**DIABETIC CONUNDRUMS: ANYTHING NEW THAT CAN HELP?**

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Diabetes mellitus (DM) is the most challenging endocrine disease to treat. Good monitoring is essential to determining what to do. When all issues accounting for poor control have been exhausted, resistance should be considered. An orderly work-up will be needed.

**Insulin**

At the current time, the insulins commonly used for maintenance in dogs or cats in the U.S. are NPH, PZIVet, Vetsulin, glargine and detemir. I prefer to start insulin BID; the majority of dogs and cats require BID therapy for good control and it may increase the chance of remission in cats. Once-daily basal insulin is starting to be investigated but now enough information is available yet. Even with once-daily basal insulin, small injections at meal time may be needed.

Vetsulin can be used successfully in dogs[1] and is currently my first choice. NPH is my 2nd choice in dogs if Vetsulin fails. Human recombinant NPH may have a shorter duration of action than the animal source NPH previously available.[2] Anecdotally, the different brands NPH do not seem equivalent. It is my clinical impression that I have greater success with Humulin N, while Novolin N (also marketed as Relion) has too short a duration of action in many dogs. With Vetsulin and NPH, I start at a dose of 0.5 u/kg BID. Some authors recommend a starting dose of 0.25 U/kg BID for dogs[3]; others recommend using 0.5 U/kg if the BG is >360 mg/dL and 0.25 U/kg if <360 mg/dL.[4]

Glargine (Lantus®, Basaglar® and Toujeo®) and detemir (Levemir®) are produced by recombinant DNA technology. Glargine's chemical structure is altered slightly from native human insulin. Lantus® and Basaglar® are 100 U/mL products while Toujeo® is 300 u/mL. In detemir, a fatty acid side chain has been added to the insulin molecule, which facilitates reversible binding to plasma proteins, particularly albumin, from where it is released slowly into plasma. Glargine and detemir insulin products are a clear aqueous solution. Detemir does not precipitate in the subcutaneous tissues. Both being a solution and not precipitating may make their absorption more predictable with less day-to-day variation.

Results with 100 U/mL glargine in diabetic dogs have been inconsistent. In one study, 10 diabetic dogs were controlled with 100 u/mL glargine and a high fiber diet at a mean of 38 days.[5] In comparison, in 12 diabetic dogs, 58%, 33% and 8% attained good, moderate and poor glycemic control, respectively by week 24[6]; thus, 100 u/mL glargine was judged to be less successful than other insulins in diabetic dogs. On the other hand, Toujeo® has a longer duration of action, is relatively "peakless" and less variability.[7] It is the most likely to be able to be used as a once-daily insulin.

Detemir can be used with success in dogs. It is VERY important to note that detemir is particularly potent in dogs; the recommended starting dose is 0.1 U/kg BID. In 10 dogs, all improved subjectively. However, 6 episodes of clinical hypoglycemia occurred in 4 dogs. Efficacy of insulin detemir at the end of the study was considered good in 5 dogs, moderate in 3, and poor in 2.[8]

Human recombinant PZI (PZIVet) has variable efficacy in dogs.[9] It is my last choice of insulin in dogs. The name brand product can be tried at a starting dose of 0.5 U/kg BID. However, a prolonged duration of action can result in hypoglycemia.[9] Compounded PZI products are unreliable; in one study, only 1 of 12 compounded products met all USP specifications in all vials tested.[10]

In cats, my first choice is 100 u/mL glargine. Compared to historical data on Levemir® and Lantus®, Toujeo® is longer-acting and has lower inter-subject variation. Thus, as in dogs, it is the most likely to be able to be used as a once-daily insulin. Vetsulin can also be used and may induce remission.[11,12] I recommend 100 u/mL glargine BID for treatment of newly-diagnosed diabetic cats. One study found detemir to be similar to glargine in diabetic cats, offering no advantage.[13] Lastly, PZIVet can be used with good success in cats.[14]

Note: although glargine is my 1st choice insulin in a newly diagnosed cat or a cat not well regulated on another insulin, if a cat has been a long-term diabetic and is well regulated, I would not "mess with success".

Recommendations are to start cats on glargine or detemir BID at 0.5 U/kg if BG is >360 mg/dL or 0.25 U/kg if BG is <360 mg/dL. For the first day, a 12-hr BG curves should be performed (i.e. the curve should be

performed for the interval between the a.m. and p.m. dose). The purpose of the BG curve is to detect hypoglycemia, if present, and lower the dose of glargine as needed. The insulin dose should not be increased for the first week no matter what the curves look like! After the first day, the cat should be sent home and then return for a curve 7 days later. Further curves will depend on the results of the first.

For glargine, I assss the curves the same as for other insulins. Some authors recommend adjusting dose based on the pre-insulin BG (compared to other insulins where we change dose based on the nadir). If at recheck, the pre-insulin BG is >290 mg/dL, increase the glargine dose 1.0 U/cat. The dose should not be changed if the pre-insulin BG is 220-290 mg/dL. In either of these first 2 scenarios, a curve should be done to ensure that hypoglycemia is not occurring. The dose should be decreased 0.5-1.0 U/cat if the pre-insulin BG is <180 mg/dL. If biochemical hypoglycemia is present, the dose should be decreased 1.0 U/cat. If clinical signs of hypoglycemia are present, the dose should be decreased 50%. Administration of glargine should not be discontinued within 2 weeks of starting treatment regardless of the curve – decrease the dose if needed, but do not stop the insulin.

To determine if a cat is in remission, insulin administration should be continued until the cat is receiving 1 U BID. Then, if the pre-insulin BG is <180 mg/dL, go to once-daily administration. If the next day, the pre-insulin BG is still <180, do not administer insulin and do a complete curve. If the pre-insulin BG is >180 mg/dL when receiving once-daily insulin, go back to BID. Weaning can be attempted again in a couple weeks.

If performance of a curve is impossible, start glargine at 2 U/cat SQ BID and have the owner monitor urine glucose concentration or water intake. A cat well-regulated on glargine should have trace glucosuria at most and urine glucose should be negative the majority of the time. If after 2 weeks of receiving glargine, urine glucose is > trace, the dose should be increased 1 U/cat/wk until urine glucose is negative or water intake is <20 ml/kg/24h if eating canned food and <70 ml/kg/24 h if eating dry food. At this point, keep the cat on the same dose for 2 wks then decrease the dose by 1 U/cat/wk until urine glucose is positive or the insulin has been discontinued.

The site of insulin injection is an important aspect. An appropriate location must be chosen, as absorption of insulin from various sites in the body differs. In dogs and cats, the dorsal neck or scruff has commonly been used as a site for injection, but this site may not be ideal due to low blood flow and increased fibrosis caused by repeated injections. A better option may be to administer the insulin at sites along the lateral abdomen and thorax. The chosen area should be rotated daily in order to prevent fibrosis at an injection site.[15]

Insulin pens may be ideal to minimize variability and maximize precision. In people, the pen needs to be held in place for 10 seconds after injection; given the low doses typically used in dogs and cats, the time does not need to be as long. Keep pens in the refrigerator to prolong their potency. If using a pen is cost-prohibitive or if using an insulin that does not come in a pen, I recommend insulin syringes, as compared to other types, due to the small needle size. A good practice is to make the injections part of a good experience. For diabetics that are meal fed and are very into their food, inject them as they are eating. For others, you can give the injections when doing a pleasurable activity.

For any patient that needs a small amount of insulin, use 0.3 mL or 0.5 mL "low-dose" syringes for accurate dosing. The scale on the syringe is easier to read for small doses. Although this seems like a minor detail, giving insulin can be nerve wracking! The syringes are not that easy to read and a small error can have big consequences when you are only giving 2 U to begin with!

**Remission**

For cats, the best case scenario is to have the DM resolve. How likely this is in general is unclear, possibly approximately 50-60%.[16-18] In one study, remission occurred after a median treatment time of 48 days (range 8-216). Unfortunately, remission is not always permanent; in approximately 30% of cats in one study, insulin therapy had to be resumed after a median of 114 d (range 30-3,370).[16] In 55 diabetic cats whose owners followed a highly intensive monitoring and blood glucose (BG) regulation (BG maintained between 50-100 mg/dL) protocol using insulin glargine and a low carb diet, cats that had received glucocorticoid treatment within 6 months prior to diagnosis of DM, that required a lower maximum insulin dose, and or that were

intensively managed using glargine within 6 months of diagnosis were more likely to achieve remission, while cats with a peripheral neuropathy present at diagnosis (such as difficulty climbing stairs or a plantigrade stance) were less likely to do so. Other factors examined that were not predictors of entering remission were age at diagnosis, gender, obesity, evidence of diabetic ketoacidosis at diagnosis, development of azotemia during therapy, concurrent hyperthyroidism and frequency of asymptomatic hypoglycemia.[18] The presence of DKA does not mean that remission is impossible.[17]

**Monitoring**

Monitoring can be a financial burden to owners. Although somewhat controversial and not perfect, I am an advocate of monitoring through performance of BG curves. Their disadvantages need to be recognized (and in part can be overcome by having owners conduct curves at home or use a Libre), but they are the only technique that not only confirms poor control but indicates how to alter an insulin dose. Measuring urine glucose and glycosylated proteins as well as assessment of clinical signs is also recommended to get as much information as possible for complete evaluation.

A recent device we have started to employ is the FreeStyle Libre Flash Glucose Monitoring system. A disposable, single-use sensor is placed on a patient; the sensor has a needle that is inserted into the subcutaneous space. Interstitial glucose is monitored every 15 minutes, which correlates with blood glucose (BG). A sensor can last up to 14 days if the dog or cat does not remove it. No calibration is needed and owners can apply the sensor at home. We put a few drops of tissue glue on the sensor to help it stick to the patient.

There are two ways to download data. The unit generates graphs in the range of 40-350 mg/dL but reports values in the range of 40-500 mg/dL. The FreeStyle Libre 14-day system is compatible with FreeStyle Libre Desktop software and the Libre View Software. Both are available on-line to download from the company's consumer website (freestylelibre.ua) and are free of charge. The Libre Desktop software allows a client to download and save their pet's information on their computer. The Libre View Software allows owners to create a report online which may be downloaded and saved as a PDF document. Numerical data can be retrieved from LibreView (the FreeStyle Libre website) by choosing the patient, then going to "Patient notes", and then scrolling down the page and following the link "Export Patient's Data". To obtain data from the sensor, an owner can use a Libre monitor (cost about $80) or download the information onto an iPhone; a new Android app is becoming available. The sensor stores information for 8 hrs, so data must be downloaded at least that often; if an owner waits longer than 8 hrs, there will be a gap. For example, if an owner downloads after 10 hrs, the first 8 hrs of data will be present followed by a 2 hr gap. The sensor will then start recording again for the next 8 hrs. The monitor can store weeks' worth of downloaded data.

For a client to get a Libre, a veterinarian needs to write a prescription for the owner to purchase the Reader kit and Sensor kit, which can be obtained at major retail pharmacies. Once the owner buys the Reader kit, there is no need to purchase that again; they just buy a new Sensor kit whenever 14 more days of monitoring is required. If the owner is going to use their smartphone, the Reader kit is not needed.

Hypoglycemia can be detected but the system is not perfect. In the only study to date, the system was able to detect 77.6% of actual low glucose events, but at times a low glucose message was displayed in error (false notification rate) and 22.4% of the time a low glucose message was NOT displayed when it should have been (missed detection rate).[19] Thus, if clinical signs are present that are suggestive of hypoglycemia, BG should be check even if the Libre says BG is not low.

We also ask owners to keep a log. Having the information is crucial in interpretation of the data and for making recommendations. We give owners a table to fill out which requests the following information:

| AM insulin -Who gave? -Where? | Appetite (note meal times and how much eaten; also any snacks) | Urinary habits (e.g. increased, decreased, accidents) | Drinking habits (e.g. increased, decreased) | PM insulin -Who gave? -Where? | Weight (once a week) | Comments: Note any changes, diarrhea, vomiting, activity level, got into wrong food, etc. |
|---|---|---|---|---|---|---|
| Time: | | | | Time: | | |

Interpretation of the information follows the same principles as a 12- or 24-hour curve. One question to ask, is what are we looking for in monitoring diabetics, or, in other words, what is the goal of therapy? At all costs, hypoglycemia should be avoided. On the flip side, how high can BG go? The goal of therapy is to eliminate clinical signs in order to provide a good quality of life for the pets and clients. The strict control aimed for in human diabetics is not practical and may not be necessary in veterinary patients. Strict control in humans is required to avoid serious diabetic complications such as nephropathy, retinopathy, vasculopathy, etc. For whatever reason, these complications are not prevalent in veterinary populations. To eliminate clinical signs, BG needs to be below the renal threshold the majority of the time, i.e. < approx. 200 mg/dL in dogs and approx. 250-300 mg/dL in cats. (Please note, this assumption may be changing!)

To construct an in-hospital curve, BG is measured in general every 2 hrs for one interval between injections, i.e. for 12 hrs if insulin is administered twice daily and for 24 hrs if insulin is given once daily. When BG is <150 mg/dL, the concentration should be measured hourly. A normal insulin/feeding schedule must be maintained as much as possible. If a patient does not eat the normal amount of the normal food at the usual time, the serial glucose curve should probably not be performed. The patient should be fed its standard diet at the usual time and the insulin given by the owner in the hospital so the owner's injection technique can be assessed. Obtaining a fasting sample for measurement of BG prior to insulin injection can aid in appraisal of glycemic control, but this may not be possible if normal feeding time occurs before the hospital opens. Furthermore, feeding a dog or cat at home may ensure that the pet will eat. If the patient is fed at home, the insulin should then be given by the owner either at home or, especially if owner technique is questionable and needs to be assessed, in the hospital in front of a technician or veterinarian. Clearly, cooperation between client and veterinarian is necessary to maximize the information obtained with minimal disturbance to routine. When first trying to regulate a diabetic patient, assessment of the owner's technique is crucial.

A curve should be performed the first day insulin is given. (We don't use a Libre for this particular curve.) Glucose concentrations may be lower than expected after the first 24 to 48 hours of insulin therapy, especially in cats as stress hyperglycemia resolves.[20] This first curve is done solely to ensure that hypoglycemia does not occur. If hypoglycemia is found, the insulin dose should be decreased 25% and another curve done the following day with the same goal in mind – to check for hypoglycemia. The insulin dose should not be increased based on the first day's curve. A patient requires ~7 days on a dose of insulin to equilibrate and reach maximal effect, so another glucose curve should be performed at that time. Based on assessment of the curve after equilibrium, the insulin dose can be changed as deemed necessary.

A serial BG curve should establish the nadir and duration of effect. The BG concentrations all must also be considered. The pattern of insulin effect should be used to determine dose, interval, and feeding schedule. In assessing a glucose curve, whether it is the first curve performed on a patient or the last of many, two basic questions need to be asked. First, has the insulin succeeded in lowering BG and how far? And, second, how long has the insulin lasted? By answering these questions, logical changes in dosing regimen, if necessary, can be made. Ideally, glucose concentrations should reach a nadir at 80 to 150 mg/dL. The highest glucose concentration should be close to 200 to 250 mg/dL in dogs or 300 mg/dL in cats. My definition of duration is the number of hours that the BG is in the desired range. The BG concentrations should be in the ideal range for the majority of the day to control clinical signs.

The first aim in regulating a diabetic is to achieve an acceptable nadir. (For insulin glargine, dose adjustment is made based on the pre-insulin BG concentration, see above.) In general, if an acceptable nadir is not achieved, insulin dosage should be adjusted depending on patient size and degree of hyperglycemia. Usually changes of approximately 10-25% are appropriate. Once an acceptable nadir is accomplished, duration of action can be determined by a glucose curve.

Hypoglycemia should always be avoided. No matter what other BG concentrations are during the day, if the value of the BG nadir is <80 mg/dL, a reduction in insulin dosage is indicated. Decrease the dose 25% if there are no signs of hypoglycemia and 50% if there are signs, and then do another curve to ensure hypoglycemia does not recur.

The Somogyi phenomenon, also called hypoglycemia-induced hyperglycemia, refers to hypoglycemia followed by marked hyperglycemia. It results from a normal physiological response when BG declines to <60 mg/dL or when BG concentration decreases rapidly regardless of the nadir. In either case, a number of reflexes are triggered that act to increase BG. Counter-regulatory hormones such as epinephrine, cortisol, glucagon are secreted, and the resultant hyperglycemia usually occurs rapidly, with BG of 400-800 mg/dL. If the Somogyi phenomenon occurs, insulin dosage should be decreased so the nadir is >80 mg/dL; counter-regulatory hormones will no longer interfere with the action of the exogenous insulin and true duration of effect will become apparent. If the duration of insulin action is truly < 8 hrs, adequate therapy with that type of insulin requires injections more frequently than twice daily, which is impractical for most owners. A different kind of insulin should be tried.

Admittedly, glucose curves are not perfect. Results of a serial glucose curve should always be interpreted in light of clinical signs. Glucose curves can be affected by deviation from normal routine and vary from day to day.[21,22] (One related important point is that due to the variation, predicting the timing of a diabetic's nadir on the basis of previous serial glucose curves and obtaining a single sample at that time is unlikely to give a reliable result[21], i.e. spot checking does not provide helpful information.) Stress hyperglycemia can falsely elevate results.

However, curves serve two very useful purposes that other techniques do not. First, they can clearly show clinically undetectable hypoglycemia. A phenomenon exists in human diabetics referred to as "hypoglycemic unawareness". In this situation, the body does not respond to mild or even moderate hypoglycemia and clinical signs do not develop. However, when severe hypoglycemia occurs, profound clinical signs appear acutely without warning. Although unproven, I believe the same occurs in veterinary patients. A glucose curve will hopefully document mild hypoglycemia that can be fixed before a seizure occurs. Thus, periodic curves can help even in a seemingly well-controlled patient. Secondly, and more importantly, other techniques and clinical signs can suggest that control is lacking, but multiple reasons for poor control including too low and too high a dose of insulin exist. The only way to know how to change the therapy to gain control is by performance of a curve.

For a glucometer, I prefer the AlphaTRAK2. Although in general glucometers underestimate BG concentration, the AlphaTRAK can either over- or underestimate BG in dogs[23], while, in cats, it tends to underestimate low and normal BG and overestimate high BG concentrations.[24] The inaccuracies, however, are of little clinical significance.

Measurement of urine glucose can be helpful for monitoring, especially cats where stress hyperglycemia prevents obtaining an accurate curve. First, urine glucose levels can be determined as needed to aid in assessment of glycemic control, especially when other data are conflicting. Consistently negative urine glucose readings may indicate that insulin dosages are either adequate or excessive. Remember, a negative urine glucose reading only means that in the period since the last urination, the BG was below the renal threshold. So, for example, the BG could be 200 mg/dL or it could be 40! The only way to know is to measure BG. With consistently negative readings, a serial glucose curve can be performed to differentiate between adequate insulin therapy and use of excessive doses that could result in hypoglycemic shock. If BG measurement is not an option, the risk of hypoglycemia is higher. Uniformly high urine glucose readings coupled with unresolved clinical signs indicate that the insulin dose is inappropriate.[15] Second, urine glucose concentrations can be determined regularly (at least weekly) to help in the assessment of ongoing control. Changes in urine glucose

levels may alert the owner and clinician to loss of glycemic control and a need for reevaluation. Third, for cats receiving glargine insulin, a protocol exists for altering insulin dose based on urine glucose measurements.

Another monitoring method is measurement of glycosylated proteins, either glycosylated hemoglobin or fructosamine. Glycosylated hemoglobin (GHb) is formed by non-enzymatic, irreversible binding of glucose to hemoglobin.[25] Fructosamine refers to glycosylated serum proteins, mainly albumin.[26] Both GHb and fructosamine form at a rate proportional to the average BG present, so the higher the mean BG concentration over time, the greater their concentrations should be. The levels of glycosylated proteins are also affected by the half-life of the native protein. Thus, GHb reflects glycemic control over the previous 2-3 months, while fructosamine reflects that over the previous 2-3 weeks.

Both parameters correlate in general with BG and are typically not affected by stress. However, the value obtained from the laboratory must be interpreted in conjunction with all other data. Normal animals or well-controlled diabetics can have elevated concentrations of either GHb or fructosamine, and, conversely, uncontrolled diabetic animals can have normal levels of either.[27,28] Fructosamine may be elevated in sick, hyperglycemic, but non-diabetic cats.[19] Given the overlap in GHb or fructosamine concentrations that can occur between well and poorly controlled diabetics, in general, I think one of the best uses of glycosylated proteins is to evaluate trends in glycemic control if measured at each recheck. I recommend not to try to normalize serum concentrations of glycosylated proteins but to aim for a concentration slightly above normal. A fructosamine below normal indicates chronic hypoglycemia.

Lastly, home monitoring of clinical signs is crucial as an adjunctive tool. If a patient is not polyphagic, polydipsic or polyuric and body weight is stable or increasing, diabetic control is likely good. Judgment of adequacy of control should not rely solely on owner reports.

**Resistance**

Insulin resistance should be suspected in any pet in which marked hyperglycemia persists throughout the day despite insulin doses of more than 1.0 U/kg per injection or when >1.5 U/kg per injection is needed to maintain adequate glycemic control. However, use of these doses does not mean insulin resistance is present. The problem could lie with owner issues, patient management (e.g., exercise, diet), or insulin choice. Lack of response to high doses of one insulin type does not mean all insulins will be ineffective.

Before a thorough and costly workup for insulin resistance is initiated, factors that mimic insulin resistance should be ruled out. The owner's technique and insulin handling should always be evaluated first. Possible causes for an unsatisfactory response to insulin include inadequate mixing of insulin before withdrawal into the syringe; use of the incorrect syringe (e.g., using a U100 syringe with U40 insulin); misunderstanding of how to read the insulin syringe; problems with insulin injection technique; and inactivation of insulin as a result of improper handling. A bottle of insulin should be discarded after 3 mths. If owner issues are suspected, a glucose curve should be performed after the owner administers insulin using a new, undiluted bottle and while being observed. Second, the owner should be questioned to ensure consistent and appropriate diet and exercise. If hyperglycemia is believed to be due to a postprandial surge from feeding a meal when the insulin's effects are waning, timing of meals should be adjusted. Alternatively, addition of an oral hypoglycemic agent such as acarbose can be considered. Third, if no response is seen to one type of insulin, then another should be tried to see if it might be effective. Fourth, absorption of insulin can vary among subcutaneous sites, so another injection site should be used; the lateral thorax or abdomen is recommended. Lastly, a glucose curve should be performed to eliminate other possible mimics of insulin resistance, such as the Somogyi phenomenon and inadequate duration of insulin action.

If insulin resistance is documented, a number of differential diagnoses should be considered. Infection, ketoacidosis, and concurrent illness can cause resistance. The urinary tract and oral cavities are common sites of infection; always perform a urinalysis and urine culture, regardless of urinalysis findings, and complete oral examination. Renal disease, hepatic insufficiency, cardiac insufficiency, pancreatitis, and starvation should be considered. Malnutrition can lead to insulin resistance and diminished insulin secretion. Obesity has been linked to glucose intolerance and abnormal insulin secretion in cats and dogs, but its role in creating insulin resistance is unclear. Hyperthyroidism, hypothyroidism, and hyperadrenocorticism can also cause insulin resistance.

Certain drugs, most notably progestogens and glucocorticoids, can cause resistance. If possible, use of these medications should be slowly discontinued in diabetics. Otherwise, the patients may need to be treated as insulin-resistant. Neoplasia has been associated with insulin resistance in 5% to 10% of diabetic cats and dogs. Hyperlipidemia should be considered as a possible cause.

Insulin antibodies are a commonly discussed cause of resistance. The clinical significance of anti-insulin antibodies (AIAs) remains unclear. Although antibodies may form against exogenous insulin, associated clinical insulin resistance appears rare. If AIAs are believed to be causing insulin resistance, the insulin source should be switched to a different one. Glycemic control should improve within 2 weeks of changing the species of insulin if AIAs are causing resistance.

When a cause for insulin resistance is sought, the easiest causes to rule out and the most likely should be eliminated first, proceeding through to the least likely. The following order, in general, has been recommended in cats: concurrent drugs, obesity, concurrent disease (including infection and ketoacidosis), hyperthyroidism, acromegaly, hyperadrenocorticism, and insulin antibodies. The order to use in dogs, in general, is as follows: concurrent drugs, diestrus/acromegaly, obesity, concurrent disease (including infection and ketoacidosis), hyperadrenocorticism, hypothyroidism, hyperlipidemia, and insulin antibodies. This order is not absolute. If strong evidence exists for a differential diagnosis lower in the order, that possibility should be ruled out first.

Management of insulin resistance requires correcting the underlying disorder, if possible. For causes such as a simple bacterial infection or concurrent administration of diabetogenic medications, eliminating the underlying problem can be relatively easy; other problems, such as acromegaly, may be more difficult to correct.

If the cause cannot be determined or eliminated, the following guidelines are suggested: (1) Administer insulin at least twice daily. (2) Avoid long-acting insulins, unless regular insulin is added. Intermediate-acting insulins are more effective in overcoming insulin resistance and lowering blood glucose concentrations. (3) Consider using mixtures of short-acting and longer-acting insulins. Large insulin doses may be required, but it will be necessary to determine the actual dosage using serial blood glucose curves, as for any diabetic.


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