Obesity in companion animals part one – appetite and satiety

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MARGE L CHANDLER DVM, MS, MACVS, DACVN, DACVIM, DECVIM-CA, MRCVS in the first of a two-part article, discusses obesity complexities in cats and dogs, including causes and risk factors, as well as the roles of appetite and satiety

NUMEROUS veterinary and newspaper articles have been written about pet obesity. It is recognised as the number one nutritional problem affecting pets of the first world, with obesity and overweight body condition affecting more than 50 per cent of cats and dogs. Imagine the veterinary and public reaction if an infectious disease was affecting more than 50 per cent of pets.

This two-part article will explore the mechanisms of appetite and satiety in part one, followed by prevention of obesity and preventing weight re-gain after weight loss in part two.

The risk factors for obesity include both pet and owner factors (Table 1). There are also well-known adverse effects of excessive body fat (Table 2). Many weight loss programmes and nurse clinics exist, and every major pet food company has diets designed to promote weight loss. We know how to achieve weight loss in pets and people – consume fewer calories than expended. However, the pathogenesis of obesity is not as simple and direct as uncontrolled gluttony.

Obesity is a complex disorder involving energy metabolism and satiety control. Multiple genetic and environmental factors control regulation of food intake, resting metabolic rate, thermic effect of food, and energy expenditure and efficiency during work.

Three common causes of obesity in pets are overeating, decreased exercise and lower metabolic

rate. While activity and eating behaviours contribute substantially to the development of obesity, much is now known about how eating and energy balance are regulated. Further, while these are now known to have – at least partially – a genetic basis, there is also good evidence that gene expression can be modified.

To better understand the roles of appetite and satiety, and potential interventions, we need to understand the complex physiology of these drives.

Appetite and satiety

Years ago, the intake of food was thought to be solely controlled by “glucostatic” regulation, where fasting blood glucose would fall and stimulate the feeding centre in the hypothalamus. The subsequent postprandial increase in glucose was believed to activate the satiety centre, which inhibited the feeding centre.

The control of food intake is now known to be much more complicated, and is often overridden in humans by social, cultural and environmental factors. These environmental factors may also result in food intake in dogs and cats, with clues from the preparation of food and even a sense of the time when food may be available. Owners who have automatic feeders may observe their pets waiting by the feeder at the time it will dispense food, without any signs from the owner.

Regulation of feeding and energy balance involves both short-term regulation of individual meals and longer-term regulation of overall energy balance and body fat. Short-term control of food intake involves the CNS and hormones from the gastrointestinal (GI) tract. Long-term regulation of food intake and adiposity involves input from the adipose tissue (fat) producing several endocrine and paracrine mediators, including leptin, adiponectin, resistin and tumour necrosis factor ?. Some of the gut hormones also appear to have a role in longer-term control.

Distension of the stomach activates stretch receptors and mechanoreceptors, which transmit satiety signals – although, generally, eating stops before the stomach is this distended. Central and peripheral signals communicate information about the current state of energy balance to key brain regions, including the hypothalamus and brainstem, often from the gut via the vagal nerve. Hunger and satiety represent coordinated responses to these signals.

GI signalling

Ghrelin

The only GI hormone that is orexigenic (increases appetite) is ghrelin – sometimes referred to as the hunger hormone. It is secreted by gastric epithelial cells and also by hypothalamic neurons and acts on the hypothalamic feeding centre.

The concentration of plasma ghrelin peaks before a regular meal and, in humans, its release is accompanied by feelings of intense hunger. In humans, blood concentrations of ghrelin are lowest shortly after the consumption of a meal.

Plasma ghrelin is suppressed in proportion to the calories ingested, although dietary fat appears to suppress ghrelin less potently per calorie than carbohydrates or protein. This may reduce satiety on a high-fat diet, leading to potential weight gain, which already is a risk of high-fat diets. The rapid postprandial drop in ghrelin is attenuated in obese humans, compared to lean ones, and obese people may be more sensitive to appetite stimulation by it.

Ghrelin appears to suppress fat utilisation in adipose tissue. It also has beneficial cardiovascular and anti-inflammatory effects. These positive effects may limit the use of ghrelin antagonists as potential treatments for obesity.

Satiety signals

Cholecystokinin

Cholecystokinin (CCK) is secreted postprandially from the small intestine and reduces food intake in addition to its effects on the pancreas and gallbladder. In humans, it has a short half-life of one to two minutes, limiting its use as an appetite suppressant. Chronic administration of CCK alone also does not result in weight loss. Protein and fat stimulate increased release of CCK from the gut. CCK acts both peripherally and centrally to prolong a feeling of satiety.

Peptide YY

Peptide YY (PYY) is secreted by the L cells of ileum and large intestine. It is a satiety signal and decreases food intake, likely via a pathway through the vagal afferent nerve to the hypothalamic actuate nucleus.

PYY also inhibits fasting small bowel motility and gastric emptying. There are suggestions some of the anorectic effects are due to nausea in humans. A veterinary drug (dirlotapide) is marketed for helping control obesity in dogs, which has its effect partially via PYY. This drug results in effective weight loss while being given, although, without management changes by the owner, the chance of weight re-gain is very high.

Oxyntomodulin

Oxyntomodulin is released from the L cells of the intestine and inhibits food intake. It is also an incretin and stimulates increase in plasma insulin. When injected in humans, it results in decreased calorie intake and an increased energy expenditure from increased voluntary activity. It also increases heart rate in rodents. As it has a short duration of action, it required three times daily

injections, which limits usefulness, although analogues may be developed.

Adipokines

Lipid cells are highly active and the adipose tissue has many endocrine functions. The term adipokines refers to factors released from adipose tissue that regulate energy metabolism. They also affect cardiovascular function, reproductive status and immune function. Leptin and adiponectin are two of the better-studied adipokines.

Leptin

Leptin is a protein hormone that helps regulate bodyweight by signalling the amount of fat stored, then decreasing food intake (and may increase energy expenditure). It increases with an increased amount of white fat in the body. It also stimulates angiogenesi, decreases insulin sensitivity and appears to be pro-inflammatory, prothrombotic and pro-oxidant. Some obese individuals develop leptin resistance and can develop very high concentrations without a marked decrease in food intake.

Adiponectin

Adiponectin is produced by mature adipocytes and is a key adipokine that regulates carbohydrate and lipid metabolism, enhances insulin sensitivity and is anti-inflammatory. There is less in obese individuals, so positive effects are only seen in lean animals. Weight loss in the obese increases adiponectin in most species, including cats; however, one study in dogs did not show a decrease in high molecular weight adiponectin after weight loss and adiponectin may not be involved in changes in insulin sensitivity in dogs. It may be obesity decreases adiponectin concentrations in intact, but not in neutered, dogs.

Other non-GI hormones

Thyrotropin-releasing hormone (TRH)

TRH can be a potent inducer of satiety in experimental animals and this may act by the direct inhibition of lateral hypothalamic enkephalin-mediated feeding behaviour. Diurnal rhythm will also affect appetite, for example, in nocturnal hunters. These peptides and adipocytes are targets for some of the drugs and functional foods involved in managing obesity, which will be discussed in part two.

• References in part two.

Figure 1. The Labrador retriever is a breed known to be at risk of obesity.

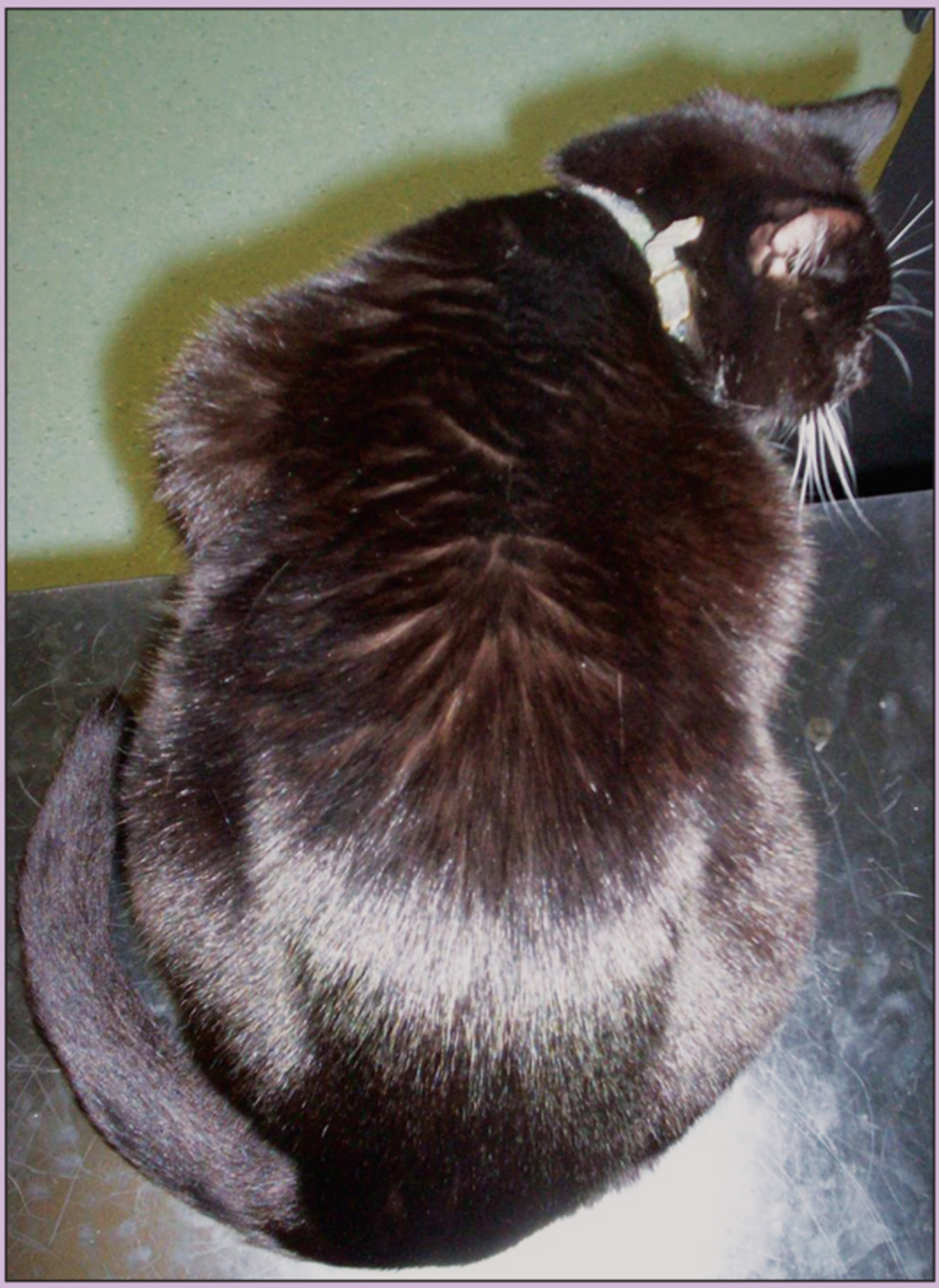

Figure 2. Some overweight cats may not be able to groom properly.

Breed – some breeds are more obesity prone (**Figure 1**)
Genetics – may affect metabolism and activity levels
Neutering – at any age
Age – middle-aged are at most risk
Palatable free choice diets – especially high fat diets
Feeding snacks, treats and table scraps
Using a large bowl or feeding utensil
Not weighing or measuring the amount fed
Sedentary lifestyle – indoor cats
Overweight owner – dogs only
Older owners
Likely factors – owners unaware of ideal body condition and weight, infrequent weighing of a pet

Table 1. Some of the factors that increase the risk of obesity in dogs and cats

Diabetes mellitus (cats)
Insulin resistance (cats and dogs)
Worsening signs of arthritis or other musculoskeletal disorders
Increased risk of pancreatitis (dogs)
Increased anaesthetic and surgical complications
Worsened heat and exercise intolerance
Complications from cardiorespiratory disorders
Some dermatological diseases (**Figure 2**)
Some forms of neoplasia
Incontinence (especially female dogs)
Tracheal collapse
Chronic bronchitis
Earlier mortality than lean animals

Table 2. Some of the health implications and disorders with increased risk in obesity

Orexigenic (stimulating appetite)	Anorexigenic (decreasing appetite)
Ghrelin	Leptin
	Peptide YY (PYY)
Neuropeptide PY (in hypothalamus)	Glucagon like peptide-1 (GLP-1)
	Cholecystokinin
Agouti-related peptides (hypothalamus)	Oxyntomodulin
	Orexin A
Endogenous opioids	Pro-opiomelanocortin (POMC) neurons (hypothalamus)
	Corticotropin-releasing hormone
Melanin concentrating hormone	Thyrotropin releasing hormone (TRH)

Table 3. Some of the hormones – neuropeptides (neurotransmitters) – that cause increased food intake (orexigenic peptides) and those that decrease food intake (anorexigenic) are listed below. Many more exist than are listed