Weight gain is associated with an increase in the risk of developing diabetes mellitus in cats. However, not all obese cats become diabetic. In humans, fasting blood glucose concentrations and results of oral glucose tolerance testing have been used to distinguish healthy individuals from those with impaired fasting glucose concentration control, impaired glucose tolerance, or diabetes mellitus. However, even in the strictly controlled environment of an experimental study, glucose concentrations measured in cats after food has been withheld (ie, baseline glucose concentrations) vary greatly within the reference range and have not been found to increase with obesity. In 2 clinical populations of obese cats, baseline glucose concentrations also were not higher, compared with concentrations in control cats of normal body condition. Contrary to reports in human patients, results of oral glucose tolerance testing were not found to be a reliable marker of glucose homeostasis in cats because of large variations in results. Because diabetes is defined as a condition of persistent hyperglycemia, it is of great interest to perform a comprehensive analysis of distinct groups of cats to identify parameters that are unique to populations at highest risk of developing diabetes or that would indicate a progression toward diabetes before persistent hyperglycemia ensues. In particular, in the study reported here, we hypothesized that, compared with cats with a normal body condition, overweight and obese cats would have evidence of altered long-term glucose control, as indicated by higher serum fructosamine concentrations.

**Materials and Methods**

The study consisted of a survey of cats examined at 9 specialized feline practices from April through October 2010. Owners of cats enrolled in the study signed an informed consent form. Signalment data and a detailed medical history were collected, including information about food type, frequency of feeding, and amount of...
food given. Each cat was then examined by the practitioner. Body condition scoring was performed, and measurements were taken for calculation of feline body mass index.* Feline body mass index was calculated according to the following formula:

\[
\text{Percentage body fat} = \left( \frac{\text{RC}}{0.7062} \right) - \frac{\text{LIM}}{0.9156} - \text{LIM}
\]

where RC was the rib cage circumference in centimeters and LIM was the length of the lower limb from the middle of the patella to the dorsal tip of the calcaneal process in centimeters. Blood samples were collected from each cat enrolled in the study for a CBC and serum biochemical testing. For the CBC, blood was placed in an EDTA-containing tube and kept at 4°C until processed; all samples were processed within 24 hours. For serum biochemical testing, blood was allowed to clot (usually 20 to 30 minutes but always < 60 minutes) and was then centrifuged at 1,500 × g for 10 to 20 minutes. Serum was then immediately collected and kept at 4°C until processed by the laboratory (within 24 hours). Serum proinsulin concentration was determined with an immunoradiometric assay.30 Serum insulin concentration was determined with a radioimmunoassay.24,31 Intra- and interassay coefficients of variation were 5.8% and 11.9%, respectively. Blood glucose concentration was measured with a hexokinase method in the laboratory and was also immediately measured with a handheld glucometer when blood was collected in the veterinary practice. Urine samples for urinalysis were requested but could not be obtained from all cats. Urine was collected by cystocentesis. Urine glucose and ketone concentrations were measured with reagent strips in the veterinary practice immediately after urine collection. All tests that required a commercial laboratory, except measurement of insulin concentration, were performed at the same laboratory by technicians blinded to cat group assignment. The study was performed according to good clinical practice standards.

**Statistical analysis**—For each parameter, summary statistics were obtained. The normality of the distribution of values was visually ascertained with normal probability plots and histograms and quantitatively ascertained with the Shapiro-Wilk and Anderson-Darling tests. Analysis of variance was performed with a general linear mixed models procedure implemented with statistical software. The generalized linear mixed models procedure fits statistical models to data with correlations or nonconstant variability and where the response is not necessarily normally distributed. The P values for multiple pairwise comparisons were adjusted as appropriate with the Tukey highly significant difference test if all possible pairwise comparisons were performed. When only a subset of pairwise comparisons of interest, rather than all possible pairwise comparisons, were performed, P values were adjusted by use of the Bonferroni method. Statistical software was used for preliminary analyses and graphics. For all analyses, values of \( P < 0.05 \) were considered significant. Summary statistics are reported as mean ± SD for normally distributed values and as median and range for nonnormally distributed data.

### Results

**Animals**—Cats enrolled in the study only had a single clinic visit and were chosen for the study either at the time of initial evaluation at the clinic or from the clinic’s patient database. For cats chosen from the clinic database, owners were asked to visit the clinic. Cats were assigned to 2 groups: cats with a diagnosis of diabetes mellitus (diabetic cats) and cats with no obvious clinical signs of diabetes mellitus (ie, polyuria, polydipsia, or polyphagia) in which diabetes mellitus had not previously been diagnosed (nondiabetic cats). Nondiabetic cats were further subdivided on the basis of BCS assigned on the basis of a 9-point scale as cats with normal body condition (BCS, 4 to 5), overweight cats (BCS, 6 to 7), and obese cats (BCS, 8 to 9). Diabetic cats were further subdivided as naïve diabetic cats and treated diabetic cats. The naïve diabetic cats had been given a diagnosis of diabetes mellitus within 1 week prior to the study visit, had at least 1 clinical sign of diabetes mellitus (ie, polyuria, polydipsia, or polyphagia), had high blood glucose and fructosamine concentrations, and had not been treated for diabetes mellitus prior to collection of blood samples for the present study. The treated diabetic cats were cats in which a diagnosis of diabetes mellitus had been made at least 3 months prior to the present study, the cats were currently being treated with insulin, and food had been withheld for at least 8 hours prior to blood sample collection.

Cats were excluded if they were pregnant or lactating, had suspected or confirmed concurrent systemic disease (eg, renal failure, acromegaly, hyperthyroidism, hepatic disease, or pancreatitis), or had been treated with a glucocorticoid or thiazide diuretic in the past 3 months or with a progestogen or megestrol acetate in the past 6 months. Cats were also excluded if they had a history of receiving a blood transfusion in the past 3 months or were known to be from the same sire or dam as another cat included in the study. Any cat that had eaten within 8 hours prior to blood sample collection was excluded, except for cats in the naïve diabetic group. Twenty-four cats were excluded. Total number of cats enrolled in the study and sex, age, and weight distributions were summarized (Table 1). Mean age was not significantly different among the 5 cat groups. Body weight was lowest in the normal body condition group and almost 2-fold higher in the obese group. Female cats in the normal body condition group had a significantly lower body weight (median, 4.1 kg [9.2 lb]; range, 2.5 to 5.3 kg [5.5 to 12.1 lb]) than did male cats (median, 5.3 kg [11.7 lb]; range, 3.6 to 5.8 kg [7.9 to 12.7 lb]; \( P < 0.05 \)) in this group. This was also the case for the obese group (females: median, 7.7 kg [16.9 lb]; range, 4.9 to 12 kg [10.8 to 26.4 lb]; males: 9.4 kg [20.7 lb]; range, 6.5 to 13.7 kg [14.3 to 30.1 lb]; \( P < 0.01 \)), but no sex differences were seen in the other groups. Median BCS of the naïve and treated diabetic cats was 6 (range, 4 to 9). In the naïve diabetic group, 7 of 21 cats had a normal body condition, 8 were overweight, and 6 were obese. In the treated diabetic group, 4 of 20 cats had a normal body condition, 13 were overweight, and 3 were obese. There was a strong correlation between feline body mass index and body weight (\( r^2 = 0.541; P < 0.001 \)) and between body weight and rib cage circumference (\( r^2 = 0.721; P < 0.001 \); Figure 1). Thirteen
of the naïve diabetic cats had eaten within 8 hours prior to blood sample collection. However, there was no significant difference between fed cats and cats from which food had been withheld for any of the parameters of interest (data not shown).

Results of hematologic testing—Mean or median Hct was within reference limits in all groups, although the lowest value was seen in the naïve diabetic cat group (Table 2). There were no significant differences among groups in other routine CBC results (data not shown).

Glucose concentration was not significantly different among the 3 groups of nondiabetic cats but was significantly higher in the diabetic cats than in the nondiabetic cats. None of the cats with a normal body condition, but 3 cats in the overweight and obese groups, had glucose concentrations outside the reference interval. However, there were no significant differences in fructosamine concentrations among the 3 groups of nondiabetic cats, and the upper range of values was similar for these 3 groups (Figure 2). Glucose and fructosamine concentrations were significantly higher among male cats in the naïve and treated diabetic groups than among female cats in these groups. Body condition score was not significantly associated with glucose or fructosamine concentration in the naïve diabetic group (data not shown). Fructosamine concentration was significantly correlated with glucose concentration ($r^2 = 0.752; P < 0.001; Figure 3$). Glucose concentrations measured with a glucometer were highly correlated with glucose concentrations determined by the reference laboratory method ($r^2 = 0.88; P < 0.001$).

Alkaline phosphatase activities were highest in the naïve diabetic group and were similar among the other groups (Table 2). There were no significant differences in BUN or creatinine concentrations among the groups, and all concentrations were within reference limits (data not shown). However, creatinine concentrations were lowest in the naïve diabetic group, leading to a significantly higher BUN-to-creatinine concentration ratio in this group, compared with the 3 groups of nondiabetic cats. Cholesterol concentration was significantly higher in the naïve diabetic group than in the overweight group. Cholesterol concentration was also higher in the naïve diabetic group than in the group of cats with normal body condition, but the difference was not significant ($P = 0.057$). For nondiabetic cats, triglyceride concentrations were highest in obese cats; naïve diabetic cats had the highest triglyceride concentrations overall. No significant differences among the groups were seen in regard to results of other routine serum biochemical tests. There was no significant difference in fPLI values among the 3 groups of nondiabetic cats; however, naïve and treated diabetic groups had significantly higher values than did the nondiabetic cats (Table 2).

Table 1—Age, body weight, and feline body mass index for 117 client-owned cats (74 nondiabetic cats classified as normal body condition, overweight, or obese and 41 diabetic cats classified as naïve or treated diabetic cats).

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of females</th>
<th>No. of males</th>
<th>Total No. of cats</th>
<th>Age (y)</th>
<th>Weight (kg)</th>
<th>Feline body mass index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondiabetic cats</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal body condition</td>
<td>16</td>
<td>9</td>
<td>25</td>
<td>10 (7–14)</td>
<td>4.4 (2.5–5.9)$^{ab,ef}$</td>
<td>30 ± 1.5$^{ab,ef}$</td>
</tr>
<tr>
<td>Overweight</td>
<td>17</td>
<td>10</td>
<td>27</td>
<td>11 (7–15)</td>
<td>5.9 (3.7–7.8)$^{ab}$</td>
<td>43 (23–58)$^{ab}$</td>
</tr>
<tr>
<td>Obese</td>
<td>13</td>
<td>11</td>
<td>24</td>
<td>10 (7–15)</td>
<td>8.5 ± 2.2$^{ab,ef}$</td>
<td>55 (31–87)$^{ab,ef}$</td>
</tr>
<tr>
<td>Diabetic cats</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naïve diabetic</td>
<td>11</td>
<td>10</td>
<td>21</td>
<td>10 (7–17)</td>
<td>5.7 (3.7–8.9)$^{ab}$</td>
<td>39 (21–57)$^{ab}$</td>
</tr>
<tr>
<td>Treated diabetic</td>
<td>8</td>
<td>12</td>
<td>20</td>
<td>11 (7–16)</td>
<td>6.5 (4.5–8.2)$^{ef}$</td>
<td>43 ± 3$^{ef}$</td>
</tr>
</tbody>
</table>

Cats were examined at 9 specialized feline practices. Nonnormally distributed data are given as median (range); normally distributed data are given as mean ± SD.

*Within a column, values with the same superscript letter are significantly ($P < 0.05$) different.

Figure 1—Scatterplots of feline body mass index versus body weight (A) and of body weight versus rib cage circumference (B) for 117 client-owned cats (74 nondiabetic cats classified as normal body condition [BCS, 4 to 5; n = 25], overweight [BCS, 6 to 7; 27], or obese [BCS, 8 to 9; 24]; 21 naïve diabetic cats; and 20 treated diabetic cats) examined at 9 specialized feline practices. The solid line represents the linear regression line.
Hormone concentrations—In the nondiabetic cats, serum insulin concentration was significantly correlated with body weight ($r^2 = 0.420$; $P < 0.001$; data not shown). Insulin concentrations were significantly higher in treated diabetic cats than in cats with a normal body condition and were lowest in the naïve diabetic cats (Table 3). Nine of the 21 naïve diabetic cats had insulin concentrations less than the lower reference limit. In 2 of these cats, concentrations were undetectable ($<$ 2 µU/mL). There was no sex difference in insulin concentrations. In the naïve diabetic group, BCS was not significantly associated with insulin concentration (data not shown). The glucose-to-insulin concentration ratio was significantly lower in obese cats, compared with ratios for the other nondiabetic groups of cats, and significantly higher in naïve and treated diabetic cats. Proinsulin concentrations were significantly higher in obese cats than in diabetic cats or cats with normal body condition. There were no sex differences in proinsulin concentrations. Four of 21 cats in the naïve diabetic group had undetectable proinsulin concentrations, whereas 1 of 20 cats in the treated diabetic group had an undetectable concentration. Body condition score was not associated with proinsulin concentration for cats in the naïve diabetic group. The insulin-to-proinsulin concentration ratio was not significantly different among the groups and ranged from 0.01 to 0.24. All cats had thyroxine concentrations within reference limits, except for 1 cat in the overweight group, which had a low thyroxine concentration (0.4 µg/dL; reference interval, 0.5 to 5.8 µg/dL). The highest thyroxine concentration (3.5 µg/dL) was seen in an overweight cat.

Urinalysis—No urine samples from cats in normal body condition or obese cats had glucose or ketones. One overweight cat had a measurable urine glucose concentration (250 mg/dL); however, this was not reflected in a high blood glucose concentration. One naïve diabetic cat had no detectable urine glucose but had a high blood glucose concentration. One other cat in this group had a urine glucose concentration of 500 mg/dL, and all other cats in this group had urine

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference range</th>
<th>Normal body condition</th>
<th>Overweight</th>
<th>Obese</th>
<th>Naïve diabetic</th>
<th>Treated diabetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hct (%)</td>
<td>24–45</td>
<td>44 (33–50)</td>
<td>44 ± 7*</td>
<td>46 ± 4*</td>
<td>39 ± 6*</td>
<td>46 ± 1*</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>70–150</td>
<td>104 ± 4*</td>
<td>103 (68–197)f,d</td>
<td>124 ± 6*</td>
<td>455 ± 25fx</td>
<td>257 ± 33f</td>
</tr>
<tr>
<td>Alkaline phosphatase (U/L)</td>
<td>0–62</td>
<td>22 (10–43)*</td>
<td>25 (7–71)*</td>
<td>32 ± 12</td>
<td>63 ± 29f</td>
<td>36 ± 16</td>
</tr>
<tr>
<td>BUN-to-creatinine ratio</td>
<td>111–125</td>
<td>120 ± 3*</td>
<td>119 ± 3*</td>
<td>118 (97–124)f</td>
<td>112 ± 5*</td>
<td>116 (107–119)f</td>
</tr>
<tr>
<td>Chloride (mEq/L)</td>
<td>82–218</td>
<td>199 ± 56*</td>
<td>173 (105–330)j</td>
<td>204 (116–424)</td>
<td>261 ± 109*</td>
<td>536 (108–536)</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>20–90</td>
<td>36 ± 10*</td>
<td>38 (24–185)j</td>
<td>79 (52–456)x</td>
<td>114 (39–644)j</td>
<td>67 (35–1,045)j</td>
</tr>
<tr>
<td>fPLI (µg/L)</td>
<td>&lt; 3.5</td>
<td>1.5 (0.5–9.4)x</td>
<td>1.8 (0.6–7.1)x</td>
<td>17 (0.7–4.7)j</td>
<td>2.5 (0.8–7.8)x</td>
<td>3.4 (1.3–12.8)x</td>
</tr>
</tbody>
</table>

Nonnormally distributed data are given as median (range); normally distributed values are given as mean ± SD.

*Values were not significantly ($P = 0.057$) different.

— = Not available.

Values designated by the same letters were significantly ($P < 0.05$) different.
glucose concentrations of 1,000 or 2,000 mg/dL. Trace amounts of ketones (5 mg/dL) were found in 2 cats and small amounts (15 mg/dL) in 2 cats; other cats in this group did not have ketone bodies in their urine. In the treated diabetic group, no urine glucose was detected in 2 cats, 1 cat had a urine glucose concentration of 250 mg/dL, 1 had a urine glucose concentration of 500 mg/dL, and all others had urine glucose concentrations of 1,000 or 2,000 mg/dL. None had ketonuria.

Feeding and diets—Cats consumed exclusively dry food (n = 52), exclusively canned food (37), or a mixture of both (28). Dry food was often fed free choice (n = 70), regardless of whether it was the only food fed or was fed in combination with canned food (Table 4).

Discussion

Results of the present study suggested that cats at risk to develop diabetes (ie, overweight and obese cats) could not be distinguished from cats with a normal body condition on the basis of results of isolated hematologic testing. A longitudinal study is indicated to follow nondiabetic cats over a period of several years to identify those that eventually develop diabetes. Our findings also suggested that dietary education of cat owners could be improved. Whereas obesity is a risk factor for diabetes mellitus in cats, not all obese cats become diabetic. The present comprehensive analysis of hematologic findings in 5 clinical populations of cats indicated that none of the measurements that were performed had the potential to be used to classify cats as at higher risk of developing diabetes or as prediabetic (ie, cats with higher-than-normal glucose concentrations but not high enough to be diabetic). None of the obese cats in this study had fructosamine concentrations higher than those in the group of cats with normal body condition, and all results were well within reference limits. Because it is known that the risk to develop diabetes is about 2- to 4-fold as high in obese cats, this might suggest that a switch from normal to abnormal glucose homeostasis occurs quickly.

Measurement of peripheral insulin resistance and fasting blood glucose concentrations in human patients has been found to be a good indicator of progression to diabetes. It appears that individuals that progress to develop diabetes have higher baseline body mass index, a steeper rate of increase in fasting glucose concentration, and higher blood pressure and triglyceride concentration, along with lower high-density lipoprotein cholesterol concentration than do nonprogressors. However, the most consistent change related to an increase in blood glucose concentration, which in many cases occurred rather rapidly instead of gradually, was a decrease in glucose-stimulated insulin secretion (ie, β-cell failure). Not all people with impaired fasting blood glucose concentration control are definite progressors, and there are individuals who develop diabetes but do not have impaired fasting glucose concentration control at baseline. In general, 33% to 50% of people with impaired fasting glucose concentration control convert to having type 2 diabetes after 10 to 20 years of follow-up. In the present study, mean baseline blood glucose concentrations were not higher in obese cats, compared with concentrations in cats with a normal body condition, supporting previous data from a long-term obese cat colony. In the present study, contrary to what has been reported in people, there was a much wider range of glucose concentrations in cats with a normal body condition. In the high-risk overweight and obese groups, 3 cats each had glucose concentrations > 150 mg/dL but none had high fructosamine concentrations (concentration was < 232 µmol/L in all 3 cats), suggesting that long-term glucose concentration control was not impaired. These cats might have had stress hyperglycemia, a temporary increase in blood glucose concentration caused by secretion of stress hormones leading to glucose production through glycogenolysis and gluconeogenesis.

Table 3—Insulin, proinsulin, and thyroxine concentrations for the same cats as in Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal body condition</th>
<th>Overweight</th>
<th>Obese</th>
<th>Naïve diabetic</th>
<th>Treated diabetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin (µU/mL)</td>
<td>4–15</td>
<td>11 (4–27)²₅</td>
<td>16 (6–43)²⁶</td>
<td>22 ± 2⁷</td>
<td>4 (UD–12)²₅</td>
</tr>
<tr>
<td>Proinsulin (pmol/L)</td>
<td>—</td>
<td>203 ± 138²⁶</td>
<td>184 (27–1,006)²⁶</td>
<td>400 ± 209²⁶</td>
<td>164 (UD–1,012)²⁶</td>
</tr>
<tr>
<td>Thyroxine (µg/dL)</td>
<td>0.5–5.8</td>
<td>2.1 ± 0.4</td>
<td>2.2 ± 0.7</td>
<td>2.1 ± 0.3</td>
<td>1.9 ± 0.6</td>
</tr>
</tbody>
</table>

UD = Undetectable. See Table 2 for remainder of key.

Table 4—Type of food fed to the same cats as in Table 1.

<table>
<thead>
<tr>
<th>Food type</th>
<th>Normal body condition</th>
<th>Overweight</th>
<th>Obese</th>
<th>Naïve diabetic</th>
<th>Treated diabetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exclusively dry</td>
<td>11 (10*)</td>
<td>12 (9*)</td>
<td>11 (9*)</td>
<td>11 (9*)</td>
<td>7 (5*)</td>
</tr>
<tr>
<td>Exclusively canned</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Mixture of dry and canned</td>
<td>6*</td>
<td>7*</td>
<td>5*</td>
<td>7*</td>
<td>3*</td>
</tr>
</tbody>
</table>

*Dry food was available free choice.
Information about previous visits was available for only 3 naïve diabetic cats in the present study. All 3 cats had been healthy 8 to 12 months before developing clinical signs of diabetes mellitus. We have previously shown that changes in baseline glucose concentrations are a very late feature of the progression to diabetes. The maintenance of normal glucose concentrations in obesity is possible because obese cats have high insulin concentrations counteracting peripheral insulin resistance, and the feline liver maintains insulin sensitivity through adjustments in glycogenolysis and gluconeogenesis. This leads to lower endogenous glucose output. The maintenance of glucose control was also seen in a recent study in which cats with normal body condition and long-term obese cats were monitored with a continuous glucose monitoring system for 7 days. There was very little interday variability of glucose concentrations in cats with normal body condition and obese cats and no difference between the 2 groups. In that study, there was only 1 obese cat that was clearly prediabetic and had higher baseline and postprandial glucose concentrations than the other cats. When challenged with a large IV dose of glucose during a glucose tolerance test, obese cats cannot dispose of the glucose load within the same time frame as do cats with normal body condition. However, these very high glucose concentrations measured during an IV glucose tolerance test are not physiologic and not observed in the postprandial state. Concentrations of fructosamine, which is an indicator of longer-term glucose homeostasis, were not different among any of the nondiabetic groups in the present study, supporting the notion that overweight and obese cats have normal glucose homeostasis. A large long-term study is now necessary to follow obese cats longitudinally to obtain information to determine whether hyperglycemia develops gradually over several years or more rapidly.

Blood glucose concentrations did not correlate with urine glucose concentrations in 2 of the cats in this study. One overweight cat had a small amount of glucose in the urine, but the blood glucose concentration was normal. One naïve diabetic cat had a normal urine glucose concentration, but blood glucose concentration was high. A second sample was not obtained, and it is therefore difficult to determine whether the results were due to testing error. Stress hyperglycemia can increase glucose concentrations high enough to lead to excretion of glucose in urine. Because a urine sample reflects the glucose concentration over time, it is possible to detect glucose in the urine even though blood glucose concentration already has returned to normal. Glucosuria due to the Fanconi syndrome has been described in cats but is rare and is associated with other disease signs, which were not seen in this cat. Only 2 of the naïve diabetic cats had small amounts of ketones in the urine. The urinalysis reagent strips used detect acetone but not β-hydroxybutyrate, and one might argue that more cats might have been found to be ketogenic had β-hydroxybutyrate concentrations been measured. This is unlikely because conversion of acetone to β-hydroxybutyrate occurs when hydrogen ion concentrations increase, and these cats had no clinical signs of ketoacidosis and their bicarbonate concentrations were not significantly different from those of the nondiabetic cats.

It has been reported that obese cats have peripheral insulin resistance. This was also suggested in the overweight and obese cats of the present study because insulin concentrations in obese cats were higher than those in the cats with normal body condition, indicating that pancreatic β-cells adapt well to insulin resistance. Disproportionate hyperproinsulinemia relative to insulin concentration and a change in the insulin-to-proinsulin concentration ratio have been found in some studies to predict progression to diabetes in humans. We have previously shown that both insulin and proinsulin concentrations are higher in obese cats from which food had been withheld, compared with cats with normal body condition, but there was no difference in the insulin-to-proinsulin concentration ratio. As expected, insulin and proinsulin concentrations also increased with increasing body weight in the cats of this study, but the ratio between the 2 hormones did not change. Although these higher values suggest that pancreatic β-cell output is increased, the large variation in concentrations among all groups do not allow the use of these hormones as predictors when only 1 blood sample is collected. Further studies are necessary to evaluate whether their measurement becomes a predictive factor if followed longitudinally. The higher insulin concentrations of treated diabetic cats likely reflected cross-reactivity with exogenously administered insulin. It would be impossible to predict the extent of this on the basis of our data.

None of the cats in this study had changes in CBC results that would indicate any disease process, and most of the biochemical values were normal. There were no significant changes in electrolyte concentrations in any of the groups except for chloride, which was below the lower reference limit in 7 of 21 naïve diabetic cats. This may have been caused by chloride loss through osmotic diuresis. Creatinine concentration was lowest in naïve diabetic cats. Lower serum creatinine concentration in people is thought to be due to lower skeletal muscle mass associated with untreated diabetes. It needs to be investigated whether this association also exists in cats. Alkaline phosphatase activity was significantly higher in the naïve diabetic group. It is not uncommon to see increases in alkaline phosphatase activity in human patients with diabetes. The increase could be due to acute cholestasis because the half-life of alkaline phosphatase is short in cats. Cholesterol concentration was significantly increased in the naïve diabetic cats, compared with concentrations in the other groups. A detailed examination of lipoproteins has not been performed in diabetic cats, only in obese cats. However, it is known from rodents and people that the increase in cholesterol concentration is caused by a decrease in the expression of the receptor for the cholesterol-carrying low-density lipoprotein, thereby increasing its plasma concentrations. The higher concentrations of triglycerides in obese and naïve diabetic cats are caused by higher very low-density lipoprotein concentrations. We and others have previously shown that very low-density lipoprotein concentration is significantly higher in obese cats, compared with
concentration in cats with a normal body condition.\textsuperscript{31,32} The increase is caused by an increase in synthesis and a decrease in lipoprotein lipase activity.\textsuperscript{33} There was no clear distinction of cholesterol or triglyceride concentrations among groups, and the values spanned a large range. Although 13 of the naive diabetic cats had eaten within 8 hours before blood sample collection, there was no significant difference in any of the measured parameters, including lipid concentrations. Lipase concentrations, which are sometimes still used for the diagnosis of pancreatitis but have low sensitivity and specificity, were not significantly different among the groups. The fPLI has also been used for the diagnosis of pancreatitis. According to laboratory information, an fPLI > 5.4 µg/L is an indicator of pancreatitis. Each one of the normal body condition and overweight cats, 3 of 21 naive diabetic cats, and 6 of 20 treated diabetic cats had an fPLI > 5.4 µg/L; all obese cats had values within reference limits. None of the cats had clinical signs of pancreatitis. It is interesting that treated diabetic cats had a higher incidence of high fPLI concentrations and higher mean concentration than did naive diabetic cats, suggesting either that treatment leads to nonspecific alterations in immunoreactivity unrelated to pancreatitis or that subclinical pancreatitis is more common in treated than untreated diabetic cats for unknown reasons.

Diet has long been implicated in obesity and diabetes. It has been stated anecdotally that a diet high in carbohydrate (usually, dry diets are higher in carbohydrates than canned diets) leads to obesity and diabetes. However, there are no long-term studies that show that this is indeed the case. In a multiyear study\textsuperscript{34} of cats, no adverse effect of carbohydrates was documented. Our study suggested that the dietary risk factor is most likely not the type of food (ie, canned vs dry) but the amount of food that is available to cats. Seventy of 117 cats, even when already overweight, obese, and diabetic, were still allowed unlimited access to food. Although we do not have detailed information about the exact amount of food that was consumed by each cat, the fact that these cats had unlimited access to food suggests that dietary education by veterinarians needs to be improved to stress to owners the importance of weight control, especially in overweight, obese, and diabetic cats.

The present study had limitations in its design because we did not have retrospective data from the diabetic cats. To identify what contributes to the development of diabetes, a prospective longitudinal study is clearly necessary. A large cohort should be followed for several years and be examined on a regular basis.

In summary, no parameters have been identified in blood or urine that are unique to cats at high risk of developing diabetes, and long-term glucose concentration control was well maintained in overweight and obese cats. The finding that obese cats, which are at high risk to develop diabetes, all had normal long-term glucose concentration control suggested that the switch from normal glucose homeostasis to diabetes may occur quickly. Additionally, because most cats, even overweight, obese, and diabetic cats, had unlimited access to food, we suggest that client education about the importance of weight control needs to be an important part of routine office visits.

References


