**THE PET HEALTH LIBRARY**

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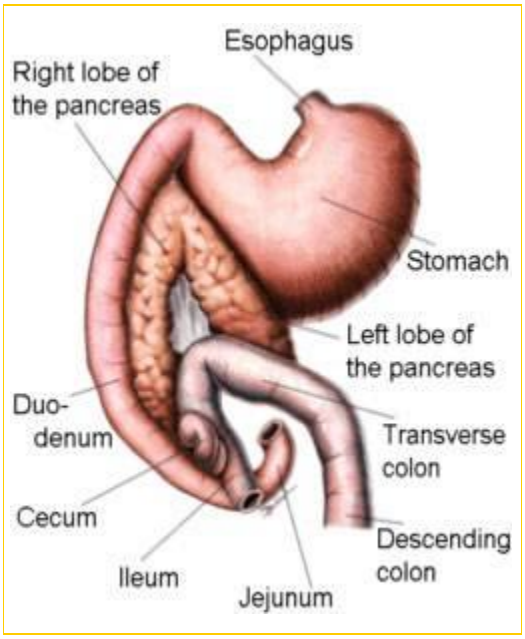
# Insulinoma

The pancreas is a small light pink glandular organ nestled under the stomach and alongside the duodenum (upper small intestine). The endocrine pancreas is the part of the pancreas that secretes hormones involved in blood sugar regulation, such as insulin and glucagon. The exocrine pancreas produces enzymes we use to digest our food. These two parts of the pancreas are not in separate areas but instead these two different types of pancreatic tissues are all mixed together throughout the entire pancreas.




The insulin-secreting cells are called beta cells and are bunched in groups called Islets of Langerhans, which are scattered throughout the pancreatic tissue. In some unfortunate individuals, the beta cells become tumorous and while the tumor itself can be small, its effects are large because it produces large amounts of insulin. Insulin-secreting tumors are called insulinomas.

**What Happens to the Patient?**

Insulin is a hormone secreted to store sugar. Normally it is secreted in response to the carbohydrates in a meal; it allows the extra sugar to be removed from the bloodstream and stored as starch and fat, thus keeping the blood sugar level within the normal range. The function of normal islets of Langerhans is tightly regulated by the body but if there is an insulin-secreting tumor, the tumor is not subject to this regulation. Insulin secretion runs wild in this situation and low blood sugar (hypoglycemia) becomes a problem.

The hypoglycemia in this situation is typically severe, most commonly resulting in seizures. Other clinical features include: listlessness, twitching, trembling, apparently drunken or wobbly gait, and reduced mental awareness.

**Testing**

One of the first steps in evaluating any sick patient is a basic blood panel. Patients presented during a seizure are commonly screened for low blood sugar. The low blood sugar is typically recognized early in the diagnostic process, although if the blood sugar has had time to recover (if the patient has eaten or depending what emergency medications have been given), the situation may be ambiguous. Sometimes the patient must return to the veterinarian in a fasted state to get an accurate blood sugar assessment.

Assuming hypoglycemia is confirmed, the history and basic physical examination generally rule out some obvious potential causes. Some examples of fairly obvious potential causes of hypoglycemia include:

- Toy breed puppy hypoglycemia
- Diabetic patient possibly overdosing on insulin

- Pregnant female in labor having a difficult delivery
- Extreme exercise exertion, as in hunting dog hypoglycemia
- Starvation
- Overwhelming bacterial infection

Other not so obvious causes of hypoglycemia include liver disease, insulinoma, and hypoadrenocorticism (Addison's Disease). The testing that is commonly needed beyond the basic panel would include: a resting cortisol level, as a normal level largely rules out hypoadrenocorticism; an ACTH stimulation test, which is the definitive test for ruling out hypoadrenocorticism; an insulin level, which must be measured at the time the patient is hypoglycemic; and possibly a bile acids liver function test if it is not clear if liver disease has been adequately ruled out by earlier findings.

**What is Hypoadrenocorticism?**

Hypoadrenocorticism is a deficiency in the production of cortisol, more commonly known as cortisone. Cortisol is produced by the adrenal gland and one of its functions is to raise blood sugar in anticipation of a fight or flight response. In simpler terms, if the body is anticipating exercise, such as fighting for one's life or escaping a predator, blood sugar must be readily available for the muscles to burn. Cortisol is secreted to make that happen. (It also makes other metabolic adaptations happen as well but that is a story for another time.) Poor cortisol secretion can create episodes of hypoglycemia and since hypoadrenocorticism is easily treated once identified, it is important to rule it out in a hypoglycemic patient.

For more information on this condition, click here.

**The Insulin Level**

To be meaningful in testing for insulinoma, the insulin level must be drawn when the patient's blood sugar level is less than 60 mg/dl because the insulin level is interpreted in light of the blood sugar level. In other words, an insulin level might be within the normal range for a normal patient but might be inappropriately high in a hypoglycemic patient.

**Ultrasound**

Once you are confident that excessive insulin is being produced, the next step is ultrasound. There are two reasons for this:

- To locate the tumor if you are planning surgery
- To obtain prognosis even if you are not planning surgery

Another reason to image the abdomen with ultrasound includes searching for tumors other than insulinoma that might cause hypoglycemia. Most notoriously, the hepatoma (also known as the hepatocellular carcinoma) and smooth muscle tumors (both benign and malignant and usually found in the spleen) also cause hypoglycemia. Other tumors potentially can consume enough blood sugar to create hypoglycemia and ultrasound is an excellent way to find any.

Unfortunately, most insulinomas in dogs and cats are malignant. This is bad news but the good news is that regardless of this fact, surgery is still helpful as the bulk of the tumor (if not all of it) can be removed. Because insulinomas can be small - sometimes too small to see during surgical exploration - ultrasound is helpful to evaluate the texture of the pancreatic tissue. In this way, even very small lesions can be identified. Furthermore, an ultrasound can evaluate tumor spread to other organs, thus helping to determine if it is worth pursuing surgery or if perhaps it is too late for this option and medication should be pursued instead.

With ultrasound, lesions in the pancreas as small as 7 mm in diameter can be identified and, in one study, ultrasound was able to locate the pancreatic tumor in 75% of cases.

*An ultrasound image of the pancreas.*

**Treatment: Surgery**

Surgical removal of the tumor is not a simple surgery. Manipulating the tumor can cause insulin surges that result in hypoglycemia during surgery; blood sugar levels must be tightly monitored both during and after surgery. IV fluids containing sugar are a must. Furthermore, manipulation of the pancreas can create inflammation (pancreatitis), which is associated with pain and nausea. Some patients have been exposed to excess insulin for so long that their normal beta cells require a prolonged period to recover, and during this time the patient may require insulin injections just as a diabetic patient would.

This all sounds like a lot of risk for the treatment of a tumor with a 90% chance of malignancy. However, 50% of dogs without evidence of tumor spread at the time of surgery have had normal blood sugars for a year after partial removal of the pancreas. This is an excellent statistic and is often well worth the surgery. Young dogs tend to have a poorer prognosis. Evidence of lymph node spread has not affected prognosis but tumor spread in the liver decreases survival time. In one study, dogs receiving partial pancreas removal had a medial remission time of 496 days and the dogs that went on to receive medical management after signs recurred had a median survival of 1316 days. Dogs with medical management alone had a median survival of 196 days.

**Treatment: Medications that Manage Hypoglycemia**

Many months of symptom control can be achieved with diet, steroids (hormones related to cortisol, which raises blood sugar), and diazoxide. This is helpful for patients where surgery is not considered an option or for whom there is non-resectable tumor spread. Frequent small meals can be used to keep blood sugar in a reasonable range. If hypoglycemic disorientation occurs, it can generally be stopped with sugar supplements such as Nutrical® or Karo® syrup.

If or when frequent feedings prove inadequate, corticosteroids such as prednisoneor dexamethasonecan be used to assist in raising blood sugar. Ideally dosing is kept as small as necessary so as to avoid side effects such as excessive water consumption, urination and immune suppression.

Diazoxide is a medication that promotes blood sugar elevation through a number of mechanisms including suppression of insulin secretions. Upset stomach is the most common side effect of this medication and giving the medication with food can help ease the upset. It also causes sodium retention and should not be used in heart failurepatients. Concurrent liver disease may exacerbate side effects.

Other medications such as somatostatin analogs have not been as reliable in achieving results.

**Treatment: Medications to Combat the Cancer**

Since insulinoma is a cancer, drugs of chemotherapy can be useful in suppressing tumor spread. You would not consider such aggressive therapy, though, unless a biopsy has confirmed the tumor.

*Streptozocin*
This drug targets beta cells of the pancreas specifically. To avoid inducing kidney failure, it must be given with aggressive intravenous fluids, thus hospitalization is required for its periodic use.

Other medications that have been used or are emerging include toceranib, doxorubicin, and alloxan.

Veterinary oncologists have the most up to date recommendations on chemotherapy. Ask your veterinarian if referral to an oncologist is best for you and your pet.

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