Metabolic Syndrome in Fat Pets

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Suppose

'Syndrome X' was …….

Reported to be a problem in at least 25-30% of the dog and cat population meaning a single veterinarian may see as many as 340 of these afflicted patients per practice year (~1 per day) and diagnostics were relatively simple and inexpensive.

What if 'syndrome X' was responsible for: reduced activity, an impaired gait, traumatic & degenerative orthopedic disorders, decreased heat tolerance & stamina plus early signs of aging?

Consider

'syndrome X' was associated with: dyspnea, congestive heart failure, dystocia, non-allergic dermatological problems, pancreatitis and hypothesized to be associated with an increased risk of several cancer types [Cystic transitional cell carcinoma Am J Epid 1991 and Mammary cancer J Tox Env Health 1989], and shown to be associated with a shortened (1-2 yrs) life span [dog data (Kealy et al 2002 and cat data Waltham Intern Symp 1997]

And we have a treatment!!!!

"Healthy but obese" patients is not acceptable because the two are mutually exclusive.

Fat is a Metabolically Active Tissue that can no longer be considered an inert tissue or dead weight. It has not be known to be a metabolically active tissue but is very active.

Obesity is a chronic pro-inflammatory state. The number and concentration of inflammatory markers is HIGHLY correlated with the degree of obesity in several species.

Obese animals and people live in a chronic low grade state of inflammation and oxidative stress. Higher circulating levels of cytokines, interleukins and acute phase proteins are found in obese vs. lean people and animals. The levels increase as adiposity increases and the levels decrease as adiposity decreases.

Metabolic Syndrome was first described in 1988 as 'syndrome x' in people then evolved in our collective thinking from a vague cluster of common chronic diseases (cardiovascular disease, diabetes and obesity) to what is now defined in people as any three of the five traits:

1. Abdominal obesity (waist circumference)
2. Impaired fasting glucose (insulin resistance)
3. Hypertension
4. Hypertriglyceridemia
5. Low HDL ("good") cholesterol

Obesity is linked to systemic disease through oxidative stress. Given oxidative stress accumulates in fat:

1. ROS (reactive oxygen species) production in obese mice was increased in only adipose: not in muscle, aorta or liver
2. Decreased expression and activity of adipocyte antioxidant systems (SOD, GPx) in obese vs. normal wt mice.
3. Circulating plasma ROS are increased in obese vs. normal wt (non-diabetic) people and mice.

There is a mismatch of adipokines from adipocytes as % body fat increases in that adiponectin (anti-inflammatory) secreted by normal fat cells is decreased in obese people and obese mice. Leptin (pro-inflammatory) is increase in obese vs. normal wt (non-diabetic) people and mice. (Furukawa et al 2004).

In summary, adipose tissue is major site of ROS production and chronic increases in adipocyte ROS production leads to increasing systemic oxidative stress. This in turn leads to changes such as:

1. vascular wall integrity which leads to hypertension and atherosclerosis.
2. underlies pathophysiology of hepatic steatosis.
3. leads to end stage glomerular injury in kidneys
4. impairs both pancreatic insulin secretion and glucose transport into muscle and adipose tissue.

There is a link between obesity and diabetes in that in the chronic inflammatory state of obesity, specifically TNF-alpha induces a serine (instead of tyrosine) phosphorylation of insulin receptor. This in turn decreases the insulin signal transduction and degrades the insulin receptor.

Animal studies – We see the same cytokine picture in several species with increased body fat

1. TNF-alpha and IGF-1 levels were sig higher when ideal wt dogs were made obese. (Blanchard et al 2004).
2. Dogs made obese had increasing levels of TNF-alpha and became progressively insulin resistant (Gayet et al 2004).
3. Weight gain in dogs resulted in increased plasma cytokine concentrations (Gayet et al 2003).
4. TNF-alpha and IL-1 were sig higher in mares with a higher % body fat (Vick et al 2007).

Animal studies – We see the same correction decreased body fat (weight loss)

1. Obese cats placed on a wt loss diet had sig decrease in markers of oxidative stress and inflammation (Saker et al 2004, Tvarijonaviciute et al 2012).
2. TNF-alpha and IGF-1 levels were sig lower when obese dogs lost wt to ideal (Blanchard et al 2004).
3. During food restriction and weight loss, cytokine levels returned to pre-obese state in dogs (Gayet et al 2003).

Animal studies – We see the same insulin sensitivity with increased body fat

1. Insulin sensitivity decreased as % body fat increased in mares (Vick et al 2007).
2. Insulin sensitivity was lowest when dogs were obese but increased when dogs lost weight to ideal (Blanchard et al 2004).
3. Dogs made obese became progressively insulin resistant (Gayet et al 2004).
4. Weight gain in dogs resulted in decreased insulin sensitivity: during wt loss, insulin sensitivity returned to pre-obese state (Gayet et al 2003).

Canine adiponectin and leptin levels change similar to people with changing body fat levels in that obese adult dogs had higher plasma leptin concentrations and lower plasma adiponectin concentrations. Adiponectin (anti) levels was negatively correlated while leptin (pro) levels positively correlated with obesity.

Purina canine life span study: 24 paired litter mates (8 wks) fed two levels of calories (full vs. 25% less) until death (~15 yrs).

	Full fed*	-25% fed
BCS	7/9	6/9
Glucose	100.7	93.5
Insulin	70.8	48.4
TG's	49.9	41.5

The antioxidant profiles (@ 5 and 10 yrs of age) were different due to diet restriction.

Summary: Excessive calorie (+25%) intake resulted in

1. Higher % body fat 6/9 vs 7/9
2. Shortened life span 13 yrs vs. 11 yrs
3. Earlier onset of signs of physical aging
4. Earlier onset of disease associated with age – same diseases but earlier onset

In summary

1. Adipose tissue is metabolically active and produces pro and anti-inflammatory cytokines.
2. Obesity produces a chronic pro-inflammatory state and additional oxidative stress.
3. Inflammatory state produces insulin resistance.
4. Increased oxidative stress limits cell life span and longevity.
5. Weight loss reduces pro-inflammatory state and oxidative stress.

In good conscience, we must be more aggressive in offering weight loss programs to our clients.

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