Chapter 8
Obesity in Humans and Dogs: Similarities, Links, and Differences

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Abstract Obesity is defined as an excess of adipose tissue and is considered as one of the most pervasive, chronic diseases leading to morbidity and decreased lifetime expectancy in both humans and dogs. For these reasons and because the prevalence of obesity continues to increase, the societal burden of obesity is increasing worldwide. Dog ownership has been related with improved lifestyle and lower obesity rates. However, the possible relationship between owner and dog obesity has been reported, suggesting common causes of obesity in humans and dogs. In this line, the specialists of both fields, human and veterinary medicine, agree not only about the main common causes but also about dangerous consequences of the obesity. Nevertheless, some discrepancies between human and dog obesity have also been described. For this reason, in this chapter, we aimed to look more deeply at the similarities, links, and differences between human and canine obesity. Better understanding of this disease would not only help to design obesity treatment approaches, but also, and more importantly, to prevent it in humans and dogs taking advantage of marvelous human-dog relationship.

Keywords Adipokines · Canine · Inflammation · Insulin resistance · Obesity consequences · Obesity grade · Overweight · Owner-dog relationship

8.1 Introduction

Obesity is defined as excess adipose tissue and is considered as one of the most pervasive, chronic diseases leading to morbidity and decreased lifetime expectancy in both humans and dogs. For these reasons and because the prevalence of obesity

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M. R. Pastorinho, A. C. A. Sousa (eds.), *Pets as Sentinels, Forecasters and Promoters of Human Health*, https://doi.org/10.1007/978-3-030-30734-9_8

continues to increase, with prevalence exceeding half of general population of both humans and dogs in some countries (WHO 2018; Muñoz-Prieto et al. 2018), the societal burden of obesity is increasing worldwide.

In order to prevent health, economic, and social consequences of obesity in humans, close follow-up of obesity prevalence is performed among different countries and different health organizations, such as Organisation for Economic Co-operation and Development (OECD) or World Health Organization (WHO). Furthermore, a growing number of countries have adopted policies to prevent obesity from spreading further. These include awareness raising, health care, regulatory and fiscal measures, taxation of unhealthy food, and sugar-sweetened beverages (http://www.euro.who.int/en/health-topics/noncommunicable-diseases/obesity). In the same manner, in recent years, the increasing societal burden is being reflected in the increasing scientific literature dealing both human and canine obesity. The specialists of both fields, human and veterinary medicine, agree about the dangerous consequences of the obesity and the importance to study it further in order to better understand its pathophysiology. This knowledge would not only help to design obesity treatment approaches, but also, and more importantly, to prevent it. In addition, possibly common actions to prevent at the same time human and canine obesity, especially in dogs and owners, could be undertaken based on the studies about links and common causes of obesity in humans and dogs (Kushner et al. 2006; Bartges et al. 2017).

The main common causes and consequences have been reported for both humans and dogs. Dogs have even been suggested as an animal model for obesity investigations (Osto and Lutz 2015; Stachowiak et al. 2016). However, some discrepancies have also been described. For this reason, in this chapter, we aimed to look more deeply at the similarities, links, and differences between human and canine obesity.

8.1.1 Metabolic Syndrome

Both humans and dogs can suffer from metabolic syndrome (MetS). MetS is a metabolic disorder resulting from obesity and is diagnosed on the basis of a combination of the presence of obesity, impaired glucose metabolism, dyslipidemia, and hypertension (Eckel et al. 2005; Tvarijonaviciute et al. 2012a) (Table 8.1). While in humans the main risk factors associated with the presence of MetS are clearly defined (cardiovascular disease, type 2 diabetes, liver disease), in dogs, the doubts about usefulness of its determination still exist (Verkest 2014). However, in dogs, the presence of MetS was suggested to be related to lipid metabolism alterations, liver and lung function impairment, presence of a prothrombotic state, and a decrease in immune function (Tvarijonaviciute et al. 2019), although further studies are needed to corroborate these results.

Table 8.1 Definitions of the human and canine metabolic syndrome (MetS)

Human MetS criteria (Eckel et al. 2005)	Canine MetS criteria (Tvarijonaviciute et al. 2012a)
Generally by different organizations, reported criteria for MetS diagnosis in humans include: Overweight/obesity (more importantly central) ↑ triglycerides (or specific treatment for this lipid abnormality) ↓ high density lipoprotein (HDL) cholesterol ↑ glucose or previously diagnosed type 2 diabetes ↑ blood pressure Some criteria also suggest to determine: Microalbuminuria ↑ high-sensitivity C-reactive protein (hsCRP)	The guidelines of the International Diabetes Federation (2006) were modified in order to produce an accessible system for dogs: Overweight/obesity And two of the following: ↑ triglycerides (or specific treatment for this lipid abnormality) ↑ cholesterol ↑ glucose or previously diagnosed diabetes ↑ blood pressure

8.2 Causes

Obesity is a multi-causal disease (Ravussin and Ryan 2018). However, food-related and physical activity-related factors were labeled as "the big two" because of the importance that these exhibit in the development of obesity (Keith et al. 2006). Furthermore, genetics, environmental, and reproduction-related factors, among others, were also shown to contribute to obesity epidemic in both humans and dogs. It is important to point out that in the particular case of the dogs, different authors highlight that neglectful or misconceived strategies of the owners are the primary causes of obesity in dogs (Burkholder and Bauer 1998; Bland et al. 2009) since most of the obesity risks in dogs are related to the chosen way of life, habits, and values of the people (Muñoz-Prieto et al. 2018).

8.2.1 Genetic Susceptibility

Insights from human and animal model studies suggest that genetics, including monogenic disorders and, more recently, polygenic clues arising from genome-wide association studies (GWAS), presents a central role of the brain in the regulation of feeding behavior (Yeo and Heisler 2012). It was shown that, specifically, monogenic alterations in the melanocortin, leptin, 5-hydroxytryptamine (5-HT; serotonin), and brain-derived neurotrophic factor (BDNF) pathways could result in disturbed energy balance and body weight gain in humans (Yeo and Heisler 2012). Furthermore, mutations in proopiomelanocortin (POMC) gene have been associated with severe hyperphagia and obesity in humans, with a subsequent increase in

risk of obesity-related diseases such as type 2 diabetes (Farooqi et al. 2006). In a similar manner, in dogs, POMC gene has been associated with food motivation and obesity in Labrador Retriever and Flat-Coated Retriever dogs (Raffan et al. 2016; Mankowska et al. 2017). However, further studies are needed in order to confirm these observations, since these alterations were not detected in other obesity-prone dog breeds (Beagles, Cocker Spaniels) and have been not related to 5-point body condition score (BCS) (Mankowska et al. 2017).

Although being true that some individuals are more genetically susceptible to develop obesity, it is not correct to blame for the epidemic on genetics alone (Ravussin and Ryan 2018). Most of the increase in obesity has occurred in the past 40 years, and the genes have not changed such much to be responsible for the high rates of obesity (Hall 2018; Ravussin and Ryan 2018). Thus, other environmental-behavioral changes were suggested to be the main causal factors for the current obesity epidemic (Hall 2018).

8.2.2 Food-Related Obesity Risk Factors

Obesity occurs when energy intake exceeds energy expenditure over an extended period (Ravussin and Ryan 2018). However, not only the quantity but also the quality, availability, palatability, and food costs together with the eating behavior (snacking, eating out of home) were described to be related to the obesity development in humans (Ravussin and Ryan 2018). In a similar manner in dogs, the number of meals per day, the type of diet, and price were linked to increased risk to develop obesity (Kienzle et al. 1998; Robertson 2003; Bland et al. 2009; Mao et al. 2013). Some human-related dog feeding conduct could also predispose for canine obesity, e.g., the presence of the owner while dog is eating (Kienzle et al. 1998). In addition, the similarities between children and dog behavior related to food have been described (Pretlow and Corbee 2016). It was argued that if the owner is constantly eating, the dog may develop the habit of begging (Carballo et al. 2015), which could result in uncontrolled caloric intake leading to the development of obesity. Furthermore, there is the belief among some owners that the affection toward the dog is best reflected by giving treats or sharing their food while eating. This fact, together with the fact that the calories of the treats usually are not included in the general count, can result in increased caloric intake and subsequent development of obesity (Kienzle et al. 1998; Bland et al. 2009).

8.2.3 Physical Activity-Related Obesity Risk Factors

Humans as well as dogs with low physical activity are prone to suffer obesity. It was stated that the changes driven by behavioral factors triggered by the obesogenic environment resulted in reduction in physical activity in humans (Keith et al. 2006; Ravussin and Ryan 2018). Even a relatively small change in energy balance was

responsible for weight gain, especially, in genetically susceptible individuals (Hill et al. 2012). For this reason, reduced physical activity was stated to be the main reason of human obesity epidemic (Church and Martin 2018).

Currently, dogs are increasingly considered more as "fellows" than "pets." The "overhumanizing" of the pet dogs was suggested to result in ignorance of the some basic needs of the dog such as exercise and occupation (Kienzle et al. 1998) that, together with excessive calorie intake, results in obesity development.

Nevertheless, a recent questionnaire-based study involving ten different European countries suggested that obesity rates among dog owners are lower than the general population (Muñoz-Prieto et al. 2018). These observations could be related to the increased physical activity, since dogs were shown to present both social and physical activity support (Jennings 1997; Kushner et al. 2006; Cutt et al. 2007; Coleman et al. 2008). Furthermore, owning a dog has been suggested to be a way to combat a sedentary lifestyle by enhanced motivation for activity (Wohlfarth et al. 2013). However, the scientific basis is weak, and further studies are required in order to confirm these observations (Christian et al. 2013). And more importantly, owning a dog does not protect owner from being obese (Muñoz-Prieto et al. 2018).

8.2.4 Reproduction-Related Obesity Risk Factors

In humans and animal models, the influence of reproduction-related factors with the risk of developing obesity in offspring has been suggested. The development of obesity was related to extremes of energy imbalance in utero (both high and low birth weight) of mother or even two generations back, when oocytes were formed in the grandmother, suggesting that the environmental changes initiated one-two generations ago could be responsible for the obesity epidemics today (Keith et al. 2006; Davis et al. 2018). In addition to this, the late pregnancy age, as women delay reproduction beyond 30 years, increases risk of offspring obesity possibly due to the accelerated loss of the brown adipose uncoupling protein 1 levels in the offspring, which may act to increase white adipose tissue deposition in later life (Symonds et al. 2004; Keith et al. 2006; Davis et al. 2018). Furthermore, taken into consideration that estimated hereditability of adiposity reaches 65%, together with the increasing obesity rates and assortative mating in terms of adiposity, and the fact that positive relation between BMI and number of offspring exists, an increased frequency of the genotypes susceptible to obesity in the following generations would be expected (Davis et al. 2018).

In dogs, possibly because of the lack of knowledge, neutering is the most important reproduction-related obesity risk factor (Lund et al. 2006; Sandøe et al. 2014). The main reasons related to body weight gain after neutering are increased food consumption, decreased metabolic rate, and reduced activity (Houpt et al. 1979; Sloth 1992; Robertson 2003). For this reason, warning the owner that neutered dogs are more likely to develop overweight/obesity than entire ones is of high importance. However, it is also important to highlight that neutered dogs can be maintained at their ideal body weight through careful feeding and adequate exercising.

8.2.5 Environmental Obesity Risk Factors

In scientific literature, there are evidences that accessibility to and quality and availability of green spaces together with their safety have a direct effect on physical activity, a key mediator of obesity (Swinburn et al. 1999; Lee and Maheswaran 2011). On the other hand, the increase in atmospheric carbon dioxide (which promotes wakefulness and increased energy intake via increased secretion of the orexin as a result of decreased pH in the organism) and the use of thermoregulation systems to reach the thermoneutrality (resulting in declined energy waists) were suggested to further contribute to obesity spreading among people (Keith et al. 2006). Although similar studies in dogs are lacking, it could be postulated that these factors could also be risks for canine obesity development, since dogs share the same environment as humans.

Furthermore, in the last years, the term "obesogenic environment" has emerged referring to "the sum of influences that the surroundings, opportunities, or conditions of life have on promoting obesity in individuals or populations" (Swinburn et al. 1999). This definition includes societal (aging population, urbanization), economical (work opportunities, economic disparity and insecurity, national gross domestic product (GDP)), physical (high mechanization, sedentary lifestyle), and nutritional (consumption of processed high-energy food) drivers shifting the focus of this disease from the individual to the systemic level (Dempsey et al. 2018).

Table 8.2 includes some additional possible contributors of the obesity epidemics. Although these factors are frapped in uncertainty and contradictions, at least in part they should be considered as possible causal factors of increased obesity rates in the general population over the last decades (Keith et al. 2006; Davis et al. 2018).

8.3 Obesity Grade Measurements

One of the cornerstones of obesity diagnostic and monitoring is an accurate determination of body adipose tissue content (Baldwin et al. 2010; Freeman et al. 2011). However, measurement of adipose tissue is not simple because it is not perfectly compartmentalized being tightly interconnected with the lean tissue. For the determination of obesity, the main conceptual division of importance is between body fat (BF) (Armstrong 1996) and lean body mass (LBM) (Burkholder 2001). The correct measurement of body condition is basic for a correct diagnosis and even more important for the weight loss monitoring to ensure that the BF, and not the LBM or bone mineral content, is lost (Diez et al. 2002).

A number of methods were developed to assess body condition in both humans and dogs. From a practical point of view, they can be divided into (1) *simple*, which are easy to perform and non-invasive and do not need specialized personnel or equipment; thus, they are economic; and (2) *complex*, which usually require specialized personnel and/or equipment. The most frequently used methods in clinic and investigation are disclosed in Table 8.3.

Table 8.2 Additional risk factors suggested contributing to the obesity development

Obesity causes	Described in humans	Described in dogs
Age	Obesity rates were positively related with age. Taken into account that in the last decades the proportion of older people have increased, the obesity epidemics at least in part could be attributed to this fact (Keith et al. 2006; Muñoz-Prieto et al. 2018)	The age of dogs and the age of the owner were associated with an increased probability of dogs being overweight (Muñoz-Prieto et al. 2018)
Behavioral Smoking Sleep debt	Since smoking has anorexigenic effects and increases metabolism, in the last decades, observed decreasing smoking could possibly contribute to the obesity epidemic (Davis et al. 2018). Nevertheless, negative health effect of smoking is profound, and its cessation should be further recommended. Decreased sleeping hours were related to increased hunger and appetite leading to increased risk of adiposity, and inversely correlated to BMI (less sleeping hours – higher BMI) (Reutrakul and Van Cauter 2018).	The dogs owned by the smokers were shown to be prone to obesity development. This could be related to the unhealthy habits of the owner (Muñoz-Prieto et al. 2018)
Gut microbiome	The possible mechanisms resulting in obesity development in persons were suggested to include an increase in energy harvest, modulation of free fatty acids (e.g., butyrate), lipopolysaccharides, gamma-aminobutyric acid (GABA), an impact on Toll-like receptors, the endocannabinoid system, and "metabolic endotoxinemia" as well as "metabolic infection" (Harsch and Konturek 2018)	Different composition of gut microbiota was described in obese dogs when compared with normal weight ones (Handl et al. 2013). Furthermore, weight loss was associated with modifications in microbiota composition (Kieler et al. 2017)
Infections	Although contradictory results exist, adenovirus 36 was suggested to accelerate the differentiation and proliferation of pre-adipocytes (Davis et al. 2018)	

8.3.1 Complex Body Condition Measurement Methods

The complex methods for body condition determination are highly accurate, precise, and objective; for these reasons, they are considered as reference methods in both humans and dogs (Burkholder and Toll 2000). However, they are mainly used for investigation purposes being limited in clinical practice due to their difficult performance and cost or time required. The mostly used methods include dual energy X-ray absorptiometry, deuterium oxide dilution, and bioelectrical impedance.

8.3.1.1 Dual-Energy X-Ray Absorptiometry (DEXA)

This method determines simultaneously the BF, LBM, and bone content (Pietrobelli et al. 1996). It is based on the fact that the emitted energy is absorbed at different degrees relative to the type of tissue it encounters, thus enabling clear imagining of

Table 8.3 Pros and cons of the most regularly used methods for body condition measurements

Type	Method	Humans		Dogs	
		Pros	Cons	Pros	Cons
Complex	DEXA	Accurate determination of the body fat, lean mass, and bone content (Rothney et al. 2009; Shiel et al. 2017)	Expensive, not practical or applicable in routine analysis (Laflamme 1997; Munguia-Izquierdo et al. 2018)	Accurate for assessing body fat and lean mass, small radiation dose, fast (Speakman et al. 2001)	Requires sedation or anesthesia, expensive, depends on lean tissue, hydration status, positioning accuracy, and patient position (Speakman et al. 2001; Santarossa et al. 2017)
	D_2O	Accurate estimation of total body weight, acceptable in all age groups (Wells and Fewtrell 2006)	Delayed results, inaccurate in diseases that affect hydration status (Wells and Fewtrell 2006)	Noninvasive, accurate estimation of BF indirectly (Burkholder and Thatcher 1998)	Depends on hydration status (Burkholder and Thatcher 1998)
	BIA	Noninvasive, simple and practical (Kopelman 2000)	Reliability of this method could be affected by the quality of electrodes used, intra-variability, body temperature, fasting, bladder condition, body positioning, menstrual cycle, etc. (Sergi et al. 2017)	Noninvasive, correlates with DEXA (German et al. 2010)	Poor precision and accuracy in dogs with high percentage of body fat; depends on hydration status (German et al. 2010)
Simple	Body weight	Objective, repeatable, can identify changes overtime	Does not quantify fat versus lean mass	Easy to perform, can indicate weight change (German and Morgan 2008)	Does not quantify fat versus lean mass, scales not calibrated (German and Morgan 2008)

(continued)

Table 8.3 (continued)

Type	Method	Humans		Dogs	
		Pros	Cons	Pros	Cons
	Anthropometric measures	Easy to use, correlates strongly with densitometry estimation of body fat percentage (Kopelman 2000)	Subjective, does not discriminate body fat from lean mass (Kopelman 2000)	Easy to use, estimates body fat percentage (Witzel et al. 2014)	Subjectivity in each determination (Witzel et al. 2014)
	Morphologic scales	Not used	Not used	Easy to use, conveys degree of body fat (Laflamme 1997; Witzel et al. 2014)	Highly subjectivity (Laflamme 1997; Witzel et al. 2014)

DEXA Dual-energy x-ray absorptiometry, *D_2O* Deuterium oxide dilution, *BIA* Bioelectrical impedance analysis

different tissues (fat mass (FM), LMB, and bone) (Rothney et al. 2009). This technique is considered the most extended system for determination of the body composition in humans (Shiel et al. 2017). In a similar manner, DEXA is a criterion-referenced method for determining bone mineral content and body composition in vivo in dogs (Speakman et al. 2001).

8.3.1.2 Deuterium Oxide Dilution (D_2O)

The fundament of this method is that body water is predominantly associated with nonfat tissue; therefore, a measure of total body water provides an indirect measure of fat-free mass. In humans, the D_2O is administrated, and, following equilibrium, the enrichment of the body water pool is measured in samples of either saliva, urine, or blood (Davies and Wells 1994). This is the best option to use in populations, where the normal hydration is known or can be assumed, being simple to carry out (Wells and Fewtrell 2006).

In dogs, D_2O dilution technique for the estimation of the body composition has been validated by Burkholder and Thatcher (1998) and is considered as a referenced method. In this species, the D_2O content is determined in serum samples obtained 2–4 hours after its administration, which then is used in an equation to calculate total body water, LBM, and FM (assuming that adipose tissue has minimal water content and that lean BM consists of 73% water) (Zanghi et al. 2013).

8.3.1.3 Bioelectrical Impedance

Bioelectrical impedance analysis (BIA) has emerged as a valid alternative for the assessment of body composition, given that it is relatively fast and inexpensive as compared to DEXA or D_2O, or even advanced technique images (such as magnetic resonance) (Sergi et al. 2017). Since it does not expose subjects to radiation risks, it can be repeated safely during the follow-up. Furthermore, because of its fast turn-around time, a large number of individuals can be examined in a short period of time (Böhm and Heitmann 2013). However, like other techniques, BIA represents some disadvantages when estimating body composition. These include factors that can influence the reliability of the measure: instrument-related factors (quality of electrodes, intra-variability), technician-related factors, subject-related factors (body temperature, fasting, bladder condition, body positioning, menstrual cycle, etc.), and environmental-related factors (temperature) (Sergi et al. 2017).

BIA has been used in dogs as a safe, noninvasive, and rapid method for assessing body composition (Santarossa et al. 2017); however, further studies are needed to validate this method for use in dogs since it was shown that BF can vary depending on electrode positioning, dog skin, different breed conformation, air temperature, etc., leading to both BF underestimation and overestimation (German et al. 2010).

8.3.2 Simple Body Condition Measurement Methods

8.3.2.1 Body Weight

Determination of body weight (BW) consists in an objective measure that is repeatable and capable of identifying changes over time. This tool exemplifies a simple technique, which is costless and, therefore, of open access for all people, although it is not capable of measuring the BF and LBM. In a similar manner, in dogs, the BW relative to the ideal BW or breed standard is used as a defining criterion for obesity (Burkholder 2001). However, the problems of using BW scale in dogs is that BW varies within breeds, and even more difficulties appear when the dog is mongrel, making it impossible to determine the body composition by this way alone (Burkholder 2001).

8.3.2.2 Anthropometric Measures

The most popular anthropometric measurements for body condition determination are the calculation of body mass index (BMI), the waist circumference (WC), and the skinfold thickness.

Body Mass Index

The BMI was firstly described by Quetelec in the nineteenth century and is the most widely applied system to study the overweight/obesity epidemiology in humans (Kopelman 2000). The BMI is calculated following the equation (Eq. 8.1):

$$BMI = \frac{Body\ weight\left(kg\right)}{\left[Height\left(m\right)\right]^2} \tag{8.1}$$

BMI individuals are categorized as underweight (BMI <18.5), normal weight (BMI 18.5–25.0), overweight (BMI 25.0–30.0), obese (BMI 30.0–40.0), and morbidly obese (BMI >40) (Kopelman 2000). This method correlates strongly with BF% through densitometry measurements, but it fails to discriminate between BF% and LBM (Kopelman 2000; Romero-Corral et al. 2008).

In the case of dogs, the attempt to calculate the BMI was made by different authors following the formula (Burkholder and Toll 2000) (Equation 8.2):

$$Canine\ BMI = \frac{Height\ at\ shoulder\left(cm\right)}{Height\ at\ shoulder\left(cm\right) * Body\ length\left(cm\right)} \tag{8.2}$$

where body length is the distance from the occipital protuberance to the base of the tail.

Furthermore, sex-specific morphometric measurement-based equations for BF percentage have been published (Equations 8.3 and 8.4):

$$Male\ BF\% = \left(-1.4 * TS\left(cm\right)\right) + \left(0.77\ XPC\left(cm\right)\right) + 4 \tag{8.3}$$

$$Female\ BF\% = \left(-1.7 * TS\left(cm\right)\right) + \left(0.93 * PC\left(cm\right)\right) + 5 \tag{8.4}$$

where TS is the distance from the tibio-tarsal joint to the stifle joint in cm and PC is the pelvic circumference at the level of the flank in cm. These sex-specific equations for BF percentage showed a good correlation (r = 0.948) with DEXA (Mawby et al. 2004).

The morphometric measurements in dogs have some limitations that should be taken into consideration. These include variability associated to the different conformation and size of different dogs (Witzel et al. 2014). In addition, this technique requires up to 10 min to accurately obtain the measurements, and the identification of the anatomical landmarks, and, therefore, results can differ among investigators resulting in bias (Burkholder 2001).

Waist Circumference

The waist circumference provides a simple and practical anthropometric measure for assessing central adiposity (Wei et al. 2006; Wells and Fewtrell 2006) and is determined by measuring at midpoint between lower border of ribs and upper border of the pelvis (in cm) in human beings (Kopelman 2000). Actually, an increasing

Table 8.4 Waist circumference action levels related to metabolic complication in humans

Level	Description	Men	Women
1	Increased risk	≥94 cm	≥88 cm
2	Substantially increased risk	≥102 cm	≥88 cm

Adapted from Kopelman (2000)

number of studies are reporting strong associations between the waist circumference, visceral adipose tissue, and obesity-related health risks (Hill et al. 1999; Sidney et al. 1999). In addition, it has been reported that the waist circumference is a better predictor of metabolic abnormalities than percent BF measured by bioimpedance method (Sidney et al. 1999) and correlates with metabolic syndrome indicators better than BF(%) determined by DEXA or BMI (Wei et al. 2006). Furthermore, different authors have suggested that the waist circumference, either singly or in combination with BMI, may have a stronger relation to some health outcomes than BMI alone (Han and Lean 1998; Janssen et al. 2004). Waist circumference action levels related to the metabolic complications are shown in Table 8.4. Nevertheless, using this system, the intra-abdominal (visceral) and intramuscular fat cannot be determined.

In dogs, although the waist circumference is considered for the BMI calculation (Formulas 8.3 and 8.4), this measurement alone is not used for overweight/obesity determination and/or monitoring.

8.3.2.3 Morphologic Scales

Morphologic scales are based on observation and palpation, and, unlike humans, they are commonly used in dogs due to its simplicity and fast performance. These methods include body condition score (BCS) and body fat index (BFI), which are currently the most used methods for body condition determination in dogs in investigation and clinics.

BCS is a subjective, semi-quantitative assessment of body composition that uses the body frame independent of BW (Burkholder 2001) with a range of categories from cachectic to severely obese (Mawby et al. 2004). This system consists in visual and palpation assessment of BF at various locations in the body (German et al. 2010) such as rib cage, pelvic bones, lumbar area, abdomen, and waist (Laflamme 1997). Different charts exist for BCS determination in dogs; the most frequently used ones are 9-point and 5-point scales and a BFI, which complements the first two (Table 8.5). All of them are based on palpable and visual characteristics. The 9-point scoring system and BFI were shown to present a strong correlation with DEXA in dogs (Laflamme 1997), while the 5-point scoring system was validated with D_2O (Paetau-Robinson et al. 2017). BFI is a relatively new method for BF determination and was designed to complement the BCS scales showing more accurate results when estimating dogs with BF up to 65% (Witzel et al. 2014).

Table 8.5 Different body composition scales to estimate the body fat percentage in dogs

	Corporal body fat	9-point BCS (Laflamme 1997)	5-point BCS (Laflamme 1997)	BFI (Witzel et al. 2014)	Description (Freeman et al. 2011)
Underweight	<5%	1/9	1/5		Ribs, lumbar vertebrae, pelvic bones, and all bony prominences evident from a distance. No discernible body fat
	5–9%	2/9			Ribs, lumbar vertebrae, and pelvic bones easily visible. No palpable fat. Some evidence of other bony prominence
	10–14%	3/9	2/5		Ribs easily palpated. Tops of lumbar vertebrae visible. Pelvic bones becoming prominent. Obvious waist and abdominal tuck
Normal	15–19%	4/9			Ribs easily palpable, with minimal fat covering. Waist easily noted (from above). Abdominal tuck evident
	20–24%	5/9	3/5		Ribs palpable without excess fat covering. Waist observed behind ribs when viewed from above. Abdomen tucked up when viewed from side
Overweight	25–29%	6/9	4/5	30	Ribs palpable with slight excess fat covering. Waist is discernible viewed from above but is not prominent. Abdominal tuck apparent
	30–34%	7/9			Ribs palpable with difficulty; heavy fat cover. Noticeable fat deposits over lumbar area and base of tail. Waist absent. No abdominal tuck. Obvious abdominal distention may be present
Obese	35–39%	8/9	5/5	40	Ribs not palpable under very heavy fat cover, or palpable only with significant pressure. Heavy fat deposits over lumbar area and base of tail. Waist absent. No abdominal tuck
	40–45%	9/9			Massive fat deposits over thorax, spine, and base of tail. Waist and abdominal tuck absent. Fat deposits on neck and limbs. Obvious abdominal distention
	46–55%			50	
	56–65%			60	
	>65%			70	

BCS body condition score, *BFI* body fat index

8.4 Analytical Alterations

8.4.1 Lipids

Many studies in humans and dogs have shown that obesity is associated with dyslipidemia. Dyslipidemia is an abnormal amount of lipids, such as cholesterol and triglycerides, in the blood and is a widely accepted risk factor for cardiovascular disease in humans. In humans, obesity-related dyslipidemia is primarily characterized by increased levels of plasma free fatty acids and triglycerides, decreased levels of high-density lipoprotein (HDL), and abnormal low-density lipoprotein (LDL) composition (Jung and Choi 2014). In obese individuals, adipose tissue (mainly intra-abdominal) releases increased amounts of non-esterified fatty acids (NEFAs) that provide substrate for triglyceride synthesis in the liver and for triglyceride-rich very low-density lipoprotein assembly and secretion (Bailhache et al. 2003). At the same time, increased hepatic lipase activity (usually found in the state of insulin resistance) reduces HDL cholesterol levels (Bailhache et al. 2003).

In canine obesity, modifications of the lipoprotein profile are also common changes. However, the alterations observed differ from those in humans since the circulating concentrations of both LDL and HDL-cholesterol are usually increased in obese dogs (Tvarijonaviciute et al. 2010b; Tribuddharatana et al. 2011). Although some speculations exist, it is not clearly the exact explanation for these differences between dog and human lipid metabolism.

8.4.2 Adipokines

Adipokines are the cytokines produced and secreted by white adipose tissue, which directly or indirectly modulate different metabolic processes in the organism (Osto and Lutz 2015). Although numerous adipokines have been described, the most studied ones are leptin and adiponectin (Clark and Hoenig 2016).

Leptin is abundantly expressed in adipose tissue and is involved in the regulation of energy homeostasis (Friedman and Halaas 1998). It inhibits appetite and food intake and stimulates energy expenditure (Friedman and Halaas 1998). However, circulating leptin levels are increased in obese humans and dogs probably due to the existence of leptin resistance (Considine et al. 1996; Friedman and Halaas 1998; Hoenig 2014). This resistance and the concurrent reduction of the body's energy metabolism may contribute to further weight gain in obese subjects because the brain is unable to adequately "measure" the body's adipose tissue reservoirs (Osto and Lutz 2015).

Leptin is positively correlated with fat mass in humans and dogs (Considine et al. 1996) being considered as a marker of adiposity in both species (Ricci and Bevilacqua 2012). It increases and decreases in response to weight gain and weight loss, respectively, but also increases more acutely in response to food intake (Weigle

et al. 1997; Romon et al. 1999; Ishioka et al. 2005; Jeusette et al. 2005, 2006). It is important to be cautious with the interpretation of plasma leptin concentrations because of the influence that several conditions could have on their concentrations. Thereby factors such as fasting (24–72 hours) (Kolaczynski et al. 1996), emotional stress (Otsuka et al. 2006), physical exercise (Hickey et al. 1997), testosterone and estrogen levels (Ahima and Flier 2000), or dexamethasone administration (Considine et al. 1997) have been shown to effect circulating leptin values. Similarly, circadian rhythm, feeding state, treatments, and thyroid gland activity (Ricci and Bevilacqua 2012) have been reported to influence leptin concentrations in dogs. Particular attention should be paid with regard to feeding state since serum leptin concentrations increase up to 5 folds in response to food intake (Ishioka et al. 2005). Thus, concentrations of this adipokine should be strictly determined in fasting, treatment, and, if possible, stress-free patients.

Adiponectin is an adipokine synthesized and secreted mainly by the adipose tissue, but recently other tissues, although in a lower level, were shown to secrete this protein (Katsiougiannis et al. 2006). Adiponectin in blood circulates in three different forms: trimer, hexamer (which is also called low-molecular-weight oligomer (LMW)), and high-molecular-weight multimers (HMW). All forms have different biological activities, and HMW is thought to be the most active form (Sinha et al. 2007). Several studies have shown that obese humans have significantly lower adiponectin concentrations (mainly HMW) than non-obese subjects and that adiponectin negatively correlates with body fat accumulation in both men and women (Arita et al. 1999). Hypoadiponectinemia in obese people is a consistent finding that results in loss of protective insulin sensitization, enhanced fatty acid metabolism, and anti-inflammatory actions of adiponectin (Ouchi et al. 2011). However, studies in dogs show variable results for adiponectin concentrations in obese dogs. Some studies, in a similar way to what occurs in humans, describe lower circulating adiponectin concentrations in obese dogs and detect negative correlation between this adipokine and fat mass, while others do not detect significant differences (Ishioka et al. 2006; Tvarijonaviciute et al. 2010a; Verkest et al. 2011b). Discrepancies also exist with regard to adiponectin concentrations after weight loss since some studies reported an increase in circulating adiponectin (Tvarijonaviciute et al. 2012a, b) where others found no effect in dogs (Wakshlag et al. 2011; Bastien et al. 2015). The possible explanation for all these discrepancies may be related with (1) the studied populations, since adiponectin presents high inter-individual variability, degree of obesity, and weight loss "amount" (as in humans, the decrease of a minimum of 10% of weight was shown to be necessary to detect improvement in adiponectin concentrations), and with (2) the different methods used for its determination in terms of the assay sensitivity and performance (Verkest et al. 2011b; Tvarijonaviciute et al. 2012a, c; Clark and Hoenig 2016). Furthermore, adiponectin decreases in inflammation and is affected by sex hormone changes in female dogs (Tvarijonaviciute et al. 2011a, 2013a). On the other hand, contrarily to leptin, adiponectin concentrations do not appear to be influenced by diurnal, fasting-eating/feeding cycles in humans or dogs (Merl et al. 2005; Tvarijonaviciute et al. 2012c).

It must be pointed out that although initially restricted to metabolic activities (regulation of glucose and lipid metabolism), adipokines currently represent a new family of proteins that can be considered key players in the complex network of soluble mediators involved in the pathophysiology of immune/inflammatory diseases (Francisco et al. 2018). Thus, in order to evaluate concentrations of adipokines, including adiponectin and leptin, in obesity, the inflammatory status of a patient should be taken into account in both humans and dogs (Yilmaz et al. 2008; Francisco et al. 2018).

8.4.3 Inflammatory Biomarkers

Obesity is associated with pathological changes in adipose tissue morphology, including infiltration of immune cells, and obese individuals have higher circulating levels of inflammatory markers than lean individuals (Herder et al. 2005, 2006).

The inflammatory process that occurs in obese people differs from the classical inflammatory response in certain aspects. This inflammatory process manifests itself systemically and is characterized by a chronic low-intensity reaction. In this context, the Toll-like receptor (TLR4) signaling pathway has been recognized as one of the main triggers in increasing the obesity-induced inflammatory response. This pathway responds to the increased exposure to saturated fatty acids and to LPS. Both of these are relevant in the context of obesity, with saturated fatty acids arising from within the adipose tissue triglyceride stores and the LPS arising from increased intestinal permeability perhaps due to an altered gut microbiota (Rogero and Calder 2018; Stephens et al. 2018).

Adipose tissue contains adipocytes (see above) and infiltrated macrophages, both of which release a spectrum of inflammatory mediators, including acute-phase proteins (like PAI-1), cytokines (like IL-6, TNFα), and chemokines (like MCP1). Consequently, circulating levels of inflammatory markers are elevated in human obese subjects and associate with obesity-related parameters (Weisberg et al. 2003; Kim et al. 2006; Maury et al. 2009; Maury and Brichard 2010).

Unlike humans, the involvement of inflammatory markers in canine obesity and weight loss is less clear. There is one report which showed that the cytokines and chemokines IL-6, MCP-1, and TNFα are expressed in adipose tissue depots of dogs (Ryan et al. 2010). Recently, concentrations of interleukin-6 (IL-6) and monocyte chemoattractant protein-1 (MCP-1), but not IL-8, were found to be increased in overweight dogs (Frank et al. 2015), whereas another study found decreasing concentrations of IL-8 and other interleukins with weight loss in dogs (Bastien et al. 2015). C-reactive protein (CRP) and MCP-1 have been reported to decrease with weight loss in some but not in other studies (German et al. 2009; Wakshlag et al. 2011; Tvarijonaviciute et al. 2012b; Bastien et al. 2015). Evidences exist that acute weight gain does not produce significant changes in positive acute-phase proteins in the dog (Tvarijonaviciute et al. 2011b). However, chronic obesity could predispose the development of inflammation (Tilg and Wolf 2005; Tvarijonaviciute et al. 2012a).

8.4.4 *Insulin Resistance, Hyperinsulinemia, and Glucose Concentrations. Relationship with Diabetes Mellitus*

One of the most well-recognized changes that occur with excess of the adiposity is insulin resistance, or a diminished cellular response to a given plasma insulin concentration (Saltiel and Kahn 2001). In humans, it has been shown that obesity leads to insulin resistance in all three major metabolic organs (adipose tissue, muscle, and the liver) (Conte et al. 2012). That is, in obese individuals, the responses to insulin in these organs are blunted, and higher concentrations of insulin are needed to keep plasma glucose and free fatty acid concentrations within normal limits. During everyday conditions, these higher concentrations of insulin are supplied endogenously: plasma insulin concentrations in obese humans are 20–50% greater than in lean humans (Conte et al. 2012).

Insulin sensitivity and resistance are classically assessed by the euglycemic–hyperinsulinemic clamp (EHC), in which insulin is infused at a variable rate to keep blood glucose within a set of predetermined parameters. The infusion rate necessary to accomplish this is an indicator of the response of peripheral tissues to insulin, that is, the lesser insulin necessary to control blood glucose, the more insulin-sensitive the individual (Clark and Hoenig 2016).

Insulin resistance with elevated fasting plasma insulin concentration and insulin to glucose ratio has also been demonstrated in obese dogs (Gayet et al. 2004; German et al. 2009). In addition, an improvement of insulin sensitivity after successful weight loss has been reported (German et al. 2009). Traditionally, compensatory hyperinsulinemia has been thought to result from an increase in beta cell mass (Weir et al. 2001; Saisho et al. 2013). However, decreased insulin clearance has been shown in obese, hyperinsulinemic dogs (Ader et al. 2014). Insulin resistance has also been demonstrated in obese dogs using EHC (Mattheeuws 1984), and decreased glucose clearance in obese dogs, starting at gain of 40% over lean body weight, has been shown using intravenous glucose tolerance tests (Bailhache et al. 2003).

Despite peripheral insulin resistance, obese dogs are able to maintain normal plasma glucose concentrations for extended periods of time. In addition, plasma glucose concentrations do not necessarily rise with obesity or decline with weight loss in dogs (Mattheeuws 1984; German et al. 2009; Tvarijonaviciute et al. 2012a) since although one study reported fasting hyperglycemia in some obese dogs (Tvarijonaviciute et al. 2012a), others did not find this (Verkest et al. 2010, 2011a, 2012).

Obesity is a known risk factor for type 2 diabetes mellitus in humans. Insulin resistance is thought to be involved in this predisposition, and it has been postulated that the increased secretory demand associated with obesity-induced insulin resistance eventually leads to depletion of pancreatic insulin stores and beta-cell exhaustion (Prentki and Nolan 2006). However, the latter mechanism has been demonstrated primarily in situations of preexisting beta-cell compromise, and many humans never develop diabetes mellitus, despite years of insulin resistance. Therefore, long-term

peripheral insulin resistance is not a sole prerequisite for the progression to a diabetic state, and concurrent beta-cell functional compromise must be present.

The relationship between obesity and diabetes mellitus in dogs is less clear; dogs might be protected from the development of type 2 diabetes by either compensating adequately for obesity-induced insulin resistance or by additional factors. Obese dogs appear to compensate for years of insulin resistance by maintaining high fasting insulin concentrations and an increased first-phase insulin secretion during glucose tolerance tests (Verkest et al. 2012). Other factors may also protect dogs from obesity-induced diabetes, i.e., factors that are involved in the pathophysiology of β-cell failure in humans and cats but not in dogs. The most important of these factors may be the lack of amylin-derived islet amyloid in canine diabetes since contrarily to humans and cats, canine amylin does not aggregate and does not form pancreatic islet amyloid in diabetes. Therefore, because islet amyloid is absent in obese and diabetic dogs, this species may be protected from the development of diabetes mellitus in obesity (O'Brien et al. 1990; Jordan et al. 1990).

8.4.5 Other Biomarkers

8.4.5.1 Cholinesterases (ChEs)

Butyrylcholinesterase (BChE, EC 3.1.1.8) is a non-specific ChE since although it hydrolyzes butyrylcholine at a higher rate, it also hydrolyzes acetylcholine and propionylcholine. BChE presents a significant positive correlation with the BW, BMI, and different serum analytes related to adiposity, such as triglycerides and total cholesterol (Randell et al. 2005; Calderon-Margalit et al. 2006; Iwasaki et al. 2007). Similarly, a correlation between BChE and the cholesterol profile and triglycerides has been reported in canine obesity (Tvarijonaviciute et al. 2010b, 2013b). In dogs, and experimentally induced overweight/obesity models, it was associated with the increased activity of BChE in serum (Tvarijonaviciute et al. 2010b) decreasing after successful weight loss (Tvarijonaviciute et al. 2013b). As a mechanism, it has been proposed that an incremental flux of free fatty acids from adipose tissue to the liver might stimulate the hepatic synthesis of plasmatic BChE (Cucuianu et al. 2002). On the other hand, increased activity of BChE was related to reduced levels of acetylcholine, an anti-inflammatory molecule, predisposing overweight in humans and dogs to local and systemic inflammatory disease (Das 2007). Thus, increased activity of BChE could be considered another factor responsible for the low-grade inflammatory status development in chronic overweight/obesity in both humans and dogs.

8.4.5.2 Ghrelin

Ghrelin is a peptide that has a unique structure with 28 amino acids secreted mainly in the stomach and is the only known circulating appetite-stimulating (orexigenic) factor being a potent stimulator of food intake and growth hormone secretion

(Álvarez-Castro et al. 2013; Dodds 2017). Ghrelin circulates in the bloodstream in two different forms: acylated and desacylated. It was thought that acylated ghrelin was the only active form of ghrelin, but some studies showed that desacylated ghrelin has also multiple biologic activities and can even counteract some of the metabolic responses of the acylated ghrelin (Gauna et al. 2005; Liu et al. 2008). Therefore, it was suggested that measuring acylated and desacylated, and total ghrelin separately, might provide further information on the role of ghrelin in the regulation of glucose homeostasis (Ukkola 2011).

Blood levels of ghrelin rise during fasting and fall rapidly after a meal consumption, indicating that ghrelin output is regulated by caloric intake (Klok et al. 2007). In humans, plasma levels of this peptide were inversely correlated with body weight being reduced in obesity possibly due to its hyposecretion (Álvarez-Castro et al. 2013). Similarly to that described in humans, obese dogs presented lower plasma ghrelin, while weight loss results in an increase in its plasma concentrations (Jeusette et al. 2005). In addition, studies in dogs suggested that ghrelin is more influenced by BW than by food consumption in this species (Jeusette et al. 2005).

It is important to highlight that care must be taken when measuring and interpreting ghrelin concentrations since their levels are altered by the fast/meal (Klok et al. 2007; Álvarez-Castro et al. 2013) and acylated ghrelin is highly unstable in both humans and dogs (Kanamoto et al. 2001).

8.5 Consequences

8.5.1 Health

Obesity was associated with the negative health outcomes in both humans and dogs resulting in decreased health-related quality of life (HRQoL) (German et al. 2012; Olszanecka-Glinianowicz et al. 2014; Yam et al. 2016) (Muñoz-Prieto et al. 2018).

The main mechanisms that lead obesity to cause divergent diseases can be grouped into two main groups:

1. *Mechanical*. Increasing body mass due to increasing fat is accompanied by excessive load to the joints, resulting in orthopedic diseases, restriction of the respiratory execution resulting in altered respiratory function, increased pressure due to visceral fat that worsens incontinence, and alterations in total blood volume leading to cardiac dysfunction (Kopelman 2000; German 2006; Raffan 2013).
2. *Metabolic*. Adipose tissue is an active endocrine organ that secretes a number of metabolically active analytes. Chronic excess of white adipose tissue results in an imbalance in the insulin-metabolism-related and pro- and anti-inflammatory molecules (see Sect. 8.4 for more details) leading to insulin resistance in both humans and dogs (Kopelman 2000; German 2006; Raffan 2013).

Table 8.6 Obesity-related pathologies in humans and dogs

Obesity-related disorders
Metabolic abnormalities
Endocrinopathies
Orthopedic disorders
Cardiovascular disease
Respiratory system dysfunction
Urogenital system
Neoplasia
Decreased life span

In the long run, the interaction of the two mechanisms, mechanical and metabolic, results in the impairment of different organ systems increasing the probability to suffer obesity-related diseases and decreased life span of both obese humans and dogs (Table 8.6) (Kealy et al. 2002; Weeth 2016; Fruh 2017). It is important to highlight that approximately 20% of all cancer cases in humans, including those of gastrointestinal and urinary tract among others, were attributed to the excess of weight (Wolin et al. 2010; Boutari and Mantzoros 2018). Although, to date, the mechanisms linking obesity and cancer were not fully elucidated, evidences exist that chronic insulin resistance, inflammation, and increased growth factor production due to increased adiposity could be the main mechanisms (Donohoe et al. 2017; Boutari and Mantzoros 2018; Stone et al. 2018).

8.5.2 Economic

A number of studies in different countries were performed to estimate the economic consequences of human obesity (van Baal et al. 2008; Swinburn et al. 2011; Cawley and Meyerhoefer 2012; Cawley 2015; Kim and Basu 2016; Biener et al. 2017; Fallah-Fini et al. 2017), while information about the health-care costs of obese dogs is very scarce (Bomberg et al. 2017). According to Biener et al. (2017), the estimates of the obesity-related medical costs are important because they are necessary (1) to calculate the cost-effectiveness of obesity prevention programs, treatments, and policies; (2) to target weight loss programs; and (3) to correct public policy making.

In humans, the medical costs in US health-care system rise highly in obese individual, in average $3429 per year (in 2013 dollars) (Biener et al. 2017). Overall, it was estimated that 20.6% of US national health expenditures are spent for obesity-related disease treatment (Cawley and Meyerhoefer 2012). However, it is important to highlight that expenditures related to BMI are not linear, but are J-shaped (Fig. 8.1). This means that expenditures are almost equal for normal weight and overweight persons and rise rapidly for the BMI range 35–40 and especially for those with BMI >40 (Biener et al. 2017). The McKinsey Global Institute (2014) estimated that the global impact of obesity is about $2.0 trillion (2.8% of

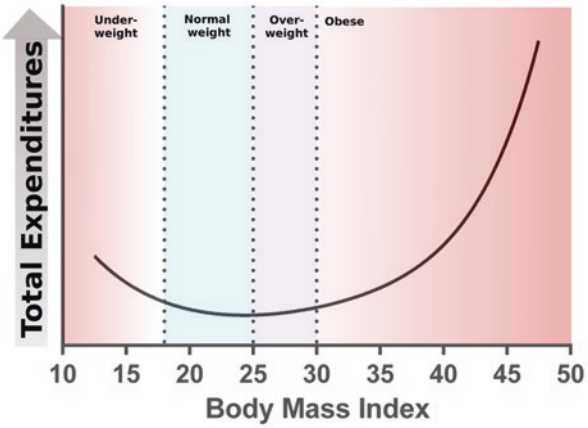

Fig. 8.1 Predicted relationship between body mass index and annual medical care expenditures for adults in the USA. (Adapted from Biener et al. (2017))

worldwide GDP), an amount almost equal to that of smoking and war, violence, and terrorism. Furthermore, the increased morbidity of the obese persons results in higher absenteeism rates, or workers who still assist to work are less productive, the fact that was estimated to have additional $1.1 trillion per year economic impact (Witters and Agrawal 2011).

In canine obesity, in a similar manner as described in humans, the average medical costs were 17% higher than of normal weight dogs (Banfield Applied Research and Knowledge. 2015). Bomberg et al. (2017) estimated that in the USA, obesity-related costs in dogs could reach $76.68 billion.

8.6 Conclusions

In this chapter, we have discussed the main causes of obesity in human and dogs, and we have highlighted the important problems that are associated with this condition. There are many links between human and canine obesity both in causes and consequences and in physiopathological mechanisms. In particular, the dog ownership constitutes a very interesting model to study the relations between human and canine obesity. One of the factors to combat obesity and increase well-being was reported to own a dog (Christian et al. 2013; Mubanga et al. 2017). However, it is also true that not in all cases this works, and furthermore, the presence of obesity in dogs due to the owner behavior with respect to dog routine care was reported, and the possible relationship between owner and dog obesity was suggested (Muñoz-Prieto et al. 2018). Further efforts in the prevention of human and canine obesity should be performed with a special focus in the benefits that the relationship human-dog can have in decreasing obesity and improving lifestyle in both humans and dogs.

Acknowledgments This work was conducted in the framework of the European Cooperation in Science and Technology (COST) Action TD 1404 "Network for the Evaluation of One Health." Financial support was provided by a grant from the Robles Chillida Foundation through its support program for the promotion of research in Health Sciences and the program "Ramon y Cajal" of "Ministerio de Economia y Competitividad," Spain, through a postdoctoral grant to AT. The University of Murcia funded AMP through a predoctoral grant. The funders had no role in study design, data collection and analysis, decision to publish, or the preparation of the manuscript.

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