Detecting, Diagnosing, and Monitoring Diabetes Mellitus in Cats: the Role of Blücare® Glucosuria Granules

Recommendations from an Expert Panel

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Abstract

Diabetes mellitus (DM) is a common endocrinopathy in cats and evidence indicates that it continues to increase in prevalence. Early diagnosis and management are essential to prolong the lives and optimize the quality of life among cats with DM. Ongoing monitoring forms a key element to the optimal care of 3 groups of cats: those with significant risk factors for and/or signs of DM, cats with insulin-treated DM, and cats experiencing diabetic remission. This white paper presents the recommendations of an Expert Panel for indications to incorporate Blücare Glucosuria granules* in these patients (**Blücare Glucosuria granules - or Glucodetect™, in some countries*).

Diabetes mellitus (DM) occurs in an estimated 0.4%–0.7% of cats,[1-5] with evidence that the prevalence of this condition is increasing.[2,6] The median survival of cats with DM was found to be 13–29 months; however, reduced survival may be associated with poor glycemic control (including non-treatment) and/or comorbidities.[7-10] Otherwise healthy cats in whom glucose is well controlled can live for many years. Thus, early diagnosis, management, and ongoing monitoring are essential to maximize both the duration and quality of life in the cat with insulin-treated DM. Additionally, monitoring refers to routine screening of cats with one or more risk factors for DM (see below) in order to improve early detection, as well as continued assessment of cats in diabetic remission.

In cats, DM is caused by failure of pancreatic β-cells and insulin resistance.[11-13] It corresponds to type 2 (non-insulin dependent) DM in the majority of cases,[14] although insulin is typically required for successful treatment. Insulin resistance can be associated with obesity, a comorbid endocrinopathy (e.g., hyperthyroidism, acromegaly, or hyperadrenocorticism), an inflammatory condition (e.g., pancreatitis, inflammatory bowel disease, or dental disease/oral inflammation), treatment with a diabetogenic agent (e.g., prednisolone), and genetics in certain lines of Burmese and other breeds.[13,15-20]

The objective of this white paper is to discuss strategies for managing the 3 groups of cats associated with DM: screening and diagnosis of the cat at risk for developing DM, management and monitoring of the cat with insulin-treated DM, and monitoring of the cat in remission. In the clinic, measurement of blood glucose (BG) and fructosamine are used to screen at-risk cats as well as those in remission. Currently, screening at-risk cats is generally not done at home as both of these require blood sampling. Blücare Glucosuria granules represent a convenient, accurate, safe, and inexpensive method to monitor urinary glucose in all of these groups of cats. Case examples are included to illustrate the appropriate use of Blücare Glucosuria granules based on the recommendations of the Expert Panel.

The At-risk Cat: Screening and Diagnosis of Diabetes Mellitus

A number of risk factors predispose to the development of DM in cats (Table 1).[1,3-6,15,21-23] Similar to other species, the main clinical signs of DM are polyuria/polydipsia, polyphagia, weight loss, and lethargy. These signs follow the onset of glucosuria.[24] Cats with DM may also exhibit generalized weakness, poor physical condition, impaired jumping, abnormal gait, and dehydration.[24,25]

Clinical evaluation of the cat with suspected DM should include obtaining a detailed history, performing a thorough physical examination, determining serum biochemistry values including BG, and performing a urinalysis. A urine culture may be indicated based on the urinalysis results and clinical signs. The veterinarian should also order a complete blood count, thyroxine level (in older cats to exclude hyperthyroidism), and serum fructosamine.[24,25] In line with other papers, the European Society of Veterinary Endocrinology ALIVE guidelines on DM provide 2 options for differentiating DM from stress hyperglycemia BG (≥14–17 mmol/L [≥250–300 mg/dL]):

1) measuring glycated proteins (i.e., fructosamine), or
2) finding glucosuria on more than one occasion on a naturally voided sample acquired in a home environment at least 2 days after any stressful events.[24-27]

If the diagnosis of DM is uncertain despite clinical testing, ongoing monitoring is recommended.[24,25] Situations that may warrant ongoing monitoring in non-diabetic cats include those in whom diabetogenic drugs have been administered, cats exhibiting inappropriate urination with polyuria, and in cats with one or more significant risk factors (Table 1) .

Table 1: Risk factors for diabetes mellitus (DM)

Significant risk

- Age >6–7 years[1,4,6]
- Obesity (body condition score >6/9)[1,4,6,21]
- Breed (some Burmese, Tonkinese, and Norwegian Forest lines)[1,3-5,15,22]
- Treatment with glucocorticoids and progestagens[4,23]

Aggravating factors

- Intact or castrated male[1,4,6]
- Physical inactivity / indoor lifestyle[3,4,21]
- Chronic inflammatory conditions
- Conditions resulting in insulin resistance such as acromegaly

Routine blood and urine testing can be performed at the clinic; however, repeat visits are stressful for both cat and client, time-consuming, and costly. Stress hyperglycemia and glucosuria may confound interpretation of test results. Home monitoring strategies are advantageous for reducing stress, cost, and help clarify in-clinic results. As well, home monitoring can help to reassure anxious owners whether, and when, glucosuria is present.

Most clients can perform home BG (HBGM) or continuous interstitial glucose monitoring;[28-30] however, these techniques have been associated with low adherence,[31] some owners are unwilling or unable to perform testing accurately,[30,32] and some cats do not tolerate the procedures.[29]

Urine glucose testing is less invasive than BG testing and is recommended in situations where the owner cannot, or will not, comply with HBGM.[24,25] Home urine testing using test strips is particularly helpful to rule out the confounding effect of stress-induced hyperglycemia. However, the need to collect pooled urine or wet urine-soaked litter is an obstacle for some owners (particularly in multi-cat households), some cats do not tolerate non-absorbent litter, and collection may stress the cat.

Blücare Glucosuria granules represent a simple and accurate semi-quantitative method to monitor for the presence of glucosuria in cats at risk for, or suspected of, having DM (Table 2). Granules are sprinkled on the cat's regular brand of litter. When urine contacts the granules, a chromogenic reaction occurs within 10 minutes and granules change from a cream color to blue. This color change remains stable for at least 48 hours. When screening at-risk cats, owners should be counseled to contact their veterinarian if the granules show any trace of blue. More detailed information about Blücare Glucosuria granules is found in the Box on page 4.

The Cat with Insulin-treated Diabetes Mellitus: Management and Monitoring

The primary goals of managing the cat with DM are to minimize or eliminate clinical signs through careful control of glucose levels, provide a good quality of life as perceived by the owner, and to avoid clinically significant hypoglycemia, defined as <3.5 mmol/L (<63 mg/dL).[24,25] Regular insulin administration and dietary modification offer the best chance for successfully mitigating clinical signs by maintaining the BG below the renal threshold, which is approximately 14 mmol/L (250 mg/dL) (Table 2).[24,25,33]

For management to be successful, client compliance and adherence are necessary. Not only do clients need to have an understanding of what is required of them, they need to be engaged and be able to perform what their veterinarian is recommending. A survey in the United Kingdom of 1192 veterinarians revealed that 1 in 10 owners opt to euthanize their cat at the time of diagnosis and that an additional 1 in 10 cats with DM are euthanized within a year due to unsuccessful management or noncompliance.[34] Treatment and monitoring recommendations must be convenient and easy for the client to adopt into his/her routine. The veterinarian is frequently required to be flexible in developing a management plan to maximize owner compliance. In the veterinarian/ owner partnership, communication goes beyond education and instruction; clients need to know that their concerns and limitations regarding caring for their cat are being heard.[25]

The treatment plan must take into account the individual cat's condition, including the presence of diabetic ketoacidosis, and comorbid conditions. Many types of insulin are available: longer-acting insulin (protamine zinc insulin [PZI]) and insulin analogues (insulin glargine and insulin detemir) are recommended over medium-acting insulins due to the potential for superior glycemic control and smaller fluctuations in BG. However, clinical data showing significant superiority are inconclusive[35,36] and there is substantial cat-to-cat variation in response to insulin than inherent differences in response to different insulins.[37] The use of oral hypoglycemic agents in cats is not supported by current evidence, and both the American Animal Hospital Association (AAHA) and International Society of Feline Medicine (ISFM) DM guidelines advocate their use only when the owner refuses insulin therapy.[24,25]

Because response to insulin varies between cats, ongoing monitoring is a vital component to optimization of therapy and maintenance of ideal glycemic control. Regular monitoring also helps the prompt identification of hypoglycemia and diabetic remission.[24,25,38] Diligent monitoring may also permit a lower BG target than that with which one might otherwise feel comfortable (Table 3), potentially reducing the risk of adverse metabolic effects of DM occurring and increasing the chance of diabetic remission.[39,40]

Current guidelines suggest that newly diagnosed cats should be monitored every 1-2 weeks while insulin type and dose are determined.[24,38] Some veterinarians perform first-day BG testing in order to detect hypoglycemia. In this case, BG should be tested over 10-12 hours after insulin administration at an interval of every 3-4 hours for cats receiving glargine and 2-4 hours for those receiving PZI.[24]

As part of monitoring, owners should be encouraged to maintain a logbook to record details of insulin therapy (date, time of administration, dose), clinical signs (appetite, water intake, urine output [number and size of clumps]), bowel movements, attitude, energy level), and additional comments and observations on the cat's behaviour and overall health.[25] The owner should also keep track of the food (brand, consistency) and quantity their cat is eating (including treats) as well as when they make changes, as these may affect their cat's diabetic regulation.

BG is the most commonly used measurement to guide insulin dose adjustments via HBGM or continuous interstitial glucose monitoring.[41] In some studies, HBGM is used by 73%–76% of owners of cats with established DM,[28,42,43] yet this does not reflect the general population.[44] Certain handheld portable glucometers have been shown to produce clinically accurate measurements in cats,[45,46] and a number

Table 2: Expert Panel recommendations for the screening and monitoring of cats with, or predisposed to, diabetes mellitus (DM)[21,22,29]

	Routine screening or preliminary investigation	Insulin-treated DM	Diabetic remission
Candidates and indications	• Hyperglycemic cats in whom there is suspicion of DM • Differentiating between stress-induced hyperglycemia and true DM • Risk factors for DM • Signs of DM including – Polyuria/polydipsia – Polyphagia – Weight loss – Lethargy • Inappropriate urination with polyuria	• Assessing treatment efficacy • Vigilance for clinically significant hypoglycemia • Monitoring for signs of remission	• Monitoring for signs of relapse
Diet recommendations	Life stage or condition-specific diet	Specific diet for DM or condition-specific diet	
	The owner should keep track of the food (brand, consistency) and quantity their cat is eating (including treats) as well as when they make changes, as these may affect their cat's diabetic regulation		
Suggested minimum frequency of Blücare® glucose granules usage[a]	At least 4 sachets[b] per year[c]	1 sachet[b] per week	1 sachet[b] per month
Interpretation	Identification of glucosuria (i.e., color change from white to light or dark blue) over several urine samples in the home environment indicates that diabetes is present.	Identification of NO glucosuria over several urine samples in the home environment (i.e., no color change) indicates that the cat may be heading towards diabetic remission; however, it may also indicate hypoglycemia. Consultation with a veterinarian should be sought promptly. Identification of blue color in the granules indicates that there is glucose in the urine and that the blood glucose level is likely higher than the normal range for at least part of the day. Owners should never change the insulin dose on the basis of a color change of Blücare Glucosuria granules alone.	Identification of glucosuria over several urine samples in the home environment (i.e., color change from white to light or dark blue) indicates that diabetes might have relapsed. Consultation with a veterinarian should be sought promptly; owners should never reinitiate insulin on the basis of a color change of Blücare Glucosuria granules alone.

[a] Suggested frequency; adjust according to clinical needs; [b] 1 sachet contains 8 g of Blücare Glucosuria granules; [c] Every 3 months for most at-risk cats but more often (monthly) for cats on diabetogenic agents with unresolved chronic inflammation or insulin resistance-inducing comorbidities

of continuous glucose monitoring systems are being used in cats.[41,47] The value of regular HBGM or interstitial glucose monitoring depends greatly on client education by the veterinarian, nurse, or technician.[29,32] Some clients are reluctant or unable to perform regular HBGM for reasons such as cost, technical issues, reticence to draw blood, and fear of hurting their cat.[30,31,48,49] In one retrospective study, 31% (8 of 26) of owners expressed an inability to perform HBGM; 6 of the 8 owners discontinued after the first few attempts.[30]

Monitoring urine glucose regularly may help with ongoing care for cats with DM, particularly for the approximately 30% of owners who cannot, or will not, perform HBGM or interstitial glucose monitoring. Blücare Glucosuria granules provide a stress-free means to perform accurate and convenient ongoing urine glucose testing in cats with DM to help detect periods without glucosuria in order to help avoid hypoglycemia. The panel recommends that testing be performed once a day over at least a 3-day period every week (ideally during the whole week), making note of the grade of coloration of granules (0 to 3+; see the Box on page 4). Recording results of weekly samples in a logbook along with other physical evaluations (e.g., thirst, appetite, weight, energy) is helpful to establish what is "usual" versus changes in a cat's diabetic status. Variation from the cat's usual degree of glucosuria, with or without changes in clinical signs, should prompt a call to the veterinary clinic based on the instructions provided to the owner.

Urine glucose testing can be helpful for the detection of hyperglycemia, signaling poor glucose control. Granules also fit in well with the "loose control" program described by Norsworthy et al.[50] Conversely, should the granules be white (0) when they have been blue (≥1) previously, there may be a concern for hypoglycemia that can occur secondary to remission or to insulin overdose and a decrease of the insulin dose should be considered in all cats that have no clinical sign of hyperglycemia and persistent negative glucosuria for ≥5 consecutive days; however the presence of blue granules does not exclude the occurrence of hypoglycemic episodes. In either case,

BLÜCARE GLUCOSURIA GRANULES CLINICAL STUDIES

Blücare Glucosuria granules provide a safe, stress-free, convenient, and accurate method to assess urinary glucose. Granules are sprinkled on the cat's regular brand of litter.[a] Upon contact with urine, the granules undergo a rapid chromogenic reaction (within 1-3 minutes) detecting the absence or presence of glucosuria that is relative to the glucose concentration (Figure).

The granules can detect urinary glucose at, or above, a concentration of 1.4 mmol/L (25 mg/dL). This threshold is the suggested cut-off for humans between physiological and pathological glucosuria,[57] and is very close to the upper reference limit of 1.48mmol/L (26.7 mg/dL found with 325 cats.[58] Although glucosuria ≥1.4 mmol/L (≥25 mg/dL) is considered pathologic, many commercially available semiquantitative Chemstrip® tests fail to detect glucosuria until it reaches a level of 2.8–13.9 mmol/L (50–250 mg/dL).[59]

While the blue color of the granules appears in less than 3 minutes, it will take up to 10 minutes to be fully developed. The color then remains stable for 48 hours.

Granule reactivity is reduced by high pH (≥7,5) and slightly reduced by high specific gravity (≥1,060); however, the test remains capable of adequately detecting glucosuria at clinically relevant levels. Even in these conditions, the granules can detect urinary glucose ≥5,6 mmol/L (≥100 mg/dL). Ketone bodies and hematuria have no significant effect on granule reactivity.

To assess the feasibility of the test at home, 16 cats (10 healthy and 6 cats with diabetes mellitus [DM]) were enrolled. Blücare Glucosuria granules[b] were sprinkled on the cat litter for 14 days.

Reliability was assessed in a field study with 132 cats at risk of glucosuria: cats with risk factors for DM (i.e., old age, overweight, receiving corticosteroids, n=118) or cats with DM (n=14), recruited from veterinary private practices. Urine was obtained by cystocentesis, standard urinalysis was performed, and glucosuria was determined by spectrophotometry (ADVIA® 1800). A cat was considered glucosuric if urine glucose was ≥1.4 mmol/L (25 mg/dL); a test was considered positive if the granule score was ≥1.

The granules were easy to use for owners and well tolerated by cats. 100% of the granules remained white for healthy cats (n=260/260). In diabetic cats, 91.2% were scored <1 in well-controlled diabetic cats (n=52/57) and 67.3% were ranked ≥2 (n=37/55) in cats with severe hyperglycemic episodes.

The field study showed that granule color was consistent with the results of the dipstick in all 132 cases (26 of which were glucosuric) and strongly correlated with glucosuria (r=0.823, p<0.0001), resulting in:

- Sensitivity: 96.15%
- Specificity: 99.06%
- Positive predictive value: 96.15%
- Negative predictive value: 99.06%

This study suggests that these granules are useful to diagnose glucosuria easily at home and may be helpful in the detection and management of feline DM.

Owners who are screening at-risk cats for glucosuria or who are monitoring cats in diabetic remission should contact their veterinarian if there is any trace of blue coloration to the Blücare Glucosuria granules. Those who are monitoring cats with insulin-dependent DM should contact their veterinarian if there is any change in the coloring of the granules from what they have been seeing in the past, including if there is no blue coloration of the granules for ≥3 consecutive days, which may be a sign of hypoglycemia.

Owners should never change the insulin dose without speaking with their veterinarian.

[a] A bentonite-based clumping litter is recommended for optimal results with Blücare granules; however, Blücare granules are compatible with most litters found on the market with the exception of wood- or plant-based litters. Blue stones found in some mineral litters may make interpretation difficult.

[b] A prototype version of the granules was used for these tests. The final version of the granules performs equally or better than the previous one on all the analysed parametres.

consultation with the veterinarian should be sought promptly and further monitoring should be performed according to the veterinarian's recommendations. The insulin dose should never be increased on the basis of persistent positive glucosuria alone.

Diabetic Remission: Monitoring for Relapse

Diabetic remission in a previously insulin-dependent cat is defined as persistent euglycemia without requiring exogenous insulin or oral hypoglycemic therapy.[41,51] It appears to be achievable in >50% of cats through optimal management.[52-54] Remission rates of 67%–84% were obtained through early (<6 months after diagnosis) intensive glycemic control with long-acting insulin.[39,40,55] However, a systematic review found inconsistencies in the duration of euglycemia used to define remission across the studies.[35] In addition to early initiation of insulin therapy and use of longer-acting insulin, factors associated with higher likelihood of remission include feeding a diabetic diet, intensive home monitoring, older age, and being purebred versus crossbred.[24,31,52]

Table 3: Guidance on setting a blood glucose (BG) target in the cat with DM

- When setting a BG target for a particular patient, one of the key patient safety considerations is how closely the BG can be monitored
- Lower targets benefit the patient but require more intensive monitoring to prevent, recognize, and treat hypoglycemic episodes
  - If monitoring is unavailable, it is safer to choose a higher glucose target range so the risk of undetected hypoglycemia is minimized
- Frequent BG monitoring is the established method to monitor a diabetic patient's response to insulin; however, this is not feasible for many owners and many cats
- Monitoring urine glucose may be a more convenient and realistic option for many cats and owners, and may help achieve the goal of tighter glucose regulation

Relapse rates in cats that have experienced diabetic remission are approximately 30%.[56]

Home glucose monitoring helps identify the onset of remission and avoid hypoglycemia. It can also be used for the initial detection of remission, to identify a return of hyperglycemia during insulin withdrawal, and to monitor for relapse (Table 2). Use of a logbook/diary (Figure 1) to record diet and clinical signs, to look for changes in body weight, and to monitor blood/interstitial and urine glucose helps to empower the client and improve the outcome for the patient.

The Blücare Glucosuria granules testing method is stress-free and easy. While useful, urine glucose may not be as easy to interpret in cats going into remission but can be very helpful for monitoring for relapse.

Conclusion

As the prevalence of feline DM continues to increase, prompt and appropriate individualized strategies for screening, management, and monitoring are required in the pre-diabetic cat, cat with insulin-treated DM, and cat in remission, respectively. Home monitoring of

Figure 1: Sample logbook/diary page

		Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday	Weekly Avg. (if veterinarian requests)
Date									
Insulin	Time given (am)								
	Value								
	Time given (pm)								
	Value								
Blood glucose (if measured)	Time measured								
	Value								
	Time measured								
	Value								
Color of granules (Select closest color)		0 1+ 2+ 3+	0 1+ 2+ 3+	0 1+ 2+ 3+	0 1+ 2+ 3+	0 1+ 2+ 3+	0 1+ 2+ 3+	0 1+ 2+ 3+	0 1+ 2+ 3+
Appetite (Compared to normal)		↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓
Water intake (Compared to normal)		↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓
mL/day									
Urine output (Compared to normal)		↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓
Number and size of clumps									
Bowel movement (Compared to normal)		NO YES	NO YES	NO YES	NO YES	NO YES	NO YES	NO YES	NO YES
Observations (diarrhea, normal, hard balls, etc.)									
Cat's energy (Compared to normal)		↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓	↑ = ↓
Observations (lethargic, grumpy, energetic, aggressive, playful, etc.)									
Weight (kg / lbs) once a week									

glucose concentrations has been shown to be key to these 3 groups of cats. Blood and interstitial glucose testing are the most commonly employed home monitoring methods, however, they are not without challenges. Glucosuria testing can be used as an adjunct in the ongoing monitoring of at-risk cats, those with DM, and those in remission. And for the ~30% of owners who cannot or will not perform HBGM or interstitial glucose testing, glucosuria testing may help with clinical management by providing information that would otherwise not be available or even prevent euthanasia due to client concerns. Blücare Glucosuria granules have been shown to be a low-stress, safe, accurate, and convenient method for regular monitoring of glucosuria.

Author Disclosures

Dr. Scherk, Dr. Buffington, Ms. Carozza, Dr. Cook, Dr. Curtis, Dr. Fleeman, Dr. Gostelow, Dr. Lutz, Dr. McKelvey, Dr. Sparkes, and Dr. Verbrugghe participated in a Blücare® Advisory Board.

Case 1: Monitoring a cat during insulin treatment

A cat with recently diagnosed diabetes mellitus (DM) is currently treated with 2 units of protamine zinc insulin every 12 hours. The elderly couple who own the cat keep meticulous monitoring records, which include daily water intake, body weight, and daily surveying of Blücare Glucosuria granules in the litter for at least 3 days every week. At today's review in the clinic, the owners reveal that they feel very anxious that the cat might become hypoglycemic. Their records show there was partial improvement of the cat's clinical signs since the last increase of the insulin dose, and persistent glucose in the urine.

Management strategy

The owners may be reassured that the now established routine of monitoring for glucose in the urine provides a means of timely detection if the blood glucose (BG) subsequently decreases below the renal threshold. It is agreed that the owners will contact the veterinarian within 3 days if the Blücare Glucosuria granules do not change color.

Case 2: Monitoring a cat with complicated diabetes

A cat with concurrent DM and chronic kidney disease has marked day-to-day glycemic variability that has resulted in both periods of severe hyperglycemia and episodes of neuroglycopenia. It has been very difficult to determine an insulin treatment protocol that results in good and stable glycemic control. The owner works long hours and so there are often periods when there is nobody at home to monitor the cat.

Management strategy

A continuous interstitial glucose monitoring device (CGMD) was placed and Blücare Glucosuria granules added to the litter to provide 2 additional methods of gathering information while the owner was away from home. The CGMD graph confirmed marked glycemic variability over the first few days. The owner noted that the interstitial glucose was trending downward when she left for work today, and so, as instructed she quickly replaced the litter in the tray and added a new sachet of Blücare Glucosuria granules. On return 12 hours later, she was disappointed to discover that there were many gaps in the 8-hour CGMD graph generated during her absence. However, it was concluded that the cat's BG had stayed below the renal threshold for the whole 12 hours when there was no color change of the Blücare Glucosuria granules.

Case 3: Differentiating between stress hyperglycemia and DM

An 8-year-old neutered male cat comes into a veterinary clinic for vaccinations and a check-up. The owner mentions that he seems to be urinating a little more frequently than normally. He is overweight with a body condition score (BCS) of 7/9 but has good muscle condition. He is mildly self-defensive but otherwise seems to be a healthy cat. The veterinarian is able to get a BG reading, which is moderately elevated (16 mmol/L [288 mg/dL]). There is also glucose in his urine. The veterinarian is suspicious that this may be due to stress hyperglycemia but would like to rule out DM.

Management strategy

Wait at least 2 days until urine produced during the stressful, event has been voided, then add Blücare Glucosuria granules to the litter box. Observe for color change identifying persistent glucosuria, which would indicate that diabetes is likely. If no color change is seen, the elevated BG seen in the clinic was most likely due to stress.

Case 4: Monitoring a cat with several risk factors for DM requiring prednisolone

An obese 10-year-old neutered male cat (BCS 7/9) is diagnosed with early low-grade alimentary lymphoma, based on clinical signs, ultrasound findings, and biopsy. Treatment is initiated with chlorambucil, vitamin B12, and oral prednisolone. As the prednisolone dose is substantial during the initial treatment period (5 mg every 12 hours), he is at increased risk of developing DM. The cat's age, sex, and body condition predispose him to this condition. The veterinarian is looking for a convenient method for the owner to periodically check the cat's urine glucose.

Management strategy

Recommend that the owner add Blücare Glucosuria granules to the litter box periodically (weekly while on high prednisolone dose, then once a month once dose has been tapered) and call the veterinarian for advice if a color change is observed, indicating glucosuria.

Case 5: Preventive health screening in a multi-cat household

A couple who live in a multi-cat household approach the veterinarian for advice. Although they are very willing to bring their cats in for annual examination, they would like to be able to screen for common diseases between visits. It is difficult for them to monitor individual cats for polyuria or polydipsia because the cats share water bowls and litter boxes. They are particularly concerned about screening for DM, as at least one cat has a history of recurrent pancreatitis and several cats are overweight.

Management strategy

Periodic use of Blücare Glucosuria granules in the litter (e.g., every 3 months) is a reliable way to screen the cats for DM. The couple should also be counselled on methods to help them achieve weight loss in their cats.

Case 6: Determining the cause of inappropriate urination and polyuria

An easily stressed, very shy, 7-year-old neutered male indoor cat frequently urinates on the owner's bed and on the tile floor adjacent to the front door of the house. The cat's owner has brought the cat into the clinic for examination, but the cat consistently urinates in the kennel on the way to the clinic, so that no urine sample can be collected during the office examination. Even with gabapentin sedation and gentle handling, the cat fares poorly during hospitalization, making in-hospitalization urine collection very stressful. Recently, the amount of urine being produced seems to have increased, and the veterinarian wishes to screen the cat for DM.

Management strategy

The owner can add Blücare Glucosuria granules to the litter, or can place them in the urine pool on the tile floor. Ideally, the urine should also be tested with Blücare Hematuria granules.[60]

Case 7: Determining whether a cat has gone into remission

A university student lives with a 7-year-old neutered female cat that was diagnosed with DM 3 months previously. The cat has been well controlled on a dose of 2 units of insulin glargine every 12 hours. The student has been routinely monitoring urine glucose levels by checking Blücare Glucosuria granules in the litter daily for at least 3 days every week, and they have consistently indicated 0 to ≥2 glucose. However, after 3 months of treatment, the student notes that all of the granules have remained white for the past week.

Management strategy

Although her next scheduled appointment with the veterinarian is in 3 weeks, she calls the clinic and is instructed to decrease her insulin dose to 1 unit and to schedule an appointment as soon as possible to discuss the possibility that her cat is in diabetic remission. Alternatively, the veterinarian could choose to discontinue insulin and check the cat as soon as possible, depending on their clinical judgement and the client's diabetes comprehension and awareness.

Case 8: Monitoring an older cat in diabetic remission

A 13-year-old spayed female cat has a history of DM that is well-controlled with insulin. After 3 months of treatment, the diabetes has apparently gone into remission: BG and fructosamine levels remain within the normal reference interval after discontinuation of insulin. The client is aware of the possibility of relapse and would like to monitor without having to collect blood samples.

Management strategy

The owner should add Blücare Glucosuria granules to the litter box regularly. A change in color would indicate that the cat has come out of remission and should be seen by the veterinarian. For the first year, the urine should be checked once a month.

References:

1. O'Neill DG, Gostelow R, Orme C, et al. Epidemiology of diabetes mellitus among 193,435 cats attending primary-care veterinary practices in England. *J Vet Intern Med*. 2016; 30(4):964-972.
2. Banfield Pet Hospital. State of Pet Health® 2016 Report. Available at: https://www.banfield.com/Banfield/media/PDF/Downloads/soph/Banfield-State-of-Pet-Health-Report-2016.pdf. Accessed on January 10, 2020.
3. Lederer R, Rand JS, Jonsson NN, Hughes IP, Morton JM. Frequency of feline diabetes mellitus and breed predisposition in domestic cats in Australia. *Vet J*. 2009;179(2):254-258.
4. McCann TM, Simpson KE, Shaw DJ, Butt JA, Gunn-Moore DA. Feline diabetes mellitus in the UK: the prevalence within an insured cat population and a questionnaire-based putative risk factor analysis. *J Feline Med Surg*. 2007;9(4):289-299.
5. Baral RM, Rand JS, Catt MJ, et al. Prevalence of feline diabetes mellitus in a feline private practice. Presented at the 21st Annual ACVIM Forum. Charlotte, NC, 4-7 June, 2003. Abstract 221.
6. Prahl A, Guptill L, Glickman NW, Tetrick M, Glickman LT. Time trends and risk factors for diabetes mellitus in cats presented to veterinary teaching hospitals. *J Feline Med Surg*. 2007;9(5):351-358.
7. Callegari C, Mercuriali E, Hafner M, et al. Survival time and prognostic factors in cats with newly diagnosed diabetes mellitus: 114 cases (2000-2009). *J Am Vet Med Assoc*. 2013; 243(1):91-95.
8. Little CJ, Gettinby G. Heart failure is common in diabetic cats: findings from a retrospective case-controlled study in first-opinion practice. *J Small Anim Pract*. 2008;49(1):17-25.
9. Goossens MM, Nelson RW, Feldman EC, Griffey SM. Response to insulin treatment and survival in 104 cats with diabetes mellitus (1985-1995). *J Vet Intern Med*. 1998;12(1):1-6.
10. Kraus MS, Calvert CA, Jacobs GJ, Brown J. Feline Diabetes mellitus: a retrospective mortality study of 55 cats (1982-1994). *J Am Anim Hosp Assoc*. 1997;33(2):107-111.
11. Zini E, Lunardi F, Zanetti R, et al. Endocrine pancreas in cats with diabetes mellitus. *Vet Pathol*. 2016;53(1):136-144.
12. Reusch CE. Feline diabetes mellitus. In: Feldman EC, Nelson RW, Reusch CE, Scott-Moncrieff JCR, Behrend EN, editors. *Canine and Feline Endocrinology*. 4th ed. St. Louis, MO: Elsevier; 2014. Pages 258–314.
13. Rand JS. Pathogenesis of feline diabetes. *Vet Clin North Am Small Anim Pract*. 2013; 43(2):221-231.
14. Gilor C, Niessen SJM, Furrow E, DiBartola SP. What's in a name? Classification of diabetes mellitus in veterinary medicine and why it matters. *J Vet Intern Med*. 2016;30(4):927-940.
15. Samaha G, Beatty J, Wade CM, Haase B. The Burmese cat as a genetic model of type 2 diabetes in humans. *Anim Genet*. 2019;50(4):319-325.
16. Rand JS, Fleeman LM, Farrow HA, Appleton DJ, Lederer R. Canine and feline diabetes mellitus: nature or nurture? *J Nutr*. 2004;134(8 Suppl):2072S-2080S.
17. Niessen SJ, Petrie G, Gaudiano F, et al. Feline acromegaly: an underdiagnosed endocrinopathy? *J Vet Intern Med*. 2007;21(5):899-905.
18. Caney SMA. Pancreatitis and diabetes in cats. *Vet Clin North Am Small Anim Pract*. 2013;43(2):303-317.
19. Niessen SJ, Church DB, Forcada Y. Hypersomatotropism, acromegaly, and hyperadrenocorticism and feline diabetes mellitus. *Vet Clin North Am Small Anim Pract*. 2013;43(2):319-350.
20. Lowe AD, Graves TK, Campbell KL, Schaeffer DJ. A pilot study comparing the diabetogenic effects of dexamethasone and prednisolone in cats. *J Am Anim Hosp Assoc*. 2009;45(5):215-224.
21. Slingerland LI, Fazilova VV, Plantinga EA, Kooistra HS, Beynen AC. Indoor confinement and physical inactivity rather than the proportion of dry food are risk factors in the development of feline type 2 diabetes mellitus. *Vet J*. 2009;179(2):247-253.
22. Öhlund M, Egenvall A, Fall T, Hansson-Hamlin H, Röcklinsberg H, Holst BS. Environmental risk factors for diabetes mellitus in cats. *J Vet Intern Med*. 2017;31(1):29-35.
23. Lowe AD, Campbell KL, Graves T. Glucocorticoids in the cat. *Vet Dermatol*. 2008;19(6): 340-347.
24. Behrend E, Holford A, Lathan P, Rucinsky R, Schulman R. 2018 AAHA diabetes management guidelines for dogs and cats. *J Am Anim Hosp Assoc*. 2018;54(1):1-21.
25. Sparkes AH, Cannon M, Church D, et al. ISFM consensus guidelines on the practical management of diabetes mellitus in cats. *J Feline Med Surg*. 2015;17(3):235-250.
26. Link KR, Rand JS. Changes in blood glucose concentration are associated with relatively rapid changes in circulating fructosamine concentrations in cats. *J Feline Med Surg*. 2008; 10(6):583-592.
27. European Society of Veterinary Medicine. Project Alive. Available at: https://www.esve.org/alive/search.aspx. Accessed on May 30, 2020.
28. Hazuchova K, Gostelow R, Scudder C, Forcada Y, Church DB, Niessen SJ. Acceptance of home blood glucose monitoring by owners of recently diagnosed diabetic cats and impact on quality of life changesin cat and owner. *J Feline Med Surg*. 2018; 20(8):711-720.
29. Casella M, Hässig M, Reusch CE. Home-monitoring of blood glucose in cats with diabetes mellitus: evaluation over a 4-month period. *J Feline Med Surg*. 2005;7(3):163-171.
30. Kley S, Casella M, Reusch CE. Evaluation of long-term home monitoring of blood glucose concentrations in cats with diabetes mellitus: 26 cases (1999-2002). *J Am Vet Med Assoc*. 2004; 225(2):261-266.
31. Gostelow R, O'Neill D, Brodbelt D, et al. Diabetic remission in cats examined in UK primary-care veterinary practices: occurrence and risk factors. Presented at the 2017 ACVIM Forum. National Harbor (MD); 8–9 June, 2017. Abstract EN09.
32. Reusch CE, Kley S, Casella M. Home monitoring of the diabetic cat. *J Feline Med Surg*. 2006;8(2):119-127.
33. Krauth SA, Cowgill LD. Renal glucose transport in the cat [abstract]. Proceedings of the American College of Veterinary Internal Medicine Forum. 1982, page 78.
34. Niessen SJM, Hazuchova K, Powney SL, et al. The Big Pet Diabetes Survey: perceived frequency and triggers for euthanasia. *Vet Sci*. 2017;4(2).
35. Gostelow R, Forcada Y, Graves T, Church D, Niessen S. Systematic review of feline diabetic remission: separating fact from opinion. *Vet J*. 2014;202(2):208-221.
36. Marshall RD, Rand JS, Morton JM. Glargine and protamine zinc insulin have a longer duration of action and result in lower mean daily glucose concentrations than lente insulin in healthy cats. *J Vet Pharmacol Ther*. 2008;31(3):205-212.
37. Gilor C, Ridge TK, Attermeier KJ, Graves TK. Pharmacodynamics of insulin detemir and insulin glargine assessed by an isoglycemic clamp method in healthy cats. *J Vet Intern Med*. 2010;24(4): 870-874.
38. Cook AK. Monitoring methods for dogs and cats with diabetes mellitus. *J Diabetes Sci Technol*. 2012;6(3):491-495.
39. Roomp K, Rand J. Evaluation of detemir in diabetic cats managed with a protocol for intensive blood glucose control. *J Feline Med Surg*. 2012;14(8):566-572.
40. Roomp K, Rand J. Intensive blood glucose control is safe and effective in diabetic cats using home monitoring and treatment with glargine. *J Feline Med Surg*. 2009;11(8):668-682.
41. Gottlieb S, Rand J. Managing feline diabetes: current perspectives. *Vet Med*. 2018; 2018(9):33-42.
42. Aptekmann KP, Armstrong J, Coradini M, Rand J. Owner experiences in treating dogs and cats diagnosed with diabetes mellitus in the United States. *J Am Anim Hosp Assoc*. 2014; 50(4):247-253.
43. Niessen SJ, Powney S, Guitian J, et al. Evaluation of a quality-of-life tool for cats with diabetes mellitus. *J Vet Intern Med*. 2010;24(5):1098-1105.
44. Albuquerque CS, Bauman BL, Rzeznitzeck J, Caney SM, Gunn-Moore DA. Priorities on treatment and monitoring of diabetic cats from the owners' points of view. *J Feline Med Surg*. 2020;22(6):506-513.
45. Zoetis Inc. AlphaTRAK 2 Blood Glucose Meter / Blood Glucose Test Strips: Product Label. ART24504-004 Rev. A 02/17.
46. Kang MH, Kim DH, Jeong IS, Choi GC, Park HM. Evaluation of four portable blood glucose meters in diabetic and non-diabetic dogs and cats. *Vet Q*. 2016;36(1):2-9.
47. Hafner M, Lutz TA, Reusch CE, Zini E. Evaluation of sensor sites for continuous glucose monitoring in cats with diabetes mellitus. *J Feline Med Surg*. 2013;15(2):117-123.
48. Adler J. The ups and downs of diabetic management. April 2018. Available at: https://www.dvm360.com/view/ups-and-downs-diabetic-management. Accessed on January 24, 2020.
49. Van de Maele I, Rogier N, Daminet S. Retrospective study of owners' perception on home monitoring of blood glucose in diabetic dogs and cats. *Can Vet J*. 2005;46(8):718-723.
50. Restine LM, Norsworthy GD, Kass PH. Loose-control of diabetes mellitus with protamine zinc insulin in cats: 185 cases (2005-2015). *Can Vet J*. 2019;60(4):399-404.
51. Bloom CA, Rand J. Feline diabetes mellitus: clinical use of long-acting glargine and detemir. *J Feline Med Surg*. 2014;16(3):205-215.
52. Zini E, Hafner M, Osto M, et al. Predictors of clinical remission in cats with diabetes mellitus. *J Vet Intern Med*. 2010;24(6):1314-1321.
53. Marshall RD, Rand JS, Morton JM. Treatment of newly diagnosed diabetic cats with glargine insulin improves glycemic control and results in higher probability of remission that protamine zinc and lente insulins. *J Feline Med Surg*. 2009;11(8):683-691.
54. Bennett N, Greco DS, Peterson ME, Kirk C, Mathes M, Fettman MJ. Comparison of a low carbohydrate-low fiber diet and a moderate carbohydrate-high fiber diet in the management of feline diabetes mellitus. *J Feline Med Surg*. 2006;8(2):73-84.
55. Hafner M, Dietiker-Moretti S, Kaufmann K, et al. Intensive intravenous infusion of insulin in diabetic cats. *J Vet Intern Med*. 2014;28(6):1753-1759.
56. Gottlieb S, Rand JS, Marshall R, Morton J. Glycemic status and predictors of relapse for diabetic cats in remission. *J Vet Intern Med*. 2015;29(1):184-192.
57. Cowart SL, Stachura ME. Glucosuria. In: Walker HK, Hall WD, Hurst JW (eds.). *Clinical Methods: The History, Physiology, and Laboratory Examinations, 3rd Edition*. Butterworth: Boston (MA); 1990; pp. 653–657.
58. Zeugswetter FK, Polsterer T, Krempl H, Schwendenwein I. Basal glucosuria in cats. *J Anim Physiol Anim Nutr (Berl)*. 2019;103(1):324-330.
59. Davidson JK, Delcher HK, Hall WD. Glucosuria and ketonuria. In: Hurst JW (ed.). *Clinical Methods: The History, Physiology, and Laboratory Examinations, 2nd Edition*. Butterworth: Boston (MA); 1978; pp 1035–1039.
60. Scherk M, Buffington CAT, Carozza E, Curtis T, Duncan K, Kruger J, McKelvey D. Blücare® granules: a novel tool for the early detection and monitoring of urinary tract disorders in cats: recommendations from an expert panel. 2018.