ESSENTIAL TOOL
The continuous glucose monitor can remain in place for several days, and the normal daily routine of the animal can be maintained.

MANAGEMENT STRATEGIES

Continuous Glucose Monitoring in Veterinary Patients

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Continuous glucose monitors (CGMs) are devices that attach to a patient for up to 2 weeks and measure interstitial glucose levels during that time. These devices have become more affordable and applicable in veterinary medicine in the past few years. CGMs have many significant advantages over traditional methods of glucose monitoring; these advantages make them essential tools for management of patients with diabetes.

Because much of the existing research on CGM use in veterinary medicine was conducted with older models, this article also reflects the author's clinical experience in an attempt to present a complete picture of current CGM use in veterinary medicine. It is likely that new data will be published in future literature to help veterinarians optimize the use of CGMs.

TECHNOLOGY AND APPLICATION

CGMs consist of 3 main components: (1) a flexible, electroenzymatic, polyurethane membrane probe that is inserted via an introducer device through the patient's skin into the interstitial (subcutaneous) space; (2) a small sensor, attached to the probe, that adheres to the surface of the patient's skin; and (3) a handheld monitor, which may be a dedicated reader (purchased separately) or smartphone (**FIGURES 1 AND 2**). Sensors are compatible with radiography, but not with computed tomography or magnetic resonance imaging. The dedicated readers are about the same size as a portable blood glucose meter (PBGM). In people, a CGM may be directly linked to an insulin delivery system.

BOX 1 describes the sensor application procedure. After application, the sensor is paired with the monitor. It is then ready to take readings in as little as 60 minutes.

FIGURE 1. The adhesive side of a CGM sensor, after removal from a patient, showing the flexible polyurethane probe that stays in the interstitial space.

Opposite: Kip Carter (2).

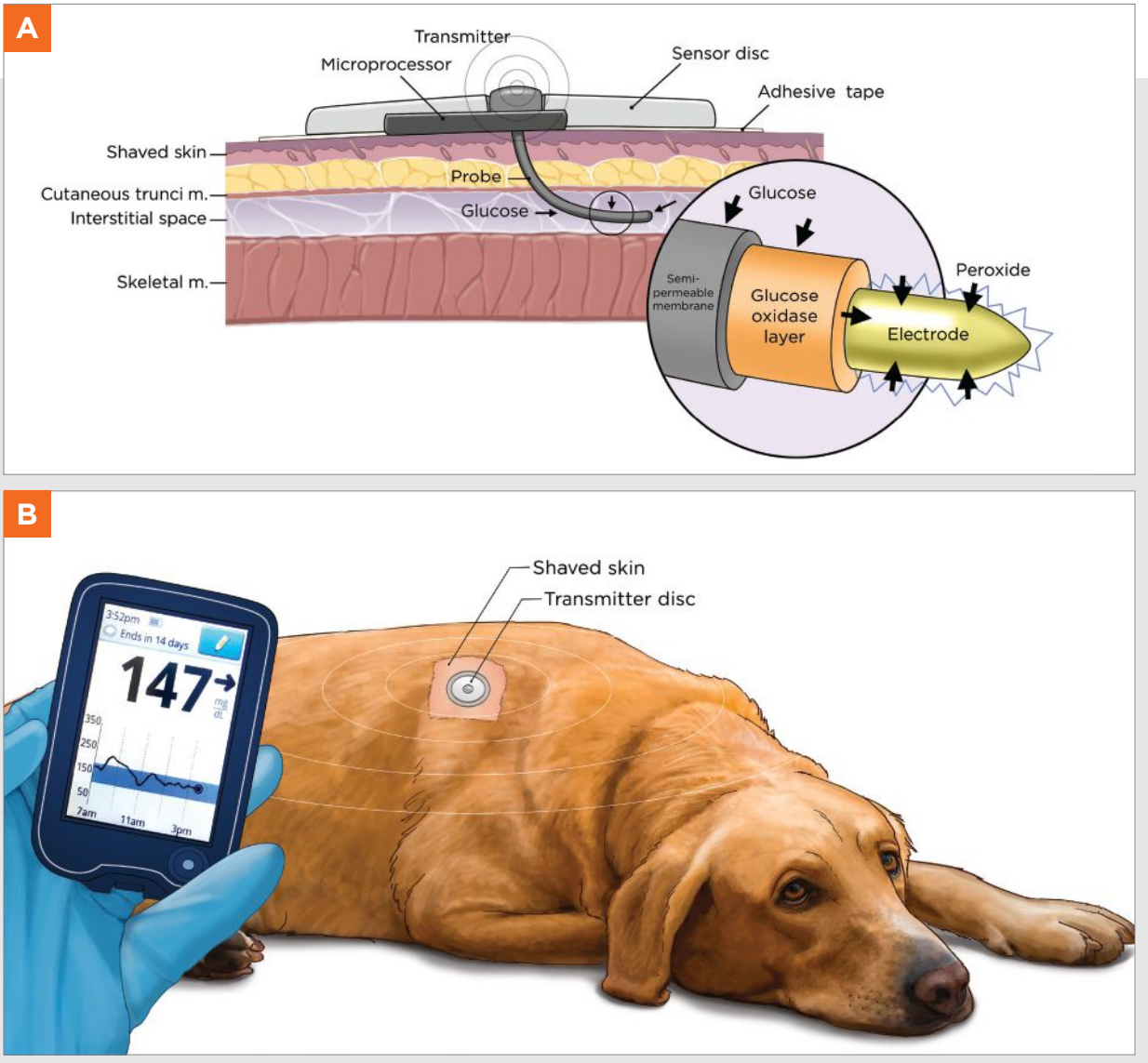

FIGURE 2. Components of a continuous glucose monitor. **(A)** The semipermeable membrane covering the subcutaneous probe allows glucose to pass through and come in contact with the inner layer, which contains glucose oxidase. The reaction of glucose with glucose oxidase creates hydrogen peroxide, generating an electrical current in direct proportion to the glucose concentration. The electrode at the center of the probe sends the signal to the external sensor, which translates the signal into a sensor glucose reading. **(B)** The sensor records, stores, and transmits the data to the monitor.

Scan the sensor at least every 8 hours to ensure data is being transmitted to the monitor. Some patients may tolerate wearing a t-shirt or bandage over the sensor; this does not interfere with data transmission.

ACCURACY AND CORRELATION WITH BLOOD GLUCOSE MEASUREMENT

It is important to remember that the interstitial glucose concentration, also called sensor glucose (SG), is not the same as the blood glucose concentration (BG).

The relationship between intravascular and interstitial glucose is quite complex,[3] and differences between SG and BG readings are expected. Briefly, because it takes time for glucose to diffuse from the intravascular to the interstitial space, changes in SG lag behind those in BG. This lag time has been shown to be as little as 5 to 6 minutes in humans,[4-6] and estimated to be 5 to 12 minutes in dogs.[7] This timeframe is short enough that clinical decision regarding insulin or glucose therapy will be impacted minimally. Some human studies have demonstrated a close correlation of SG and BG, particularly when BG levels are

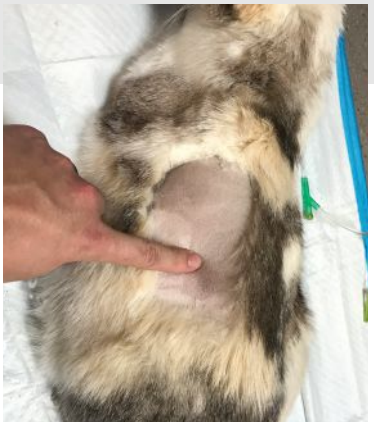

FIGURE A

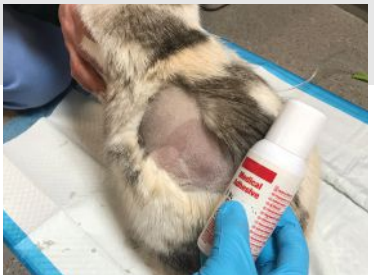

FIGURE B

FIGURE C

BOX 1 Application of a Continuous Glucose Monitor

Application of a CGM to a dog or cat is quick and simple. Detailed instructions for human application, including pictures, accompany each sensor and should be followed accordingly; the steps below provide tips for veterinary use.

1. Gather the necessary materials, including clippers, alcohol wipes, sensor, gloves, and medical adhesive.
2. Select and shave an application site (FIGURE A). This site should be difficult for the patient to reach, have limited subcutaneous motion and sufficient interstitial space for the sensor to be placed, and be comfortable for the patient. Common locations include the caudal cervical, caudodorsal to scapula, lateral epaxial, and caudodorsal thoracic regions. The ideal location for placement of a CGM in dogs and cats has been investigated, but has not been yet optimized.[1,2] The shaved area should be just large enough for the sensor, about 2 to 3 square inches.
3. Clean the shaved area with an alcohol wipe and allow it to dry.
4. Because of the variable adhesiveness of cat and dog skin, a medical adhesive may be used to help keep the CGM in place (FIGURE B). Apply the adhesive in a doughnut-shaped pattern and allow it to partially dry. Alternatively, tissue glue may be used; however, it will make removal of the sensor more difficult.
5. Check the sensor and applicator device lot numbers and expiration dates. Follow the manufacturer directions to insert the application device into the senor apparatus. A "click" is heard when the sensor is correctly placed in the application device. The needle can be seen, but should not be touched (FIGURE C).
6. Apply the application device firmly to the patient with moderate pressure until a click is heard (FIGURE D). Firm pressure may be applied for 10 to 20 seconds to ensure good sensor contact. Gently remove the application device (FIGURE E).

FIGURE D

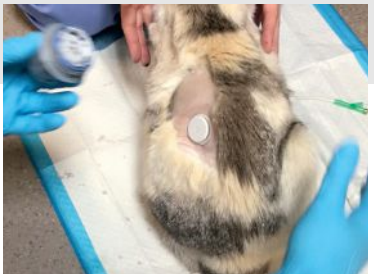

FIGURE E

stable.[7-9] However, with large swings in BG—which are common in veterinary patients with diabetes—the magnitude of BG peaks, troughs, and changes (such as with insulin therapy) are more pronounced than those in interstitial glucose. In the author's experience, SG may be up to 20 mg/dL (1.1 mmol/L) lower than BG at peak levels. Nonetheless, acceptable correlation has been found in diabetic dogs and cats, and SG readings are considered accurate estimates of BG in dogs with diabetic ketoacidosis (DKA).[10-12]

ADVANTAGES

Convenience

The first CGMs were bulky, had cumbersome cords, required charging stations, did not provide immediate readings, and required calibration several times a day with ear-prick PBGM readings. In addition, the data obtained on these older models could only be viewed after the monitoring session had been completed and the information was downloaded to a computer.[13,14]

Current CGM models are smaller, factory calibrated, and allow real-time access to reliable SG readings within 1 to 2 hours of placement. They also adhere much better to dog and cat skin and have a low profile, making them well tolerated by most veterinary patients with a high rate of success in use.[1,2] The Freestyle Libre 14 (Abbott, **freestylelibre.us**) and Dexcom G6 (Dexcom, **dexcom.com**) are affordable, commercially available, water resistant, and user friendly for owners and allow veterinarians to remotely access collected data. The author's practice uses the Freestyle Libre.

Consistency and Comfort

CGMs have the potential to eliminate the need for in-hospital glucose curves performed with multiple blood draws or ear pricks.[15] By avoiding the need for multiple blood draws, they also eliminate the need to place a sampling catheter, thereby minimizing patient stress, discomfort, and potential for adverse effects, such as iatrogenic anemia and hematoma.

Enhanced Data Collection

CGMs have been used to detect clinically relevant hypo- and hyperglycemic episodes in dogs.[16] They can also collect data at times that were not previously feasible (e.g., while patient is asleep) and in situations where owners were unwilling or unable to collect glucose measurements at home.

Other advantages of CGMs include the use of fewer resources (e.g., needles, strips, central lines, syringes) and less staff time, the ability to more rapidly adjust insulin therapy, and the ability to collect data from fractious patients, thereby improving staff safety. Few complications are associated with their use, and they have been determined to be sufficiently accurate for making therapeutic changes in veterinary patients.[17]

USES AND APPLICATIONS

CGMs may be valuable for a variety of diabetic patients: those with a new diagnosis, those with poorly regulated diabetes, and those with complications of diabetes, such as hypoglycemia (insulin overdose or alterations of insulin requirements), DKA, and hyperosmolar states (**BOX 2**).

Diagnosis and Regulation

Achieving glucose stability within 3 months of diagnosis has been shown to result in longer survival time in dogs, and successful at-home monitoring is associated with remission of diabetes mellitus in cats.[18,19] The current standard for monitoring patients with diabetes mellitus is generation of ear-prick glucose curves on which recommendations regarding insulin dose can be based. Many owners are willing to perform this monitoring in the hospital, and some may be willing to do it at home; however, it has been demonstrated that the results of a glucose curve performed at home are significantly different from those obtained in the hospital, and this may affect insulin dose.[15] Use of CGMs to collect home glucose curves may help primary care veterinarians achieve consistent results on which to base dose recommendations, although this has yet to be investigated.

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Diabetic Ketoacidosis

A CGM used to manage a single dog with DKA demonstrated that periods of hypo- and hyperglycemia that were not detected with standard PBGM techniques may be identified with a CGM;[20] this advantage may become apparent in future studies and improve monitoring of these patients.

Use of CGMs can also safely facilitate the use of more intensive insulin therapy in patients with DKA. Recent veterinary evidence supports such therapy, including use of long- and short-acting insulin in combination, higher doses of insulin, and early institution of insulin therapy.[21-23] This more intensive insulin therapy has resulted in faster resolution of acidemia and ketosis, improved appetite, and shorter hospitalization times.

BOX 2 Case Example

An 8-year-old spayed female domestic shorthaired cat presented laterally recumbent and in shock after 2 days of vomiting and inappetence. She had a 2-month history of polyuria/polydipsia (PU/PD) and weight loss.

Initial physical examination and routine blood work findings demonstrated that the patient was dehydrated and in hypovolemic shock secondary to diabetic ketoacidosis (DKA). After volume resuscitation and rehydration, she became fractious with handling and blood collection. She was sedated for placement of a continuous glucose monitor (CGM; **FIGURE A**) and hospitalized for 3 days for treatment of DKA. She received an insulin constant-rate infusion, and the CGM was used to monitor sensor glucose (SG); she tolerated the device well.

The patient was sent home with the CGM and treated with glargine insulin (1 U SC q12h). The CGM sensor dislodged 5 days later. Two months after discharge, the owner reported that the patient was doing well but still had PU/PD; her in-house blood glucose (single check) was 350 mg/dL. The insulin dose was increased to 1.5 U q12h and a second CGM was placed. Seven days later, the patient unintentionally removed the CGM. The collected data were sent to the veterinarian and demonstrated adequate diabetic control (**FIGURE B**).

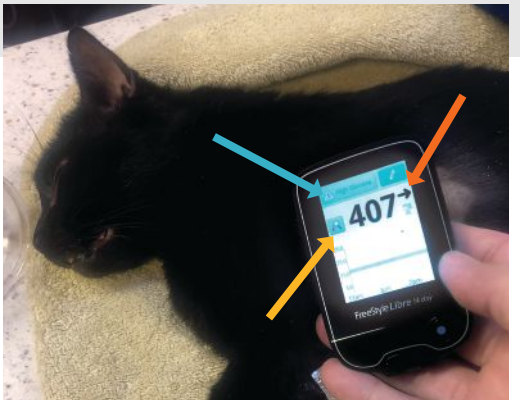

FIGURE A. The display notes the current SG reading of 407 mg/dL along with an arrow pointing to the right **(orange arrow)**, indicating the patient's SG has been stable (not rising or falling). When a high glucose is detected, a warning **(blue arrow)** is given to confirm this reading with a peripheral blood glucose monitor **(yellow arrow)**.

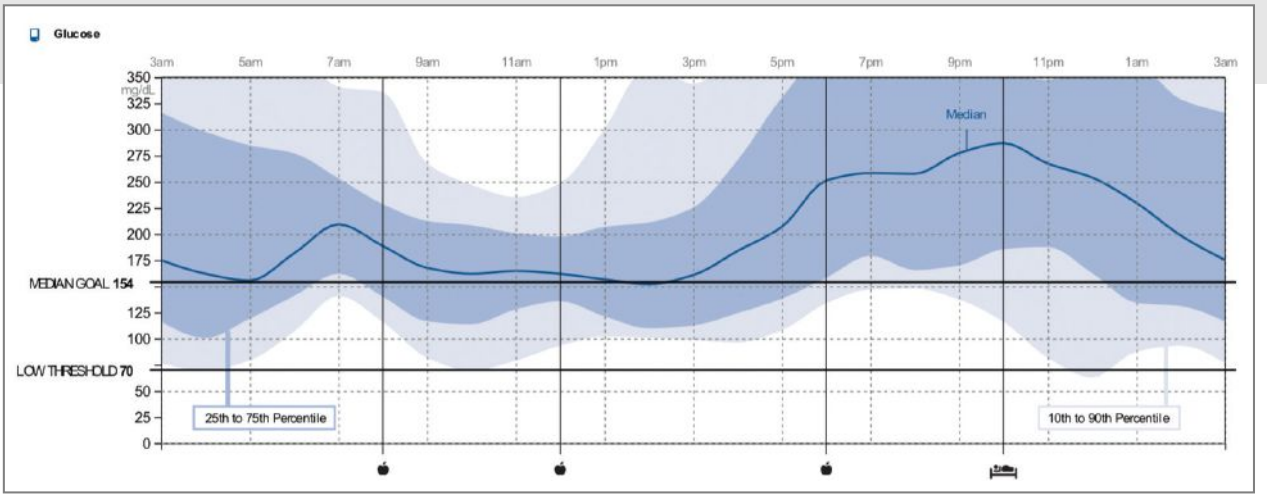

FIGURE B. This graph shows the patient's median SG (blue line), SG in the 25th to 75th percentile (blue shading), and SG in the 10th to 90th percentile (gray shading). This is cumulative data collected over a 7-day period.

Other Potential Uses

Patients with hypoglycemia from a variety of other disease processes, such as sepsis, insulinoma, xylitol ingestion, neoplasia, or liver disease, may benefit from monitoring with CGMs; use of CGMs for these conditions has not been investigated. Studies of CGM use in patients undergoing anesthesia have found some variability in accuracy.[24-26]

AVAILABILITY AND COST

No commercially available CGM has been approved for veterinary use; however, some veterinary distributors now carry these devices for sale to veterinary clinics. A prescription is required for an owner to obtain one from a human pharmacy. Prices vary by pharmacy and geographic location; at the time of publication, a Freestyle Libre 14-day sensor cost $73 to $121, and the optional reusable reader cost $89 to $153. For the amount of information these devices provide, this cost

is relatively low, and may even be less expensive than a traditional glucose curve at many hospitals.

OBTAINING AND INTERPRETING DATA

A standard glucose curve is based on 8 to 10 readings collected over a single day. By contrast, the Dexcom G6 takes a reading every 5 minutes and the Freestyle Libre every 1 minute (totaling more than 1400 readings per day) over the course of several days. These data can be displayed in a variety of ways to give clinicians a better understanding of glucose trends and management of the patient. Feeding, exercise, and sleep cycles can be monitored as well. CGMs may be able to detect previously unobserved persistent hyperglycemia and Somogyi events.[27,28]

If the SG is out of the sensor's range (40 to 400 mg/dL [2.2 to 22.2 mmol/L] for the G6, 40 to 500 mg/dL [2.2 to 28 mmol/L] for the Freestyle), the monitor displays a HI or LO alert. This should prompt collection of an ear-prick sample to be read by a PBGM. The readers designed for use with the Freestyle and Dexcom systems include a PBGM in the handheld monitor; however, separate test strips are required, and these have not been validated for veterinary species.

Data collected by the Freestyle Libre system may be displayed on the handheld monitor or, after downloading, on a computer (**FIGURES 3 AND 4**). On the monitor, individual SG readings are clearly displayed along with an arrow showing the recent trend and any necessary alerts. Daily graphs or percentage of time in target range may be displayed (**FIGURE 3**). When the data are downloaded, the entire recording period can be summarized, specific parameters analyzed, or events on individual days displayed (**FIGURE 4**).

LIMITATIONS

CGMs do have limitations. In veterinary patients, even with correct placement technique, a percentage of sensors do not function properly or may not work at all in individual patients. In one study, as many as 10% to 25% of sensors failed even when placed in the best location by veterinary professionals.[2] Patient or sensor movement, limited subcutaneous space (body condition), adhesive failure, bleeding, biofouling, and other factors may all affect sensor performance. In addition, although current CGMs are designed for 10- or 14-day use, this should be considered their maximum useful time. In the author's experience, most CGMs last 5 to 10 days in veterinary patients and provide a significant amount of data in that time. The author has observed failure rates similar to those in the abovementioned study, including failure of two or more

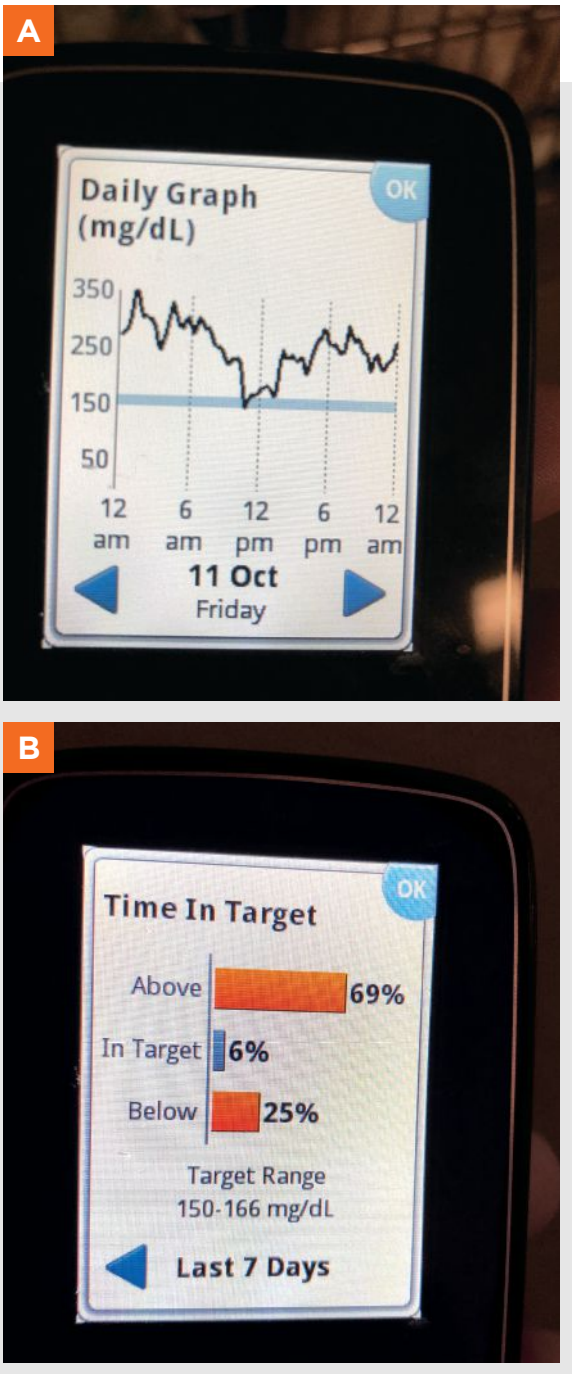

FIGURE 3. Examples of information displayed on a Freestyle Libre CGM reader. **(A)** Daily graph. **(B)** Percentage of time spent in target range.

sensors on a single patient. The use of CGMs in these patients is reconsidered.

Incorporation of CGMs into practice requires client education, as well as sensor placement and data interpretation. All of these processes require valuable veterinarian and staff time, and charging appropriately for this time is necessary.

WHAT THE FUTURE HOLDS

With the improvements in CGM technology in the past 2 decades and ongoing development, use of CGMs is likely to become much more common in veterinary patients with diabetes. Long-acting, subcutaneous sensors are already available for human patients; when these sensors are paired to an insulin pump, the result is, essentially, a synthetic endocrine pancreas. This technology is being developed and tested in veterinary patients and may be available in the future.[29,30]

Because veterinarians do not have to manage diabetic patients for decades (avoiding some of the long-term effects seen in human patients), the tight glucose control that is desired in human medicine may never be a goal of veterinary medicine, and some more advanced applications may not apply to veterinary patients. However, even with current technology, management of diabetic patients can improve drastically. TVP

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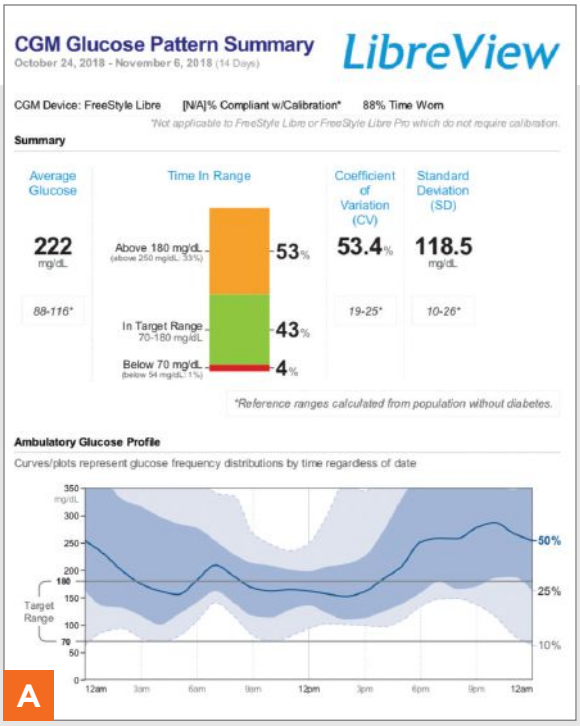

FIGURE 4. Examples of information displayed when the data from the Freestyle Libre monitor is downloaded to a computer or the Freestyle website. **(A)** Summary of recording period (24 hours) outlining quartiles averaged over that period and percentage of time outside of target range. **(B)** Percentage of data captured. **(C)** Event data from a single day, including feeding, hypoglycemic events, and when individual readings were performed.

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