

BLOOD GLUCOSE CURVES: WHEN, WHY AND HOW

Richard W. Nelson, DVM, DACVIM
University of California, Davis, CA

Serial blood glucose curves are indicated during the initial regulation of the diabetic dog and cat and when poor control of the diabetic state is suspected after reviewing the history, physical examination and body weight, not when the history, physical exam and body weight support good control. The serial blood glucose curve provides guidelines for making rational adjustments in insulin therapy. Lack of consistency in results of serial blood glucose curves creates frustration for many veterinarians. It is important to remember that this lack of consistency is a direct reflection of all the variables that affect the blood glucose concentration in diabetics. The purpose of serial blood glucose measurements is to obtain a glimpse at the actions of insulin in that diabetic animal and hopefully identify a reason that could explain why the diabetic dog or cat is poorly controlled. Reliance on history, physical examination, body weight, and serum fructosamine concentration to determine when a blood glucose curve is needed helps reduce the frequency of performing blood glucose curves, minimize the animal's aversion to these evaluations, and improve the chances of obtaining meaningful results when a blood glucose curve is needed.

A serial blood glucose curve can be generated in the hospital (common for diabetic dogs) or in the home environment by the client (common for diabetic cats). Hyperglycemia induced by stress, aggression, or excitement is the single biggest problem affecting accuracy of the serial blood glucose curve, especially in cats. Once stress-induced hyperglycemia develops, it is a perpetual problem and blood glucose measurements can no longer be considered accurate. The biggest factors inducing stress hyperglycemia are hospitalization and multiple venipunctures. An alternative to hospital-generated blood glucose curves is to have the client generate the blood glucose curve at home using the marginal ear vein (cats) or footpad (dogs) prick technique and a portable home blood glucose monitoring device that allows the client to touch the drop of blood on the ear or foot pad with the end of the glucose test strip. The ear vein and foot pad prick techniques decrease the need for physical restraint during sample collection, thereby minimizing the pet's discomfort and stress. Accuracy and interpretation of blood glucose results are similar when blood for glucose determination is obtained by the ear vein or foot pad prick and venipuncture. However, blood glucose results obtained by portable blood glucose monitoring devices designed for use in human diabetics typically underestimate the actual blood glucose values obtained with reference methods when used in dogs and cats. Interestingly, the AlphaTRAK (Abbott Laboratories) glucose meter designed for use in dogs and cats can error low or high (i.e., underestimate and overestimate), when compared with blood glucose values measured from the same blood sample using standard reference methods. The inherent error of the glucose meter must be considered when interpreting blood glucose results obtained by a portable home blood glucose monitoring device.

There are several web sites on the internet that explain in detail the marginal ear vein or foot pad prick techniques in layman's terms and provide information on client experiences with the

technique and with different portable home blood glucose meters. At the time diabetes is diagnosed, a web site is provided to the client and they are asked to visit the web site and see if they would be interested in monitoring blood glucose concentrations at home. Time is spent teaching the technique to those individuals willing to give it a try and advice is given on how often to perform a blood glucose curve (ideally no more frequently than one day every 2 to 4 weeks), and how often to measure the blood glucose concentration on the day of the curve (typically at the time of insulin administration and 3, 6, 9 and 12 hours later). By measuring blood glucose concentrations throughout the day, the clinician will be able to determine if the insulin is effective in lowering the blood glucose concentration, identify the blood glucose nadir, and estimate the duration of insulin effect; information which is necessary when trying to decide how to adjust the insulin treatment regimen.

Use of the ear vein and foot pad prick technique in cats and dogs has produced excellent results. Stress is often significantly reduced, and accuracy of the blood glucose measurements improved. Problems with home blood glucose monitoring include:

- Overzealous clients who start monitoring blood glucose concentrations too frequently.
- Interpretation of blood glucose results and adjusting insulin by the client without veterinarian input, resulting in insulin overdosing and induction of the Somogyi response.
- Difficulty obtaining blood from the ear vein or foot pad.
- Cats who do not tolerate manipulation and pricking of the ear.

The protocol I use when generating a serial blood glucose curve in the hospital is as follows:

- The insulin and feeding schedule used by the client is maintained
- The dog or cat must eat the morning meal
- The dog or cat is dropped off at the hospital as early as possible
- In the hospital, blood is obtained every 1 to 3 hours throughout the day for glucose determination; the timing of blood samples is dependent on the severity of hyperglycemia, the rapidity of the decrease in the blood glucose concentration, and the potential for development of hypoglycemia.
- The glucose nadir must be identified; if the glucose nadir has not been identified by the time of the next insulin injection, the glucose curve should be continued, the scheduled insulin injection aborted, and the dog or cat fed its evening meal

By measuring blood glucose concentrations throughout the day, the clinician will be able to determine if the insulin is effective in lowering the blood glucose concentration, identify the blood glucose nadir, estimate the duration of insulin effect, and determine the average blood glucose concentration for the time period of the glucose curve.

The *ideal* goal of insulin therapy in diabetic dogs and cats is to maintain the blood glucose concentration between 5 and 15 mmol/L and 5 and 17 mmol/L, respectively, throughout the

day and night and to have the average blood glucose concentration be less than 15 mmol/L during the time period of the glucose curve. Typically, the highest blood glucose concentrations occur at the time of each insulin injection, but this does not always occur.

- If the blood glucose nadir is greater than 8.5 mmol/L, the insulin dose may need to be increased
- If the blood glucose nadir is less than 4.5 mmol/L, the insulin dose should be decreased
- Duration of insulin effect can be assessed if the glucose nadir is greater than 4.5 mmol/L and there has not been a rapid decrease in the blood glucose concentration after insulin administration.
- Assessment of duration of insulin effect may not be valid when the blood glucose decreases to less than 4.5 mmol/L or decreases rapidly because of the potential induction of the Somogyi response (see below), which can falsely decrease the apparent duration of insulin effect.
- A rough approximation of the duration of effect of insulin can be gained by examining the time of the glucose nadir.
- For most well-controlled diabetic dogs and cats, the initial blood glucose concentration near the time of insulin administration is less than 17 mmol/L, the glucose nadir is greater than 4.5 mmol/L, the glucose nadir occurs approximately 8 hours after injection of insulin, and the average blood glucose concentration throughout the day is less than 15 mmol/L.
- An initial blood glucose concentration greater than 17 mmol/L combined with a glucose nadir occurring less than 8 hours after insulin administration and subsequent blood glucose concentrations exceeding 15 mmol/L is supportive of short duration of insulin effect.
- A glucose nadir occurring 12 hours or longer after insulin administration is supportive of prolonged duration of insulin effect. Dogs and cats may develop hypoglycemia or the Somogyi response if the duration of insulin effect is greater than 14 hours and the insulin is being administered twice a day.

The Somogyi response is a normal physiologic response to impending hypoglycemia induced by excessive insulin. Hypoglycemia or a rapid decrease in blood glucose stimulates hepatic glycogenolysis and secretion of diabetogenic hormones, most notably epinephrine and glucagon. The physiologic response to hypoglycemia increases the blood glucose concentration, minimizes signs of hypoglycemia, and causes marked hyperglycemia within 12 hours of hypoglycemia. By the next morning, the blood glucose concentration can be greater than 22 mmol/L. Secretion of diabetogenic hormones (e.g., cortisol, growth hormone) during the Somogyi phenomenon may induce insulin resistance, which can last 24 to 72 hours after the hypoglycemic episode.