Metabolic Effects of Obesity and Its Interaction with Endocrine Diseases

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KEYWORDS

• Obesity • Canine • Feline • Insulin resistance • Dyslipidemia • Diabetes
• Hepatic lipidosis • Adipocytokines

KEY POINTS

- Obesity in dogs and cats leads to numerous metabolic and endocrine abnormalities, including insulin resistance, altered adipokine secretion, blood lipid disorders, and ectopic fat accumulation.
- The effects of insulin resistance are initially limited by a compensatory increase in insulin secretion; if concurrent beta cell dysfunction develops, diabetes may ensue, particularly in cats.
- Altered lipid metabolism and hepatic triglyceride deposition may contribute to the predisposition of obese cats to hepatic lipidosis.
- Although the concept of a "metabolic syndrome" has been investigated in dogs and cats, no system currently exists to predict development of obesity-related metabolic complications.

INTRODUCTION

Obesity in pet dogs and cats is a significant problem in developed countries, and seems to be increasing in prevalence.[1] In dogs and cats, as in other species, accumulation of excess body fat has numerous adverse metabolic consequences. Adipose tissue, once thought to be an inert storage depot, has been recognized as an endocrine organ that actively participates in carbohydrate and lipid metabolism, energy regulation, and the inflammatory and coagulation cascades.[2] In the setting of overnutrition and obesity, control of these processes is altered; although this may not be immediately apparent clinically, altered glucose and lipid metabolism can ultimately

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predispose to diabetes mellitus (DM) and/or hepatic lipidosis (HL), and changes in energy metabolism may contribute to difficulty correcting obesity, particularly in cats. This article reviews the metabolic and endocrine changes known to occur with development of obesity in dogs and cats, and discusses their clinical significance.

NORMAL METABOLIC FUNCTION OF ADIPOSE TISSUE

Lipid Storage and Release

Mammalian white adipose tissue is specialized for the uptake, processing, and storage of circulating lipids. Lipids circulating as triglycerides (either dietary or endogenous) are hydrolyzed to yield glycerol and nonesterified fatty acids (NEFAs) on encountering the enzyme lipoprotein lipase on endothelial cells. These NEFAs are quickly taken up by fatty acid transporters on the surfaces of adipocytes, and most are re-esterified into triglycerides for intracellular storage. During times of energy deficit, triglycerides are hydrolyzed and NEFAs are released through the actions of intracellular lipases (eg, adipocyte triglyceride lipase, hormone-sensitive lipases).[3]

NEFAs may be taken up by other tissues such as muscle and liver to be used for energy or re-esterified for export or storage. Unlike adipose tissue, however, liver and muscle are not specialized for lipid storage, and accumulation of large amounts of intracellular triglyceride would be detrimental to normal cellular function. Therefore, in times of fuel surfeit or increased NEFA concentrations, uptake and sequestration of lipids by adipose tissue seems to act as a buffer protecting lean tissues from ectopic lipid deposition.

Endocrine Functions

Adipose tissue contains receptors for a wide variety of endocrine hormones, including insulin, glucagon, growth hormone, thyroid hormone, angiotensin, incretins, and glucocorticoids, as well as for catecholamines and cytokines such as interleukin (IL)-6 and tumor necrosis factor (TNF)-α.[2] Thus, it is able to respond to metabolic signals from other organ systems to help coordinate fuel storage and utilization. In turn, adipocytes themselves produce and release substances that participate in interorgan communication. These include the adipose-derived cytokines (or "adipokines"), adiponectin and leptin, along with proteins for lipid transport and components of the inflammatory and coagulation cascades. Adiponectin, produced exclusively by adipose tissue, has insulin-sensitizing and antiinflammatory properties, whereas leptin exerts central control of appetite and energy expenditure.[2]

The importance of adipose tissue in overall fuel and energy metabolism can be appreciated by observing the effect of adipose tissue depletion: laboratory mice that lack adipose tissue develop severe insulin resistance, diabetes, dyslipidemia, and ectopic lipid deposition, and similar metabolic derangements are observed in humans with lipoatropy or lipodystrophy.[4,5]

Obesity, adipose tissue dysfunction, and the metabolic syndrome

Although a deficiency of adipose tissue is clearly detrimental from a metabolic standpoint, excess adipose tissue has equally deleterious consequences. In humans, the development of obesity is associated with a constellation of metabolic abnormalities that predispose to type 2 DM and cardiovascular disease. These abnormalities are collectively termed "the metabolic syndrome," and include central adiposity, evidence of insulin resistance, blood lipid disorders, and systemic hypertension.[6] In addition to DM and cardiovascular disease, nonalcoholic fatty liver disease (a chronic hepatopathy characterized by excessive lipid accumulation in the liver, with subsequent inflammation and hepatic dysfunction) and reproductive disorders