

VCA Clinical Consults

What's Your Diagnosis?



PATIENT HISTORY

SIGNALMENT AND HISTORY: “Sheldon” is an 8-year-old neutered male Pug weighing 36 pounds (16.4 kg). “Sheldon” had been diagnosed with diabetes mellitus 3 months prior to presentation and was receiving 25 units of Novolin NPH insulin SQ BID. This equated to a 1.5 U/kg dosage of insulin BID. “Sheldon” seems well controlled to his owners based on weight stability and lack of polyuria and polydipsia. However, despite gradually increasing insulin dosages, every time his veterinarian performs a blood glucose curve the numbers are within the 380-450 mg/dL range with no appreciable nadir. “Sheldon” was referred for workup of insulin resistance.

SIGNALMENT AND HISTORY: “Teddy” is an 11.5-year-old neutered male Shih Tzu weighing 19 pounds (8.6 kg). “Teddy” had been diagnosed with diabetes mellitus 3 years prior to presentation. “Teddy” is receiving 12 units (1.4 U/kg) of Novolin NPH insulin SQ BID and his owners are noting intermittent polyuria and polydipsia. He is intermittently getting them up in the middle of the night and occasionally having accidents in the house. “Teddy’s” veterinarian has been monitoring fructosamine values which are all showing poor regulation of diabetes. “Teddy” was referred for workup of poorly regulated diabetes mellitus.

SIGNALMENT AND HISTORY: “Maxwell” is a 10-year-old neutered male DLH cat weighing 12 pounds (5.45 kg). “Maxwell” had been diagnosed with diabetes mellitus 2 years prior to presentation. He had been

DIFFICULT DIABETICS—

Get Them Regulated in a Flash!



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placed on a high protein, low carbohydrate diet and Lantus® insulin and approached, but never fully achieved, diabetic remission. He had been maintained on 0.5 units of Lantus® insulin SQ BID until the time of presentation. The owner had been monitoring “Maxwell’s” blood glucose with the AlphaTrak®, a portable blood glucose meter (PBGGM) at home. “Maxwell’s” normal daily blood glucose readings were well controlled in the range of 100-250 mg/dL. Approximately two weeks prior to presentation, “Maxwell’s” readings were consistently 300-500 mg/dL. Despite an insulin dose adjustment, “Maxwell’s” blood glucose remained elevated and he became systemically ill with lethargy, vomiting and anorexia. “Maxwell” was referred for evaluation for concurrent disease.

SIGNALMENT AND HISTORY: “Sophia” is a 14.5-year-old FS DSH weighing 12.4 pounds (5.64 kg). “Sophia” has a long history of presumptive inflammatory bowel disease characterized by intermittent vomiting, diarrhea and inappetence. She has been managed with a hypoallergenic diet and other

supportive therapy, such as famotidine, metronidazole, and mirtazapine as clinically indicated. Four months prior to referral she was diagnosed with diabetes mellitus. “Sophia” was relatively well regulated on 3 units of Lantus® insulin. An attempt was made to change her food to a higher protein, lower carbohydrate food, however, she developed clinical signs of vomiting and diarrhea, so her diet was changed back to the hypoallergenic diet. Unfortunately, her gastrointestinal signs did not abate and she experienced progressive inappetence, lethargy, intermittent vomiting and diarrhea. Serum cobalamin/folate levels were performed and she was severely hypcobalaminemic and supplementation was instituted. “Sophia” was referred for further evaluation. An abdominal ultrasound revealed marked diffuse small intestinal thickening, a small segmental GI mass and marked mesenteric lymphadenopathy. She underwent sampling and histopathology was diagnostic for small cell gastrointestinal lymphoma. Prednisolone and chlorambucil were prescribed for “Sophia” which presents a challenge in a diabetic cat.

SIGNALMENT AND HISTORY: “Kevin” is a 10-year-old MC West Highland White Terrier weighing 22 pounds (10 kg). “Kevin” was diagnosed with copper storage hepatopathy and hepatocutaneous syndrome. His predominant clinical sign at the time of diagnosis was inappetence. He was undergoing treatment with D-penicillamine, vitamin B6, denamarin and a hepatic formulated diet when he developed diabetes mellitus. “Kevin” was started on Vetsulin® 3 units SQ BID as his appetite was very poor.

What do all of these dogs and cats have in common? Each of these pets is experiencing a situation in which their diabetes has become poorly regulated or they have a concurrent disease which will make their diabetes very difficult to regulate in the future.

Historically, as veterinarians, we have relied on clinical signs as well as traditional blood glucose curves (BGC) to make insulin dosage decisions in our diabetic patients. During a BGC, a pet is generally hospitalized for 10-12 hours and the capillary blood glucose concentration is measured every 2 hours. Some pet owners are even willing to perform these curves using a PBGM (like the AlphaTrak®) at home. The limitations of these BGC interpretations is the number of blood samples that can sometimes be difficult to obtain and become a source of stress. Also, the glucose nadir or peak can be missed when sampling only every 2 hours. Asymptomatic hypoglycemia and Somogyi phenomenon may be missed with this traditional monitoring. BGCs done in the clinic are also time consuming and expensive.

More recently, the usage of continuous glucose monitoring systems (CGMS) has been described in dogs and cats and have been proven to be easy to use, cost-effective and accurate for interstitial glucose measurement in diabetic dogs and cats.

DISCUSSION

A detailed discussion of diabetes mellitus is beyond the scope of this article and the reader is directed to the listed references.

Continuous glucose monitoring systems (CGMS) measure the interstitial glucose (IG) concentrations in the subcutaneous interstitial fluid. Such devices consist of a sensor that is

FIGURE 1.

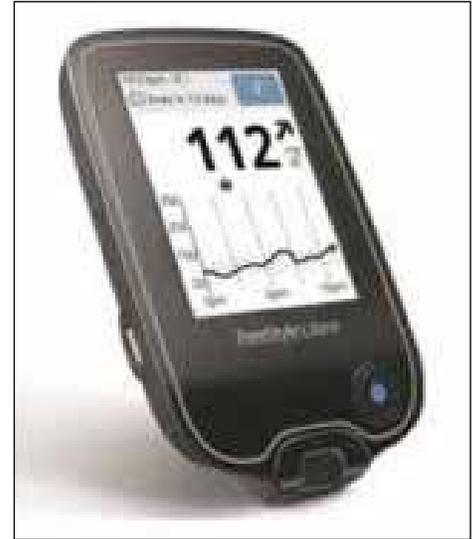


applied on the surface of the body to measure glucose concentrations (see Figure 1) and a transmitter by which the glucose data are displayed (see Figure 2). **Clinical Note: Newer generation smartphones can also be used as a reader for the Freestyle Libre 14-day sensor and this has specific advantages over the Freestyle Libre reader. The detection limits of the sensor are between 20 and 500 mg/dL; however, the reader is not capable of detecting readings above 350 mg/dL. These readings are simply recorded as “HI” on the reader screen. The smartphone app is capable of detecting these higher blood glucose numbers and displaying them at the time of scanning and may be preferable for dogs and cats.**

The Freestyle Libre 14 day® is a flash glucose monitoring system which measures interstitial tissue glucose levels every minute via a disposable water-resistant round sensor (35 mm in diameter x 5 mm thick) with a small catheter (0.4 mm x 5 mm long) inserted under the skin that can be worn for up to 14 days. This is factory-calibrated and does not require blood glucose measurements for calibration (like the older generation CGMS). It is designed for human diabetic patients to replace blood glucose monitoring and for use in day-to-day treatment decisions.

The sensor is based on the glucose-oxidase method, which measures an electrical current

FIGURE 2.



proportional to the glucose concentration. The electrode has a long carbon chain that holds both glucose oxidase and an osmium mediator (called a “wired enzyme”). After glucose has reduced by the glucose oxidase, the enzyme passes its electrons to the osmium mediator rather than oxygen. The mediator then passes the electrons to the electrode for measurement. This avoids using oxygen and thus the requirement for a limiting membrane on the sensor.

The system starts working 60 minutes after application. When the sensor is scanned by the reader (or the smartphone), it shows the measurement within 1 second. Although the CGMS is generating information every minute, it automatically records the glucose concentration every 15 minutes, storing that data in a rolling 8-hour log. There are several reports that can be generated from the reader (or smartphone) such as the 24-hour daily graph, which is helpful in making treatment decisions in dogs and cats. The reader has a USB port which can be used to charge it as well as to download data onto a computer. **Clinical Note: When downloaded onto a computer, the data from the reader will display the higher blood glucose readings (i.e., those above 350 mg/dL which could not be displayed on the reader).** A helpful website is www.FreestyleLibre.us.

At the end of the wearing period, the sensor is fully disposable (in the sharps container)

FIGURE 3.



but the reader can be re-used with a new sensor. See Figure 3 for patient photos wearing the Freestyle Libre 14 day[®]. To apply the Freestyle, a standard clip (generally about 5 cm x 5 cm) is followed by an alcohol prep which is allowed to fully dry. The application of 4 drops of surgical skin glue to the sensor and use of the spring-loaded applicator that comes with the Freestyle Libre 14 day[®] has been used successfully by the author in the application process. Both dogs and cats tolerate the application very well. The surgical glue helps the sensor stay adhered better and most of the sensors I apply have lasted the full 14 days. A mild amount of erythema at the site is quite normal after removal. **Clinical Note:** *Some clinicians place extra tape over the top of the sensor. I have not found this to be necessary when using the surgical glue.*

CGMS MONITORING AND PATIENT UPDATES

“SHELDON:” “Sheldon’s” owners reported him to be feeling completely clinically normal. All spot blood glucose measurements performed were in the 380-450 mg/dL range despite increasing insulin dosages. A Freestyle Libre was placed at his referral visit. The owners were instructed to continue administering 25 units of Novolin NPH insulin SQ BID. Within 48 hours of wearing the CGMS sensor, a marked hypoglycemic

episode was documented as seen in Figure 4, indicated by “LO” on the Freestyle Libre reader. This was documented by the owner on an Alpha Trak 2 with an actual blood glucose measurement of 37 mg/dL. Figure 5 depicts the following day with a marked rebound hyperglycemia. This documented “Sheldon” was experiencing a classic Somogyi phenomenon. **Clinical Notes:** *Hypoglycemia is often clinically silent. Hypoglycemia in diabetics is also often intermittent and frequently occurs overnight. If a patient is only being taken to the veterinarian on a rebound hyperglycemia day, this explains how an insulin dosage can continue to be increased.* The use of the CGMS helped identify the issue in “Sheldon” within 48 hours. “Sheldon’s” insulin was gradually incrementally decreased and he was found to be well controlled on 19 units of Vetsulin SQ BID (as opposed to the 25 units SQ BID he was originally receiving).

“TEDDY:” “Teddy” had been a long-term diabetic receiving 12 units (1.4 U/kg) of Novolin NPH insulin SQ BID with intermittent and erratic clinical signs of polyuria and polydipsia and urinary accidents in the house. A Freestyle Libre was placed on “Teddy” at his referral visit. After several days of blood glucose monitoring, it became apparent Novolin NPH had too short of a duration of action for “Teddy” and was lasting only 4-6 hours (not pictured). He was

FIGURE 4.

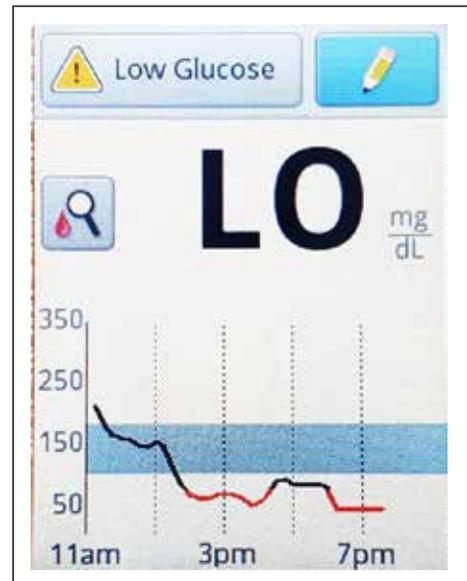
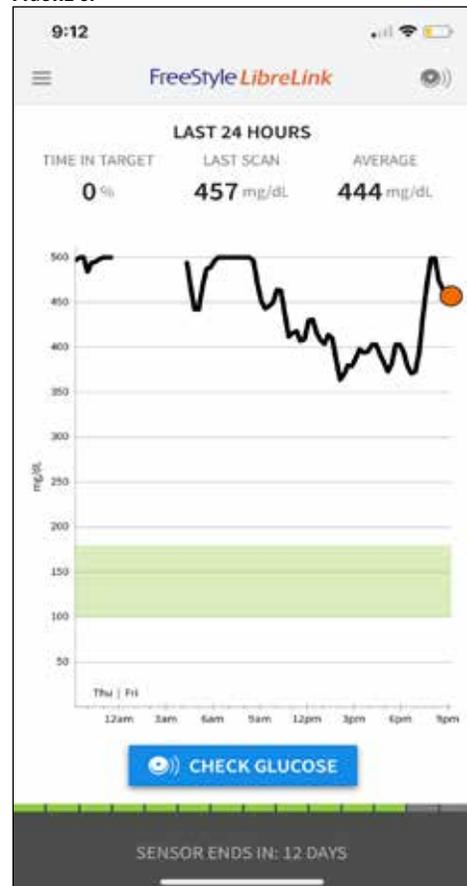


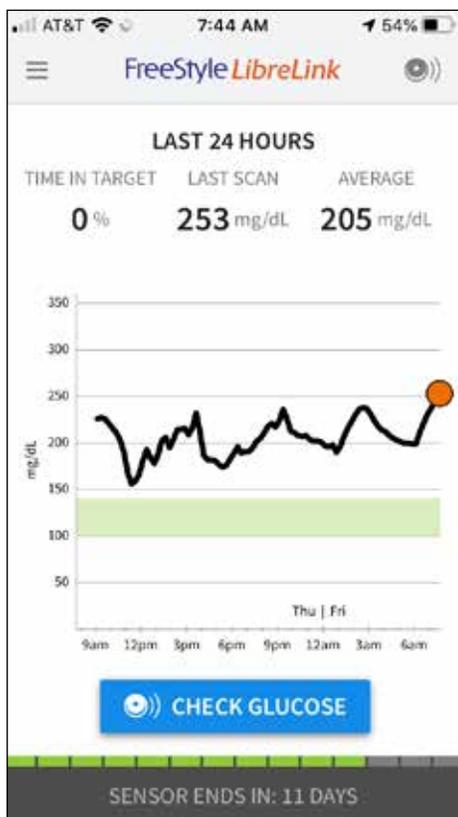
FIGURE 5.



changed to Vetsulin® insulin for a longer duration of action and his blood glucose curve improved dramatically (see Figure 6). His intermittent polyuria and polydipsia resolved once his blood glucose was better controlled throughout the day.

“MAXWELL:” “Maxwell” was diagnosed with diabetic ketoacidosis upon presentation and pyelonephritis which was dysregulating his diabetes. He had a fever, leukocytosis, azotemia, active urinary sediment and a positive urine culture for *E. coli*. This underlying disease was felt to be responsible for his insulin resistance with recent elevated blood glucose readings at home. With treatment of his pyelonephritis, his insulin needs were likely to change significantly, so a Freestyle Libre was placed to assist with insulin dosage adjustments. He initially required 6 units of Lantus® SQ BID while he had active infection to control his blood

FIGURE 6.



glucose between 150-300 mg/dL. Within 2 weeks of antibiotic therapy, the Lantus® had been incrementally decreased based on the CGMS readings to 1 unit SQ BID and the blood glucose was still in the same range. Without the benefit of the CGMS, this would have been difficult to manage.

“SOPHIA:” “Sophia” is the geriatric cat with diabetes mellitus and a recent diagnosis of small cell gastrointestinal lymphoma. Prednisolone and chlorambucil had been prescribed for “Sophia” which clearly represents a challenge in a diabetic cat. The underlying disease as well as the prednisolone can be expected to lead to insulin resistance, so a Freestyle Libre 14 day® was placed to monitor her blood glucose. Over 14 days, her Lantus® insulin was gradually increased from 3 units to 5.5 units based on the CGMS readings to keep her blood glucose 175-300 mg/dL and her

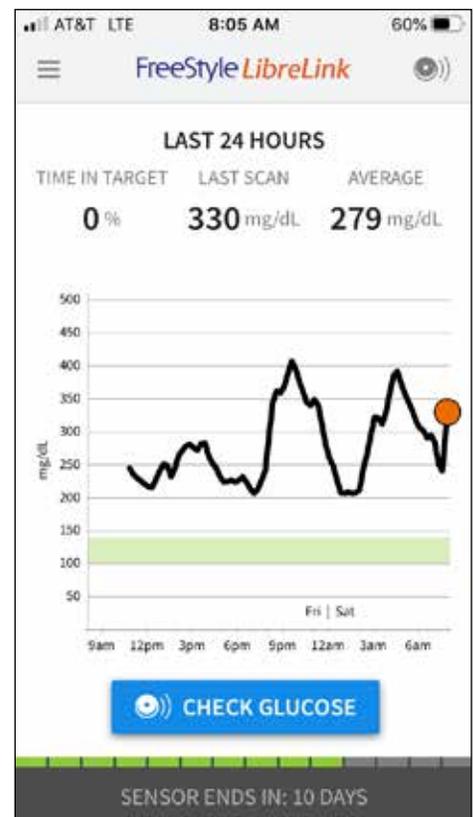
FIGURE 7.



clinical signs of diabetes well controlled.

“KEVIN:” “Kevin,” the Westie with copper storage hepatopathy, hepatocutaneous syndrome and diabetes mellitus had a very poor appetite. A Freestyle Libre was placed to monitor his blood glucose more closely and adjust his insulin with his extremely variable appetite. He initially required only a very low dosage of Vetsulin® (3 units SQ BID) to keep his blood glucose controlled as his appetite was very poor and hypoglycemia was of concern (see Figure 7). He eventually had a percutaneous endoscopic gastrostomy (PEG) tube placed and another Freestyle Libre was placed after PEG tube placement to re-establish his insulin dosing. Figure 8 shows his blood glucose curve transitioning from inappetence to feeding with the PEG tube. He was incrementally increased to 9 units of Vetsulin® SQ BID when his feedings were up to full volume.

FIGURE 8.



SUMMARY

Continuous blood glucose monitoring systems have proved to be accurate in small animal patients for monitoring sick and hospitalized patients with DKA, as well as long-term stable diabetic patients. All patients in this report greatly benefited from the CGMS. Their diabetes was much easier to control in a shorter period of time AND at a much lesser expense to the owner than when using traditional blood glucose curve (BGC) methods.

The most important advantage of CGMS over traditional BGC is that it facilitates detection of brief periods of hypoglycemia and provides information overnight. A much greater number of data points are obtained over a much longer time frame, allowing for identification of asymptomatic, or silent, hypoglycemia and Somogyi phenomenon

that could easily be missed with traditional monitoring.

It is also less time consuming for veterinary staff compared with traditional BGC monitoring, it decreases patient stress and stress-related hyperglycemia (especially in cats), and reduces the frequency of venipuncture or ear pricks associated with PBGM like the AlphaTrak®.

The disadvantages to the CGMS are very few. While there is some initial expense to the purchase of a system, it is still less than one single traditional BGC. The 14-day sensors generally cost \$25-60 each and the reader \$60-90 (one-time purchase). There have been some initial studies looking at the effect of body condition score, skin thickness, lactate concentration and severity of illness

and no variables have seemed to influence the agreement between interstitial glucose and blood glucose results. Future studies may find limitations, but to date, these have been minimal. Anecdotally, during times of rapid blood glucose changes and at times of marked hyperglycemia (>400 mg/dL), the sensor seems to be less accurate.

The other potential disadvantage is the labor-intensive nature of data-sharing between the client and the veterinary clinic. Each veterinarian should determine how data is to be shared between the client and the clinic in order to obtain meaningful information with which to make treatment decisions but not be inundated with data. Clear instructions must be outlined for the client and the veterinary support staff in order for CGMS to be used successfully.

REFERENCES

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Corradini S., Pilosio B., Dondi, F. et al. **Accuracy of a Flash Glucose Monitoring System in Diabetic Dogs.** Journal of Veterinary Internal Medicine 2016; 30: 983-988.

Surman, Sean, Fleeman, Linda. **Continuous Glucose Monitoring in Small Animals.** Vet Clin Small Anim Practice 2013 Mar; 43 (2): 381-406.

www.freestylelibre.us



CLINICAL ASSESSMENT

1 Interstitial tissue glucose and blood glucose are highly correlated in dogs and cats. **True or False?**

2 Continuous blood glucose monitoring systems are highly accurate at determining the interstitial tissue glucose concentrations in dogs and cats. **True or False?**

3 It has been proven that mild dehydration, body condition score, lactate concentration and ketosis do not affect the accuracy of interstitial tissue glucose measurements by CGMS. **True or False?**

4 The Freestyle Libre is unique amongst CGMS in that it is factory-calibrated and does not require additional calibration with blood glucose measurements, which represents an advantage over other CGMS. **True or False?**

5 Traditional blood glucose curves typically readily identify the Somogyi phenomenon. **True or False?**

6 Which of the following are potential advantages of a CGMS?

- a. Detection of brief periods of hypoglycemia
- b. Provision of glucose information overnight
- c. Greater number of data points
- d. Storage of data points in an 8-hour rolling log
- e. All of the above

7 Which of the following are potential disadvantages of a CGMS?

- a. Labor intensive data collection with clients
- b. Cost
- c. Less accurate at higher blood glucose numbers
- d. All of the above

8 Patient stress and stress-related hyperglycemia will be minimized when using CGMS. **True or False?**

9 Which of the following are possible indications for use of a CGMS?

- a. New diabetic for determination of the best insulin dosage
- b. Long term diabetic who has destabilized and needs an insulin dose adjustment
- c. A diabetic with concurrent disease (pancreatitis, pyelonephritis, Cushing's, etc.) and may have new insulin requirements due to insulin resistance
- d. A diabetic undergoing surgery who may have inappetence or not be feeling well post-operatively
- e. All of the above

10 One of the largest challenges is getting the CGMS to adhere to patient skin for the 14 days. **True or False?**

CLINICAL ASSESSMENT ANSWERS:

1. **True.** Multiple studies in dogs, cats and other species have shown very good correlation between interstitial glucose and plasma glucose concentrations.
 2. **True.**
 3. **True.**
 4. **True.** Older CGMS offered only retrospective analysis of glucose concentrations after disconnecting the sensor and uploading the data, whereas the newest generation measure and display the data immediately, allowing direct intervention on a day-to-day basis. The main shortcoming of most CGMS (aside from the Freestyle Libre) is that they need to be calibrated and require capillary blood sampling every 8-12 hours.
 5. **False.** Traditional blood glucose curves frequently miss brief episodes of hypoglycemia and the Somogyi phenomenon. With the CGMS obtaining data points every minute and recording them every 15 minutes in an 8-hour rolling log, these brief episodes are much more likely to be noted.
 6. **E. All of the above.**
 7. **D. All of the above.**
 8. **True.**
 9. **E. All of the above.**
 10. **True.** The sensor has an adhesive also pre-applied but this seems to not be adherent enough to dog and cat skin. The addition of skin glue is helpful or additional tape over top of the sensor helps to keep the sensor in place.
- 