

Troubleshooting

The uncontrolled diabetic is one with poor control of clinical signs. This may include hypo- and hyperglycemic pets, those with insulin resistance (decreased responsiveness to the insulin, defined by >1.5 U/kg per dose in dogs or >5 U/dose in cats), or those with frequent increases or decreases in insulin doses. A common misconception is that a patient who does not respond to insulin has insulin resistance, but this is not necessarily true; other insulin-related factors should be considered.

Any dog or cat with persistent clinical signs (PU/PD/PP) and unintended weight loss should be re-evaluated using the following protocol:

See the [“Troubleshooting” algorithm](#).

1. **Rule out client and insulin-handling issues first.**
 - a. Observe client’s administration and handling of insulin, including type of syringes used.
 - b. Assess insulin product and replace if out of date or if the appearance of the insulin changes (i.e., becomes flocculent, discolored, or, in the case of glargine [Lantus] or detemir [Levemir], cloudy).
2. **Review diet and weight-loss plan.**
3. **Rule out concurrent medications that could cause insulin resistance**, such as glucocorticoids, cyclosporine, and progestins. Specifically ask owners about steroid-containing eye and ear drops and progestins that might be transferred from an owner via medicated cream used as hormone-replacement therapy in women.
 - a. If the concurrent medication can be discontinued, the patient should be reassessed 2 wk later. For example, if the patient is placed on a short course of steroid eye drops before or after cataract surgery, the insulin dose does not usually need to be changed despite a short period of increased clinical signs.
 - b. If the comedication cannot be discontinued within 2 wk, the insulin dose may need to be increased. Consultation with or referral to a specialist may be helpful in these situations, particularly if the diabetic patient has a concurrent immune-mediated disease that is being managed with glucocorticoids.
4. If not already done, **obtain a BGC to rule out hypoglycemia**. At-home monitoring is preferred. If hypoglycemia is detected, the insulin dose needs to be decreased.
5. **Rule out concurrent disease.**
 - a. Repeat a physical exam. Specifically, evaluate the teeth and gums for dental disease. Ovariohysterectomies must be performed in intact, diabetic female dogs and cats. Note that anesthesia is not contraindicated in otherwise healthy, stable, nonketoacidotic diabetic patients. See AAHA’s Resource Center for [sample protocols](#)

for managing diabetic patients under anesthesia.

- b. Perform baseline laboratory testing (CBC, serum biochemistry with electrolytes, and urinalysis with culture both in dogs and cats; BP, UPC, and total T4 in cats), if not already completed recently.
- c. Consider second-level diagnostics, such as abdominal and thoracic radiographs, abdominal ultrasound, species-specific pancreatic lipase immunoreactivity (specPLI), trypsin-like immunoreactivity (TLI), B12/folate, and SDMA for IRIS staging.

These diagnostic tests, in conjunction with baseline diagnostics, will help identify many causes of insulin resistance, including renal disease, pancreatitis, urinary tract infection, and neoplasia.

Acute and chronic pancreatitis can both destabilize a previously controlled patient and make it difficult to regulate a pet initially. Diagnosis is sometimes challenging, and requires a multifaceted approach because not all abnormalities will be present in a given patient. Evaluation of clinical signs in conjunction with clinicopathologic abnormalities, species-specific PLI, and abdominal ultrasound is critical. Pets with chronic pancreatitis may have variable insulin requirements that increase when the patient has a flare-up, and decrease with improvement. If insulin doses are increased, hypoglycemia can occur when insulin resistance resolves with improvement of the pancreatitis. Thus, conservative dose adjustments should be made, and home monitoring for hypoglycemia is ideal.⁴⁴

- d. Consider specific diagnostics for (HAC), acromegaly, and thyroid disease. Hyperadrenocorticism can cause insulin resistance in dogs and cats, and cause persistent PU/PD in diabetic dogs who otherwise appear to be well regulated. Both species may have alopecia and dermatologic disease, and fragile skin is a hallmark feature of HAC in cats.

Note that ALP is often increased in diabetic dogs, so increased ALP alone does not suggest HAC. Generally, endocrine testing for HAC should not be performed before diabetic regulation has been attempted for approximately 1 mo, because unregulated diabetes can lead to false-positive results in dogs who do not have HAC. ACTH stimulation tests and low-dose dexamethasone suppression tests can be used for diagnosis in dogs. The ACTH stimulation test is more specific (fewer false positives) but less sensitive (more false negatives) than the low-dose dexamethasone suppression test.⁴⁵ The low-dose dexamethasone suppression test is preferred in cats, but requires a higher dose of dexamethasone than that used in dogs (0.1 mg/kg).⁴⁶

Acromegaly is more common in diabetic cats than once believed, and may occur in up to 32% of diabetic cats.^{47,48} Acromegalic cats are sometimes on high insulin doses, reported to be as high as 35 U q 12 hr.⁴⁷ They may lose weight initially, but gain weight (or maintain weight) later in the course of the disease despite inadequate regulation and severe PU/PD/PP. Owners may report recent onset of snoring. Physical examination may reveal a large head with prognathia inferior, cranial organomegaly, or stertorous respiration. Insulin-like growth factor 1 (IGF-1) concentration is most often used for acromegaly screening in the United States. Consider testing once a cat has had approximately 6 wk of exogenous insulin.

Hyperthyroidism and hypothyroidism can both cause significant insulin resistance.

Diagnosis of hyperthyroidism in cats is often possible with a total T4 at initial diagnosis of diabetes, but diagnosis of hypothyroidism in diabetic dogs can be challenging. Many euthyroid diabetic dogs will have a decreased total T4 concentration due to euthyroid sick syndrome, so a decreased total T4 alone cannot confirm hypothyroidism. In most cases, testing for hypothyroidism should be delayed for a few weeks after the diagnosis of diabetes to decrease the effects of euthyroid sick syndrome. If there is clinical suspicion of hypothyroidism in a diabetic patient, a total T4, free T4 by equilibrium dialysis, and TSH (thyroid-stimulating hormone) should be evaluated concurrently.⁴⁹

- e. If the cause of insulin resistance is identified, the clinician should focus on resolving and treating that cause, then return to regulating the DM.
6. If the patient has never been regulated and has only been administered one type of insulin thus far, consider switching insulin type. This may be attempted prior to item 5c, based on clinician preference.
7. Finally, consult with a specialist if the patient cannot be regulated.