

# Hypothyroid-mediated insulin resistance in the dog



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#### 1. INTRODUCTION

Hypothyroidism and diabetes mellitus are two common endocrine disorders in the dog but they do not usually appear concurrently. Hypothyoiridism has been suggested to be a cause of insulin resistance through different mechanisms and can lead to the development of diabetes mellitus. Besides, if hypothyroidism emerges in a diabetic dog, glycemic control and insulin dosage become hard to manage. Therefore, knowledge of the role of hypothyroidism on glucose homeostasis may be crutial to success in glycemic control in diabetic dogs and to avoid later development of diabetes mellitus in a hypothyroid dog.

- ✓ Understand the mechanisms of how hypothyroidism can affect insulin sensitivity.
- ✓ Be aware of glucose tolerance alterations in hypothyroid dogs.
- ✓ How to diagnose hypothyroidism in a diabetic dog showing insulin resistance, and to early detect diabetes mellitus emerging in a hypothyroid dog.
- ✓ How to treat insulin resistance mediated by hypothyroidism.

Decreased expression of triiodothyronin-responsive region in glucose transporter protein 4 (GLUT4)

Decreased somatostatin secretion (GH inhibitory hormone)

> Abscence of a positive thyroid hormone responsive element (TRE) or presence of a negative TRE in the GH gene

Transdifferentiation of somatotrophs to "thyrosomatotrophs" and secrete **GH** and **TSH** 

Drecreased **GLUT4** expression

> Growth hormone (GH) excess

Obesity

Reduced endotheliumdependent vasodilation

Marked impaired insulin sensitivity in hypothyroid dogs is mediated by different factors, such as decreased glucose transporter protein 4, excess in circulating growth hormone (GH), obesity and reduced endothelium-dependent vasodilation.

> Resistance to increased leptin and adiponectin (adipocytokines that help overcome insulin resistance)

> > Interference of insulin signalling in muscle

Accumulation of fat in the adipocyte → downregulation of GLUT4

Impairment of insulin-mediated suppression of glucose production in the liver

> Marked impairment of vasodilatory response to insulin

## 5. DIAGNOSTIC

### Hypothyroidism in diabetic dogs

- Insulin > 1.5 U/kg
- Blood glucose concentration > 300 mg/dl
- Erratic glycemia control and changing insulin requirements
- Historical, physical and clinicopathologic findings (may also be Early detection of diabetes mellitus: found in euthyroid dogs with poorly controlled diabetes)
- TSH or TRH stimulation test (more accurate than baseline serum) Glycosuria and periodic blood fructosamine levels thyroid hormone concentration)

### Insulin resistance in hypothyroid dogs

**Initial euglycemia**  $\rightarrow$  Increased insulin secretion + unchanged glucose effectiveness

Later decompensation  $\rightarrow$  Diabetes mellitus

- Monitoring hypothyroidism therapy
- GH measurement

#### 5. TREATMENT

Insulin resistance is reversible targeting the concurrent disease, so in the diabetic dog:

- Treatment with sodium levothyroxine has to be intiated
- Insulin dose must be adjusted

In the hypothyroid dog developing diabetes mellitus, sodium levothyroxine treatment • needs to be rechecked.

# 6. CONCLUSIONS

- Pathogenesis of hypothyroid-mediated insulin resistance seems to be multifactorial.
- Hypothyroidism causes marked insulin resistance but glycemia is initially unaffected. However, diabetes mellitus may develop if the compensatory mechanisms collapse and its early detection is not straightforward or well established.
- Diagnosis of hypothyroidism in a diabetic dog must be initiated when insulin resistance is suspected but its recognition is difficult because many findings compatible with hypothyroidism are not specific of thyroid hormone defficiency.
- Treatment of insulin resistance consists in treating hypothyroidism with sodium levothyroxine, and later adjusting insulin dose in the diabetic dog.