

# Insulin Resistance in Diabetic Patients: Causes and Management*

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**ABSTRACT:** Insulin resistance can occur secondary to many diseases in dogs and cats. The most common causes of insulin resistance in dogs are hyperadrenocorticism, bacterial infections, hypothyroidism, and diestrus. In cats, the most common causes are acromegaly; hyperadrenocorticism; renal, hepatic, or cardiac insufficiency; bacterial infections; hyperthyroidism; and use of diabetogenic drugs. Common mechanisms of insulin resistance include decreased insulin-receptor concentration, decreased receptor affinity, and defects in the postreceptor pathways. Management of insulin resistance includes a thorough search for an underlying cause and dietary changes.

Insulin resistance is a condition in which a normal amount of insulin causes a subnormal response in blood glucose levels.[1,2] Insulin resistance progresses to overt diabetes mellitus (DM) when the existing insulin-producing beta cells cannot compensate for the insulin resistance, thus allowing hyperglycemia to occur.[1] Insulin resistance should be suspected in a dog or cat when more than 2.2 U/kg per injection of insulin is required to maintain adequate glycemic control.[1,3] In addition, insulin resistance in dogs and cats should be considered in the presence of persistent, marked hyperglycemia throughout the day, despite insulin doses of more than 1.5 U/kg per injection.[2,3] The differential diagnosis of insulin resistance is quite extensive, and some of the possible diseases cause previously subclinical diabetic patients to become clinically diabetic, whereas other possible diseases exacerbate preexisting DM.[2] In dogs, the most common causes of insulin resistance are hyperadrenocorticism, bacterial infections, hypothyroidism, and diestrus.[2] In cats, the most common causes are acromegaly; hyperadrenocorticism; renal, hepatic, or cardiac insufficiency; bacterial infections; hyperthyroidism; and use of diabetogenic drugs.[2]

*A companion article on mechanisms and classifications starts on page 262.

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## CAUSES

### Hyperadrenocorticism

Hypercortisolism is an excess of exogenous or endogenous systemic glucocorticoids. In normal animals, insulin suppresses hepatic production of glucose and increases peripheral tissue glucose use.[3] Glucocorticoids cause insulin resistance partly by decreasing glucose uptake by peripheral tissues.[1,3,4] Glucocorticoids may decrease periph-

eral tissue use of glucose as a result of decreased binding of insulin to the receptor or through an impaired postreceptor intracellular response to insulin because of reduction in the number or efficacy of glucose transporters.[2,3,5] In addition, glucocorticoids cause increased hepatic gluconeogenesis, glycogenolysis, and ketogenesis.[1–4]

### Dogs

Hyperadrenocorticism is the most common cause of insulin resistance in dogs.[2] Approximately 45% of dogs with hyperadrenocorticism are hyperglycemic, and approximately 8% to 10% have overt DM.[3,4,6] Most dogs with hyperadrenocorticism do not become diabetic because of increased beta-cell insulin secretion and subsequent compensation for mild insulin resistance.[3] However, in conditions of low insulin reserve, or when there is pronounced insulin resistance, significant hyperglycemia and possible ketoacidosis can occur.[3]

Identification of concurrent hyperadrenocorticism and DM can be very challenging for practitioners. In these cases, it is suspected that hyperadrenocorticism develops first and unmasks subclinical DM. However, DM is usually diagnosed first. Glycemic control may be adequate in the early stages but becomes more difficult as hyperadrenocorticism progresses over weeks to months.[2] At the initial diagnosis of DM, the clinical signs that distinguish hyperadrenocorticism from DM, such as endocrine alopecia, thin skin, and abdominal enlargement, are not usually apparent. However, these signs often become evident weeks to months later as hyperadrenocorticism continues to progress.[2] Early indicators of concurrent hyperadrenocorticism in diabetic dogs include an alkaline phosphatase concentration greater than 500 IU/L, a finding of adrenomegaly during an ultrasonographic examination, and a urine-specific gravity less than 1.02 (especially in the presence of glycosuria).[2] Diagnosis of hyperadrenocorticism in a dog with DM can be challenging because of the stimulating effect of diabetic ketoacidosis on adrenocortical function and subsequent function tests. Recommended adrenocortical function tests include the adrenocorticotropic hormone stimulation test and/or low-dose dexamethasone suppression test.[2] Repeated testing may be required once the patient's diabetic regulation has been stabilized.[2] Dogs with concurrent DM and hyperadrenocorticism require a reduced insulin dose during treatment of hyperadrenocorticism with mitotane therapy because of the eventual increase in insulin sensitivity.[4,6]

### Cats

Naturally occurring hyperadrenocorticism is uncommon in cats and, as in dogs, is usually a pituitary-dependent disease process.[2] Insulin resistance in cats secondary to hyperadrenocorticism can be marked, as shown by the fact that approximately 80% of cats with hyperadrenocorticism develop DM.[2,3]

The diagnosis of hyperadrenocorticism in cats is made with abdominal ultrasonography, a dexamethasone suppression test, and sometimes an adrenocorticotropic hormone stimulation test.[2] The current recommended treatment is bilateral adrenalectomy.[2] However, bilateral adrenalectomy in a debilitated cat carries a guarded prognosis and is often complicated by perioperative management of Addison's disease. Perisurgical management includes reduction of the insulin dose by 50% during times of fasting, close monitoring of blood glucose concentrations, and dextrose supplementation during periods of low blood glucose concentrations. In addition, physiologic doses of glucocorticoids and mineralocorticoids are required peri- and postoperatively.[2] Clinical signs and physical examination abnormalities of hyperadrenocorticism typically resolve 2 to 4 months after adrenalectomy.[2] In addition, in a study[7] of cats with naturally occurring hyperadrenocorticism, four of six cats with DM secondary to hyperadrenocorticism reverted to non–insulin-dependent DM 2 to 8 months after surgery. Recent literature[8] describes the use of trilostane in cats with pituitary-dependent hyperadrenocorticism. However, cats that were diabetic remained so despite reduction in the clinical signs associated with hyperadrenocorticism.[8] If this is shown to be consistently effective in controlling hyperadrenocorticism in a larger population of cats, it may replace surgery as the treatment of choice for feline hyperadrenocorticism.

*In animals with concurrent hyperadrenocorticism and diabetes mellitus, hyperadrenocorticism develops first, but diabetes mellitus is usually identified first.*

### Progestogen

Insulin resistance secondary to diestrus should always be considered in any newly diagnosed or poorly controlled diabetic, intact female dog regardless of the history concerning recent estrus activity.[2] Insulin resistance during diestrus can be directly due to the increased blood progesterone concentration and indirectly due to stimulation of growth hormone release.[1,2] Exogenous administration of progestogen (e.g., medroxyprogesterone acetate, megestrol acetate) can also stimulate the release of growth hormone.[1] Progesterone causes insulin resistance by reducing insulin binding to receptors and glucose transport within tissues.[2] Growth hormone contributes to insulin resistance through downregulation of insulin receptors and inhibition of postreceptor glucose transport pathways. It is suspected that inhibition of glucose transport occurs from effects on the expression of glucose transporter genes.[1,2,9]

As progesterone secretion from the corpora lutea increases, so does the plasma growth hormone concentration from the dog's mammary tissue. Insulin resistance can quickly become marked, and life-threatening diabetic ketoacidosis can develop.[2] Serum progesterone concentrations can be tested to confirm that a bitch is in diestrus.[2] Bitches with transient DM secondary to diestrus have a high likelihood of developing permanent insulin-dependent DM during the next estrus phase. It is important to note that attempts to closely regulate a dog's diabetic condition while it is under the influence of hyperprogesteronism can be ineffective and involve extensive time and expense. Therefore, the recommended treatment for animals with DM secondary to diestrus is ovariohysterectomy. Carbohydrate intolerance sometimes resolves once growth hormone levels return to normal, whether through ovariohysterectomy, spontaneous regression of the corpus lutea, or withdrawal of progestogen therapy.[1,2] Responsiveness to insulin can begin to improve within hours after ovariohysterectomy and is often significantly better within 7 days.[2]

In cats, progesterone does not stimulate secretion of growth hormone.[2] However, exogenous administration of progestogens or progesterone-secreting adrenocortical tumors can cause insulin resistance and the development of DM.[2] It has been suggested that the intrinsic glucocorticoid activity of progestogens contributes to the development of DM in affected cats but that many of these cats had preexisting subclinical DM before treatment.[1,2]

### Acromegaly

Acromegaly is caused by chronic hypersecretion of growth hormone and is characterized by overgrowth of connective tissue, bone, and viscera.[2,3] Acromegaly in dogs is usually caused by exogenous or endogenous progestogens that lead to growth hormone overproduction from foci of hyperplastic ductular epithelium in mammary tissue, thus restricting the syndrome to females.[1–3] As noted previously, progestogens and the subsequently released growth hormone in dogs can lead to insulin resistance. Common clinical signs include an increase in body size, thickened skin, and inspiratory stridor secondary to an increase in laryngeal soft tissue.[2] Not all dogs with acromegaly become diabetic, and DM may be permanent even after resolution of the acromegalic state.

Acromegaly in cats is secondary to a growth hormone–secreting tumor in the pituitary.[1,3] In contrast to dogs, more than 90% of acromegalic cats are male.[3] Acromegaly occurs in older cats, and the associated conformation alterations, including an increase in body size, prognathia inferior, and weight gain despite poorly regulated DM, have an insidious onset and are often not noticed by owners.[2] Because of this insidious onset, severe insulin resistance and clinical DM are usually the earliest and most recognized clinical manifestations of acromegaly.[3] Insulin resistance can be quite severe, sometimes requiring more than 30 U of insulin twice daily. Another common cause of severe insulin resistance in cats is hyperadrenocorticism.[2] However, acromegaly and hyperadrenocorticism can often be differentiated clinically because, unlike acromegaly, hyperadrenocorticism is a debilitating disease resulting in progressive weight loss, cachexia, dermal and epidermal atrophy, and thin and very fragile skin.[2]

*Infection causes the release of diabetogenic hormones, such as glucagon.*

Definitive diagnosis of acromegaly in cats requires documentation of an increased baseline serum growth hormone concentration or detection of increased levels of insulin-like growth factor I.[2] Growth hormone assays are not readily available in the United States, but serum

insulin-like growth factor can be measured. However, diagnosis is often based on identification of conformational changes in a cat with insulin-resistant DM, persistent increase in body weight despite DM, or evidence of a pituitary mass.[2] Treatment generally consists of radiation therapy and rarely includes surgery. The diabetic state may persist despite treatment of acromegaly.[2]

### Hypothyroidism

Hypothyroidism is a common endocrine disorder in dogs and can occur concurrently with DM. The mechanisms of carbohydrate intolerance in humans with hypothyroidism are controversial but appear to be multifactorial.[2,3] Most research supports the existence of a postreceptor defect in the insulin-mediated transport and metabolism of glucose.[2,3] However, the effect on insulin secretion and insulin receptors is not as clear.[2] Research has shown differing results, such as increased and decreased insulin secretion or increased, decreased, or unaffected insulin-receptor concentration and binding affinity.[2] In addition, obesity and hyperlipidemia are often associated with hypothyroidism and may also affect insulin sensitivity.[2]

A true hypothyroid canine patient can be distinguished from a sick euthyroid patient by determining serum levels of total $T_4$, free $T_4$, and thyroid-stimulating hormone. A sick euthyroid patient often has a low total $T_4$ level and possibly low free $T_4$ level. However, the free $T_4$ tends to be decreased to a lesser extent than the total $T_4$. In addition, the thyroid-stimulating hormone level is typically normal in sick euthyroid patients.[2] Insulin resistance appears to be reversible with treatment of hypothyroidism.[2,3] The insulin requirements of hypothyroid and diabetic dogs reportedly decrease by 50% to 60% within 2 months after initiating thyroxine treatment.[2,10] Therefore, if supplementation is started, concurrent reduction in insulin dosage requirements should be anticipated, and glycemic control should be monitored weekly for the first month of treatment.[2]

### Hyperthyroidism

Insulin resistance has been noted to occur with feline hyperthyroidism. The exact mechanism is unknown. Suggested mechanisms in humans include decreased insulin synthesis and secretion, impaired insulin-receptor binding affinity, postreceptor defects, a disproportionate increase in nonfunctional proinsulin by the beta cells, and increased insulin clearance.[2,11] Thyroid hormone administration in normal cats has been shown to result in decreased glucose clearance.[12] Similar alterations have been reported in cats with naturally occurring hyperthyroidism. Cats have been shown to have a persistent decrease in glucose clearance 6 months after treatment with radioiodine.[13] Therefore, the clinical effect of treating hyperthyroidism with diabetic regulation is unknown but anecdotally appears to decrease the daily insulin requirements in diabetic cats.[2,3]

### Concurrent Illness

Concurrent illness, including infection, increases secretion of counterregulatory hormones such as cortisol, glucagon, catecholamines, and growth hormone.[3] Glucagon has an antagonistic action of insulin in that it increases blood glucose through stimulation of hepatic gluconeogenesis and glycogenolysis.[1,9,14] Glucagon also decreases insulin-receptor binding affinity.[1,14] Hyperglucagonemia has been documented in diabetic humans with insulin resistance associated with bacterial infections, renal failure, metabolic acidosis, and glucagon-secreting tumors.[1]

*The kidneys remove approximately 50% of circulating insulin.*

#### *Infection*

The increased risk of infection in diabetic patients is well documented in human and veterinary medicine.[2] Increased infection risk in humans is believed to be due to impaired resistance secondary to microangiopathy, which causes a decreased blood supply and therefore diminished delivery of oxygen, phagocytes, and antibodies to infection sites. In addition, multiple impairments of the immune system have been proposed, such as decreased humoral immunity, decreased antibody production, abnormal neutrophil chemotaxis, defects in phagocytosis and intracellular killing of organisms, and impaired cell-mediated immunity.[2]

Infections induce secretion of insulin-antagonizing hormones such as glucagon, cortisol, and epinephrine. Sustained hyperglucagonemia and insulin resistance have been documented in diabetic humans with concur-

rent infections.[2] The role of glucagon in diabetic dogs and cats has not been documented, but clinical improvement of diabetic regulation has been noted with resolution of infection. In addition, increased glucagon levels have been documented in normal dogs that have been experimentally infected.[15,16]

### *Chronic Pancreatitis*

Chronic pancreatitis is likely underdiagnosed in diabetic patients because of difficulty in confirming a diagnosis. Histologic evidence of chronic pancreatitis has been identified at necropsy in approximately 35% of diabetic dogs and 50% of diabetic cats.[2,17,18] Insulin resistance is likely secondary to the release of diabetogenic hormones (e.g., glucagon, cortisol), which can exacerbate any beta-cell depletion as a result of pancreatitis. Common clinical signs include a poor appetite, lethargy, and depression. Frequently,

*Identification and correction of an underlying cause of insulin resistance can usually improve glycemic control.*

affected patients have blood glucose concentrations greater than 300 mg/dl with fluctuating insulin requirements.[2] Concurrent management of chronic pancreatitis and DM can be very difficult.[2] Unfortunately, treatment is primarily supportive and many animals are euthanized because of a poor quality of life.[2]

### *Pheochromocytoma and Other Neoplasia*

In humans, pheochromocytomas can be associated with mild carbohydrate intolerance.[2] The catecholamines released have both direct and indirect effects that cause insulin resistance. Epinephrine increases hepatic glycogenolysis and hepatic and renal gluconeogenesis.[2] It mobilizes muscle glycogen and stimulates lipolysis, providing muscle tissue with an alternative fuel source other than glucose. Epinephrine also mobilizes gluconeogenic precursors, such as lactate, alanine, and glycerol, which inhibit the use of glucose by insulin-sensitive tissues, such as skeletal muscle.[2] In humans, mild carbohydrate intolerance does not usually require therapy because of the episodic nature of catecholamine release. In addition, most of the insulin-antagonistic effects are secondary to epinephrine rather than norepinephrine, and most human pheochromocytomas primarily secrete norepinephrine.[2] Pheochromocytomas do not typically cause severe insulin resistance in small animals, probably for similar reasons.[2]

Other tumors have been associated with insulin resistance in small animals. The most common are lymphoma and mast cell tumors.[2] The mechanism is unknown but likely relates to diabetogenic hormone secretion, hepatic function, lipid metabolism, and/or tissue responsiveness to insulin.[2]

## Hyperlipidemia

In diabetic patients, relative insulin deficiency causes lipolysis and the release of free fatty acids and glycerol. These fatty acids are absorbed by the

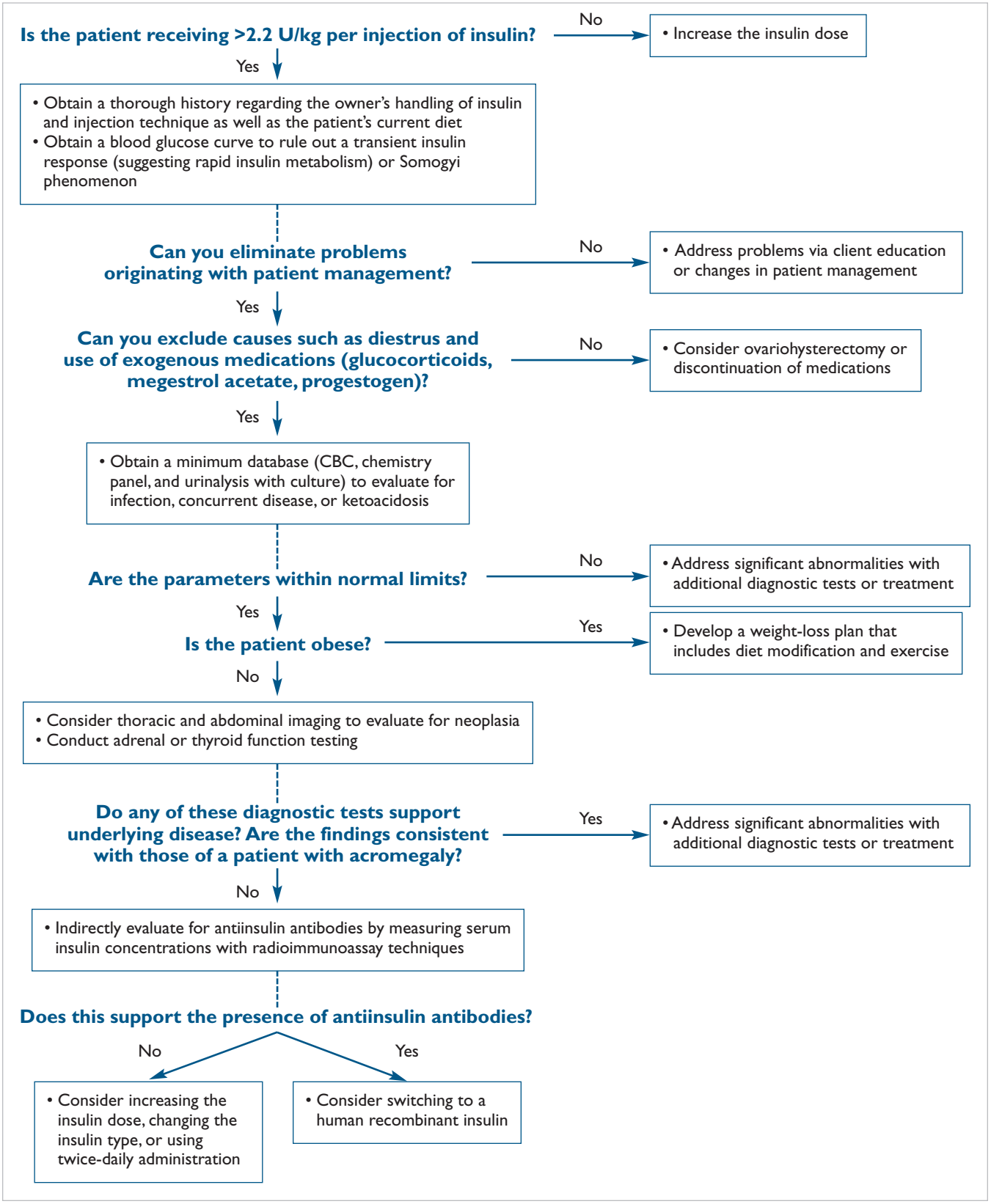


**Figure 1.** **Diagnostic approach to dogs and cats with suspected insulin resistance.**

liver and converted into phospholipids, cholesterol, and triglycerides, which are released into the blood within lipoproteins.[14] Fasting hyperlipidemia is common in diabetic dogs and is usually due to hypertriglyceridemia.[2] Hypertriglyceridemia can lead to insulin resistance by reducing the insulin-receptor binding affinity, promoting downregulation of insulin receptors, and causing a postreceptor defect in insulin action.[2,3] In addition, hyperlipidemia causes increased hepatic glucose secretion, which further compounds carbohydrate intolerance.[2]

Differentiating hyperlipidemia due to poorly controlled DM or independent of DM can be difficult and may require reevaluation when DM is controlled.[2] Most dogs with hyperlipidemia do not develop DM. However, when hyperlipidemia is marked in animals that are also diabetic, insulin resistance can occur.[3] Hyperlipidemia combined with insulin resistance is typically associated with diabetic dogs that have an additional reason for hyperlipidemia, such as hypothyroidism, hyperadrenocorticism, or idiopathic hypertriglyceridemia.[2] The diagnosis of hypertriglyceridemia requires a 24-hour fast. In general, serum triglyceride concentrations are less than 500 mg/dl in poorly controlled diabetics without concurrent disease. Fasting serum triglyceride concentrations greater than 800 mg/dl should raise suspicion for a concurrent disorder causing hypertriglyceridemia.[2] Treatment generally consists of a low-fat diet with less than 20% fat on a metabolic energy basis and omega-3 fatty acid supplementation. Drug therapy, such as niacin or gemfibrozil, can be considered, but because of potential side effects, it should be instituted only if the serum triglyceride concentration is greater than 500 mg/dl.[2,19]

## Obesity

Research in humans and cats has shown a relationship among obesity-induced insulin resistance, carbohydrate intolerance, and the development of non–insulin-dependent DM.[3] The pathogenesis in humans and cats may be similar.[3] Carbohydrate intolerance and hyperinsulinemia have been documented in obese dogs and cats.[1] Obese, diabetic dogs and cats generally remain responsive to insulin treatment, unlike humans, who tend to show mild insulin resistance with obesity.[3] Insulin resistance secondary to obesity is thought to be due to downregulation of insulin receptors, reduced insulin-receptor binding affinity, and postreceptor defects in intracellular glucose metabolism.[1,2] Worsening carbohydrate intolerance suppresses beta-cell insulin secretion through a phenomenon called *glucose toxicity*. This occurs because chronic hyperglycemia impairs insulin secretion by beta cells, promotes downregulation of glucose transport systems, and causes a defect in posttransport insulin action, thereby inducing peripheral insulin resistance.[21] The effects of obesity and glucose toxicity on insulin resistance are reversible, and insulin sensitivity improves with correction of obesity and hyperglycemia.[2,3,20]

## Renal Insufficiency

Abnormal renal function can occur secondary to DM or may be an independent problem in a patient.[2] Humans with concurrent DM and renal disease are at increased risk for hypoglycemia due to decreased renal clearance

of insulin and decreased renal gluconeogenesis.[2] The kidneys remove approximately 50% of insulin from circulation, and renal glucose production can account for 5% to 40% of blood glucose concentrations.[2,21] Problems noted in dogs and cats with concurrent DM and renal insufficiency include prolonged duration of insulin effect and insulin resistance, thereby causing hypoglycemia and hyperglycemia, respectively.[2] There is also evidence pointing to decreased tissue insulin sensitivity.[2] The combination of these effects can result in DM that is very difficult to control. Furthermore, renal disease can make patient monitoring more difficult because polyuria and polydipsia cannot be used as a reliable indicator of glycemic control.[2]

### Genetic Syndromes of Severe Insulin Resistance

Two genetic syndromes in humans, designated as types A and B, are associated with abnormalities in the insulin receptor and can cause severe insulin resistance.[2,9] Type A is an insulin-receptor mutation involving a decreased number of insulin receptors or target-cell defects in insulin action and is characterized by markedly elevated endogenous insulin levels.[2] Type B involves circulating autoantibodies to the insulin receptor.[2] Most humans with type B syndrome have additional clinical or laboratory evidence of autoimmune disease.[9] Similar genetic syndromes have not been identified in dogs or cats.[2]

## MANAGEMENT

Managing insulin resistance requires a thorough search for an underlying cause so that correction can be attempted. The diagnostic approach to a patient with insulin resistance can be overwhelming. However, possible underlying causes can be systematically eliminated (Figure 1). Identification of possible underlying causes of insulin resistance must first include a detailed history and physical examination. Thorough questioning of the owner regarding insulin handling and administration is essential. Additional diagnostics may be required to investigate possible underlying diseases. Correcting the predisposing factors can often lead to improved diabetic control or resolution of insulin resistance.[3]

Diet modification can often improve glycemic control. Dietary therapy is aimed at improving overall health and weight loss as well as restoring optimum blood glucose and serum cholesterol, triglyceride, and lipoprotein concentrations.[20] Increasing dietary fiber has two advantages: enhanced weight reduction and improved glycemic regulation through direct actions that minimize postprandial fluctuations in blood glucose and enhance control of hyperglycemia.[20] Cats have low levels of hepatic enzymes that phosphorylate glucose and convert it to glycogen.[22] This suggests that cats primarily gain their energy from gluconeogenic amino acids and fat rather than carbohydrates.[2] Recent work[23] indicates that low-carbohydrate, high-protein diets improve glycemic control in cats, and this is the current popular recommendation for that species.

Chromium supplementation has been advocated as a treatment of insulin resistance. Chromium is an essential cofactor for insulin function and is ubiquitous in the environment. Chromium is believed to increase insulin sensitivity through a postreceptor mechanism.[2] The evidence supporting a clinical benefit from chromium supplementation is controversial in human and veterinary medicine. The results of chromium supplementation in veterinary medicine have ranged from no effect to small changes in glucose tolerance, of which the clinical significance is not clear.[2,24,25] Chromium supplementation is not currently recommended in most cases of insulin resistance.

If the cause of insulin resistance cannot be identified, mild insulin resistance can often be overcome by increasing the insulin dose.[2] Glycemic control is sometimes improved by administering insulin twice daily versus once daily.[3] Increases in the insulin dose or frequency are more likely to overcome predisposing factors that cause decreases in insulin sensitivity.

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**1. In dogs with concurrent hyperadrenocorticism and DM,**
a. hyperadrenocorticism usually develops first, but DM is usually identified first.
b. the alkaline phosphatase concentration is usually within the normal range.
c. there are usually signs of both diseases at presentation.
d. DM usually develops first, but hyperadrenocorticism is usually identified first.

**2. Hyperadrenocorticism in cats**
a. is usually secondary to an adrenal tumor.
b. is usually a benign disease in which cats show very few clinical signs.
c. causes severe insulin resistance as well as DM in 80% of cats.
d. always leads to permanent insulin dependence, even with surgical correction.

**3. Insulin resistance secondary to progestogens in dogs**

a. occurs only from endogenous progestogens.
b. should always be considered in any intact female.
c. is usually mild and subclinical.
d. is always resolved by removal of progestogens.

**4. Acromegaly in cats**

a. causes severe insulin resistance, and DM is usually the first clinical manifestation recognized.
b. is easy to definitively diagnose.
c. is a debilitating disease with obvious clinical signs.
d. is due to growth hormone–secreting cells in the mammary glands.

**5. Which statement regarding causes of insulin resistance is true?**

a. Infections are uncommon in humans and animals with DM.
b. Chronic pancreatitis is easily managed in dogs and cats with concurrent DM.
c. Pheochromocytomas are usually associated with severe insulin resistance.
d. Glucagon and other diabetogenic hormones are a cause of insulin resistance with concurrent illnesses.

**6. Hyperlipidemia and insulin resistance**

a. are usually due to hypercholesterolemia in dogs.
b. typically have a direct cause-and-effect relationship.
c. are usually associated with other diseases in dogs, such as hypothyroidism, hyperadrenocorticism, or idiopathic hypertriglyceridemia.
d. almost always require drug therapy.

**7. Which statement regarding hypothyroidism in dogs is correct?**

a. Hypothyroidism in dogs usually causes insulin resistance through the release of diabetogenic hormones.
b. Treatment of hypothyroidism in dogs can decrease insulin requirements by 50% to 60%.
c. Hypothyroidism in dogs can usually be diagnosed in a diabetic dog using only a total $T_4$ level.
d. Hypothyroidism in dogs causes irreversible insulin resistance.

**8. Renal insufficiency**

a. can lead to insulin resistance due to decreased insulin production.
b. usually causes a predictable increase in insulin requirements.
c. does not affect glucose production.
d. can make monitoring difficult because of the presence of polyuria and polydipsia.

**9. Identifying the underlying cause of insulin resistance does *not***

a. always result in resolution of insulin resistance.
b. require a thorough history.
c. involve careful questioning of the owner regarding insulin handling and administration.
d. require diagnostic testing, such as blood work.

**10. The goals of dietary therapy do *not* generally include**

a. improving overall health and weight loss.
b. minimizing postprandial blood glucose fluctuations.
c. providing chromium supplementation.
d. optimizing serum lipid concentrations.

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