CELLULAR OXIDATIVE STRESS & CHRONIC INFLAMMATORY DISEASE RESULTS IN OBESITY, INFECTIONS AND CANCERS, PART 1

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Objective: To understand the mechanisms that underlie cellular oxidative stress which leads to chronic inflammation and disease. This article deals with the basics of the cellular responses to stress, obesity and infections, and how they can be managed.

Introduction

1. Chronic Cellular Inflammation from the increased free radical formation of oxidative stress leads to a wide variety of diseases. [1-5] Chronic inflammation occurs when the tissues or organs receive inflammatory "mediator" messages that cause them to react as though the "trigger" or pathogen was still present. Rather than repairing themselves, these cells remain in an ongoing state of inflammation that can wax and wane for an entire lifetime. As a result, tissues become deficient in antioxidant mediators, such as malonedialdehyde, glutathione, cysteine, ascorbic acid and other antioxidant vitamins, which is associated with poor clinical outcome. These effects also pertain to the lipid oxidation and risk of rancidity in pet foods with their higher fat and oil content. [1, 2]

2. Summary of Factors Involved

a. Chronic Obesity, Weight Control & Nutrigenomics [6]

Pet obesity is a national epidemic. [7] A 2012 survey conducted by the Association for Pet Obesity Prevention (APOP) revealed that 52.5% of dogs and 58.3% of cats are overweight or obese. [8] Banfield Pet Hospital's *State of Pet Health Report 2012* provides startling insight into the link between obesity and illness. The report, which analyzed data from more than two million dogs and 430,000 cats, found that: [9]

- 42% of dogs with diabetes are overweight (and 40% of cats).
- 40% of dogs with arthritis are overweight (and 37% of cats).
- More than 40% of dogs with high blood pressure are overweight.
- 61% of hypothyroid dogs are overweight.

Overweight dogs are at increased risk for numerous diseases and live an average of two years less than their ideal weight counterparts: [6, 9]

Cardiorespiratory diseases, including airway obstruction syndrome (seen in brachycephalic dog breeds) and laryngeal paralysis.
Endocrine disorders, including hyperadrenocorticism (Cushing's disease) and hypothyroidism.
Functional alterations, such as decreased respiratory capacity, exercise intolerance, heat intolerance/stroke and decreased immune functions.
Metabolic abnormalities, such as hyperlipidemia/dyslipidemia.
Neoplasia, including transitional cell carcinoma (TCC) of the bladder.
Orthopedic disorders, such as osteoarthritis, anterior cruciate ligament rupture and intervertebral disk disease.
Urogenital system conditions, including TCC bladder tumor.

Scientists have identified "obesity gene" variants in people, however many lean individuals carry these obesity genes and never become overweight. [10, 11] This means that the determining factor for becoming obese may be an individual's lifestyle.

One meta-analysis of data from more than 200,000 people who carry a specific gene predisposing them to obesity found that physically active adults who carried the obesity gene were nearly one-third less likely to become overweight or obese than those who didn't exercise. [6] Genetic predisposition does not mean that obesity is our destiny, or our dog's destiny. [12]
Over the last half-century, there has been an unsettling parallel between the spike in human obesity and obesity in companion animals. [7] This parallel relates to the similar environmental and lifestyle changes that have occurred. [6, 7]

Calorie restriction has been shown to *increase* lifespan by increasing the amounts of dietary activators of **sirtuins,** proteins that regulate metabolism and lifespan, such as resveratrol and other polyphenols (green and black tea, grape seed extract) fed to dogs. [6, 13-16]

Banfield's separate survey of pet caretakers found that 76% of dog guardians and 69% of cat guardians believed their pet were at a healthy weight, when in fact they were not. [9]

Studies show that obesity can affect gene expression, resulting in a host of chronic diseases. [6, 10, 12] Once the body becomes "programmed" for fat, it's like a never-ending cycle because fat cells lead to more fat cells.
Essentially, obesity is a state of chronic inflammation, which leads to a host of chronic inflammatory diseases. [6]
Acute inflammation is normal and serves a purpose. Chronic inflammation, however, leads to a variety of diseases. [1-5]
Furthermore, **food intolerances/sensitivities** can lead to weight gain because food sensitivities lead to inflammation, and obesity is an inflammatory condition. [6]

Since inflammation generates obesity, a key step in helping a pet to lose weight is to feed him lots of fat-fighting anti-inflammatory foods, while also removing pro-inflammatory foods.[11, 17]

b. Fat-Fighting Functional Foods are discussed below in Section h.
Commercial weight-loss foods may not be the best choice. These products are typically high in unhealthy carbohydrates, contain pro-inflammatory ingredients and don't contain enough high quality animal protein. Opt instead to recommend fresh, wholesome ingredients that promote healthy gene expression, maintenance of lean body mass and overall optimum health. [6, 11, 17]

c. Genetic Predisposition. [6] Certain breeds of dogs have been identified as genetically predisposed to obesity, including: Basset Hounds; Beagles; Boxers; Cairn Terriers; Cavalier King Charles Spaniels; Cocker Spaniels; Dachshunds; Doberman Pinschers; Golden Retrievers; Labrador Retrievers; Scottish Terriers; Shetland Sheepdogs; and West Highland White Terriers. In contrast, sighthounds appear to be less susceptible, and German Shepherds had the lowest incidence of obesity.

c. Spaying/Neutering Linked to Obesity. [16] A recent study found that dogs who had undergone gonadectomy were significantly more likely to become overweight in the two years following the procedures, compared with sexually intact dogs. There was no difference between males and females, and the increased risk was not influenced by the ages at the time of the procedures.

d. Other Factors [6]
Decrease in physical activity.

Progression away from fresh, wholesome foods to highly processed foods packed with ingredients that send unhealthy messages to the genes.
Proliferation of readily available, energy-dense convenience foods.
Genetic screening for obesity does not take into account environmental and behavioral factors.

Individuals who know they are genetically predisposed to obesity might actually feel discouraged to exercise and eat healthy.
It fails to take into account the larger societal influences at play.
It has a low predictive power to determine whether an individual will actually become obese.

e. Obesity Regulates Gene Expression [10, 11]

Studies clearly show that poor diet doesn't just lead to health problems by creating fat in our bodies; it actually changes the expression of obesity-related genes.
Feeding your dog foods that suppress his genomic expression for obesity may therefore not only result in a loss of weight, but also in the reduced risk of a whole host of obesity-related diseases.
Once the body becomes "programmed" for fat, it's like a never-ending cycle because fat cells lead to more fat cells. [6]
The more fat cells there are in the body, the more these cells secrete pro-inflammatory **cytokines** and the more chronic, systemic inflammation that is created. The fat regulating hormones are **adiponectin** and **leptin.** [6, 10]

f. Food Sensitivities: Hidden Cause of Weight Gain [6]

Food intolerances/sensitivities are a major cause of cellular inflammation, which creates small fissures between the cells, allowing foreign invaders, such as bacteria and partially digested food molecules, to cross from the gastrointestinal tract into the bloodstream, creating a further reaction from the immune system.
Eating reactive foods can lead to obesity because food intolerances/sensitivities lead to inflammation, and obesity is an inflammatory condition.

g. Feeding "Recommended" Amounts [6]

Manufacturers' feeding recommendations can result in overfeeding and weight gain.
They don't take the specific age, health, lifestyle, activity level or any other individual factors of the pet into account.
They also tend to *over*estimate the amount of daily calories the pet needs to consume.

h. Fat-Fighting Functional Foods [6]

Some of the most important are:

i. High quality, bioavailable novel protein

Coconut oil (virgin, expeller-pressed, preferably organic), a medium chain saturated fat (MCFA), also known as a medium-chain triglyceride (MCT), is packed with health benefits ranging from immune-boosting to heart-protective properties. Coconut oil also digests differently than other fats, creating a higher thermogenic effect that boosts metabolic rate.

Omega-3 fatty acids, another powerful canine functional superfood, exert a strong anti-inflammatory effect and thus play an important role in weight loss.

L-Carnitine, an amino acid synthesized in the liver and kidneys from lysine and methionine, improves nitrogen retention, which increases lean mass and reduces fat mass.

White kidney bean extract (*Phaseolus vulgaris*), an extract derived from the white kidney bean. In human studies, *Phaseolus vulgaris* has been shown to act as a starch blocker that works by blocking the activity of alpha amylase, a digestive enzyme found in saliva that breaks down starch. While dogs produce amylase in the pancreas, but not in the saliva, clinical effectiveness is seen in canine in patients supplemented with *Phaseolus vulgaris*.

ii. Antiangiogenic Foods

These foods that prevent angiogenesis, the creation of new blood vessels, can actually *shrink* fat cells by cutting off their blood supply. They include: Apples; Artichokes; *Berries* (blackberries, blueberries, raspberries); Bok choy; Cherries; *Curcumin* (turmeric); Ginseng; Kale; Lavender; *Maitake mushrooms;* Olive oil; Parsley; Pumpkin; and Sea cucumber.

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