beef/pork insulin should also be changed to another insulin type in case anti-insulin antibodies are contributing to the problem.
**Progress Notes**

The urinary tract infection was treated with oral cefadroxil\(^b\) for 10 days and the insulin was changed to 55 IU recombinant human Lente insulinc every 12 hours, subcutaneously. The food was changed to a commercial dry veterinary therapeutic food that was lower in fat, higher in digestible carbohydrates and higher in dietary fiber (Prescription Diet w/d Canined) than the current foods (Table 1). The estimated daily energy requirement for weight loss was 1,000 kcal/day (4.18 MJ); this was met by feeding 2.25 cups twice daily shortly after insulin administration.

Reassessment one month later showed that insulin continued to be ineffective despite increasing the dose to 60 IU every 12 hours, subcutaneously. The owner reported recent lethargy, weakness and excessive shedding in addition to continuing polydipsia and polyuria. Results of serum biochemistry analysis, urinalysis, blood glucose curves and a complete blood count had not changed from those values at the initial presentation. Baseline serum thyroxine concentration was low (0.6 µg/dl, reference = 1.5 to 3.5 µg/dl) and decreased to 0.5 µg/dl four hours following administration of 200 µg of thyrotropin-releasing hormone (TRH). Hypothyroidism with insulin resistance, diabetes mellitus and obesity became the working diagnoses. Levothyroxine sodium\(^c\) (0.8 mg, per os, every 12 hours) was initiated and the insulin dosage was reduced (30 IU, subcutaneously, every 12 hours). The feeding plan was unchanged.

Over the next three months the insulin dosage was stabilized at 28 IU, subcutaneously, every 12 hours. The dog's activity level and coat improved. A weight loss of 5 kg was attained as well. Abnormalities in the serum biochemistry profile were alleviated except for the hyperglycemia. Serum thyroxine concentration six hours after levothyroxine administration was 4.8 µg/dl (normal = 1.5 to 3.5 µg/dl).

**Additional Comments**

Diabetes mellitus in dogs is most often insulin-dependent. When conventional therapy fails to work, other disease processes should be considered as well as other modalities of treatment for diabetes control. The use of a low-fat, high-fiber food in this case was beneficial for weight reduction and maintaining glycemic control.

**Endnotes**

a. Friskies Petcare Co, Glendale, CA, USA.
b. Cefa-Tabs. Fort Dodge Laboratories, Fort Dodge, IA, USA.
c. Humulin L. Eli Lilly & Co, Indianapolis, IN, USA.
d. Hill’s Pet Nutrition, Inc., Topeka, KS, USA.
e. Soloxine. Daniels Pharmaceuticals, St. Petersburg, FL, USA.

**Bibliography**


**Table 1.** Nutrient levels in foods fed to a diabetic dog.

<table>
<thead>
<tr>
<th>Nutrients (DM)</th>
<th>Dry grocery brand food*</th>
<th>Moist grocery brand food**</th>
<th>Dry veterinary therapeutic food***</th>
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<tbody>
<tr>
<td>Crude fat (%)</td>
<td>13.3</td>
<td>21.8</td>
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<tr>
<td>Crude fiber (%)</td>
<td>4.3</td>
<td>1.1</td>
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<tr>
<td>Energy (kcal/g)</td>
<td>3.7</td>
<td>4.4</td>
<td>3.3</td>
</tr>
<tr>
<td>Protein (%)</td>
<td>24.8</td>
<td>39.7</td>
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<tr>
<td>Digestible carbohydrate (%)</td>
<td>52.2</td>
<td>28.3</td>
<td>50.1</td>
</tr>
</tbody>
</table>

Key: DM = dry matter.

*Alpo Beef Flavored Dinner. Friskies Petcare Co, Glendale, CA, USA.
**Cycle Adult. Friskies Petcare Co, Glendale, CA, USA.
***Prescription Diet w/d Canine. Hill’s Pet Nutrition, Inc., Topeka, KS, USA.