1. Introduction

Throughout the preceding decade, there has been widespread recognition that a specific constellation of clinical abnormalities, collectively known as the “metabolic syndrome” or “cardiometabolic syndrome,” portends significant risk for, amongst others, cardiovascular disease and diabetes in affected people.1–7 The metabolic syndrome affects ~27% of adults in the United States, and its prevalence continues to increase as obesity and lack of physical activity become progressively more common in modern society.3,6,7 Obesity and insulin resistance (IR) (or glucose intolerance) represent the cornerstone of the definition of metabolic syndrome.1–7 Other clinical abnormalities that contribute to the definition of human metabolic syndrome include hypertension, atherogenic dyslipidemia (hypertriglyceridemia, low high-density lipoprotein [HDL] cholesterol, and high low-density lipoprotein cholesterol), presence of a prothrombotic state (elevated plasma concentrations of fibrinogen and plasminogen activator inhibitor-1), and presence of a proinflammatory state (elevated C-reactive protein).8

Although it has long been recognized that metabolic syndrome is associated with obesity, it has more recently become evident that it is excessive visceral fat (omental and mesenteric fat depots) rather than total fat that is the principle metabolic risk.9,10 Genetic and gestational factors also have been linked to a pre-disposition to IR; sedentary lifestyle, acquired visceral obesity, and other factors are more likely to precipitate the cardiovascular and endocrinopathic consequences of IR in those individuals that have been born with IR.11–13 That laminitis in horses is commonly associated with obesity and IR has led to the (controversial) use of the term “equine metabolic syndrome,” although some specific aspects of the human syndrome characteriza-
tion are lacking for horses. Specifically, although there seems to be an association between obesity and IR regarding the risk of laminitis, there is currently a paucity of data pertaining to the role of hypertension, inflammation, procoagulable state, and dyslipidemia in the equine metabolic syndrome.

In the absence of substantial epidemiological data, obesity in horses and ponies has commonly been suggested to be a risk factor for laminitis. It is reasonable to infer that, by virtue of relatively increased weight bearing, obesity could contribute to an increased likelihood of laminitis simply through the effect of the additional force of distraction at the level of the hoof-lamellar interface. However, there is evidence that ponies (reduced body weight compared with horses) are at greater risk for the development of laminitis than horses. Evidence has been published to support the hypothesis that IR does indeed represent an important metabolic and hormonal pre-disposing factor for laminitis in ponies. Moreover, there seems to exist an underlying genetic pre-disposition to the development of IR in some breeds of ponies.

Relative to horses, IR has been more readily seen in (certain) pony breeds. Laminitis has been commonly associated with both Cushing’s syndromes (pituitary pars intermedia dysfunction [PPID]) and the exogenous administration of synthetic glucocorticoids. A satisfactory explanation for the mechanism by which glucocorticoids might cause laminitis is presently lacking. However, glucocorticoids represent a potent cause of IR. Whether or not glucocorticoid-associated IR leads to laminitis is unknown; glucocorticoids could theoretically lead to laminitis risk through multiple diverse pathways.

Compelling experimental data have been published to suggest that glucose is essential for the health and strength of the equine hoof-lamellar interface. Hemidesmosomes (HD) represent the important attachment link between keratinocytes and the underlying lamellar basement membrane. Keratinocyte glucose starvation may weaken HD, which leads to separation of the keratinocyte from the basement membrane. Situations associated with cell-glucose starvation, such as IR, might increase the risk for laminitis.

In insulin-resistant states, those tissues that depend on insulin to facilitate cellular glucose uptake are relatively deprived of glucose (energy) compared with those tissues that do not depend on insulin. However, it has not been ascertained whether or not equine hoof lamellar keratinocytes are responsive to insulin. Being a part of the integument, an argument could be made that insulin does not play a role in the promotion of glucose availability to keratinocytes. Because glucose supply should be abundant, keratinocytes might not be (relatively) starved of glucose because of IR. That being the case, an alternative mechanistic explanation for the risk of laminitis associated with IR and obesity should be determined.

Stimulated glucose uptake by insulin-responsive cells is facilitated by the presence of type-4 glucose transporters (GLUT-4). In the presence of insulin, GLUT-4 is inserted into the cell membrane such that the movement of glucose from the extracellular fluid into the cytoplasm is increased. Although GLUT-4 has been demonstrated in equine hoof lamellar keratinocytes, it has not been ascertained if its insertion into the cell membrane is regulated by insulin or a different mechanism. Interestingly, the expression of GLUT-4 (and GLUT-1) by equine hoof keratinocytes seems to be reduced in chronic laminitic states.

2. Endocrinopathic Consequences of Obesity

Substantial new information regarding the endocrinopathic consequences of obesity has been made available from the human and laboratory animal perspective in the last few years. However, much less work has been published regarding the consequences of obesity on equine health. Our team has been interested in the role that glucocorticoids might play in terms of risk of laminitis.

In this context, glucocorticoids are important from the perspectives of both their direct implication for risk of laminitis in horses and their potential role as a cause of IR. Moreover, newer work in humans suggests that glucocorticoids play a critical role in the development of visceral obesity and metabolic syndrome.

3. “Thriftiness”

As a herbivorous species, horses evolved with a reliance on grass forage for their nutritional requirements. Accordingly, during the fall season, horses ingest increasing quantities of grass and gain adiposity in preparation for the winter season when food tends to be relatively scarce. Stimulated appetite and adipogenesis at this time along with the acquisition of a thick haircoat are kindled in herbivores by an increase in the secretion of pro-opiomelanocortin peptides from the hypothalamic-pituitary axis. These changes represent a critical survival mechanism that affords the provision of (stored) energy, in the form of body fat, throughout the winter months.

In nature, the period of environmental harshness is finite, and the acquired fat stores should be depleted before the onset of spring and the growth of new grass. In the healthy state, the acquisition of adipose tissue is, therefore, important for survival, but the acquisition of excessive adiposity and its chronic persistence exert diverse adverse effects on the health of the individual. Both IR and the development of a mild to moderate proinflammatory state have been regarded as key components of the survival mechanism during this limited period of environmental harshness. Additionally, both seem to develop and resolve parallel with the acquisition
and depletion of additional adiposity at the onset and conclusion of winter.

Some animals, by virtue of the impositions of natural selection, have inherited genetic traits that have facilitated their survival through periods of environmental harshness. These animals are said to have inherited “thrifty genes.” Although it is likely that multiple diverse physiological processes contribute to the concept of thriftiness, IR seems to be an important component. A good example of the effect of natural selection on thriftiness is the Ossabaw Island swine. After abandonment on a barrier island off the coast of Georgia (Ossabaw Island) by Spanish colonists ~500 yr ago, isolated swine evolved a thrifty genotype to survive seasonal cycles of feasting and famine. When allowed to consume excess food in “modern” captivity, these Ossabaw Island swine quickly develop the highest levels of total body lipid of any mammal as well as IR, impaired glucose tolerance, hypertriglyceridemia, and hypercholesterolemia compared with lean Ossabaw and domestic swine. Ossabaw Island swine develop coronary atherosclerotic lesions that are virtually indistinguishable from lesions in humans. To that end, these swine are currently being investigated as “large-animal” models of metabolic syndrome with relevance to human medicine.

Another example of the inheritability of the thrifty genotype is the Pima Indian tribe in the southwestern United States. Historically, the Pima Indians were lean and active; however, exposure to inactivity and modern Western diets have produced obesity in the majority of adults and the highest incidence of type-2 diabetes in the world. The extent to which different breeds of horses have inherited thrifty genes requires further investigation, but it is reasonable to consider that some pony breeds, being more insulin resistant than horses, may represent equine-specific examples of this phenomenon.

4. Fat Tissue Acts Like a Gland

Adipose tissue is no longer regarded as either a simple repository of stored energy or a passive, space-filling connective tissue. Since the discovery that leptin is an adipocyte-specific secretory protein in 1994, the role of adipose tissue as an endocrine organ with novel implications for the pathogenesis of disease in obese individuals has broadened exponentially. The results of this work have led to a new field of study called adipobiology. Adipose tissue is unique in that it is characterized by a remarkable potential to expand, a property that is vital for staving off the risk of starvation; however, when persistent, this trait increases the risk of obesity-associated conditions such as vascular disease and diabetes. Although there exist two major (white) adipose-tissue repositories in the body at the visceral and the SC locations, many other smaller deposits are present at numerous locations including the epicardium, peri-cardium, kidneys, adrenal glands, brain, and around large blood vessels. Smaller, organ-specific adipose tissue is being recognized as an important modulator of local organ function/dysfunction in the obese state.

Although, at first glance, the histological appearance of adipose tissue is similar regardless of its location, new exciting findings are showing that the cellular composition and secretory capacity of adipose tissues from different locations is quite variable. The most pronounced regional difference between tissue locations is that between adipose tissues in the SC versus the visceral locations. As noted above, the risk of vascular dysfunction and diabetes in obese individuals is much greater for visceral obesity than it is for SC obesity.

Obesity is defined as an expanded mass of adipose tissue within the body. Although mature adipocytes represent the most numerous and prominent cell type within adipose tissue, other cells probably play an equally important role in the endocrinological function of adipose tissue. Other cells that are important in this context include stromal cells such as macrophages, fibroblasts, and pre-adipocytes. The role of endothelial cells and nerve fibers within adipose tissue should not be ignored. For example, visceral adipose tissue is specifically and distinctly characterized by a population of tissue-specific macrophages.

Before the discovery of leptin (and subsequent adipokines), obesity had been linked with IR, and the release of fatty acids from visceral adipose tissue was believed to be specifically important in this context. For example, obesity is accompanied by elevated plasma levels of non-esterified fatty acids that contribute to IR in skeletal muscle and tend to cause hepatic lipid infiltration. The recognition that adipose tissue releases a plethora of multifunctional adipokines has led to substantial rethinking of the mechanisms responsible for the risk of cardiovascular and endocrinological diseases associated with obesity. In fact, adipokines have recently been claimed to represent the “missing link” between IR and cardiovascular disease.

5. Adipokines or Adipocytokines

Adipose tissue-derived effector molecules include cytokines, chemokines, prostaglandins, growth factors, enzymes, hormones, complement factors, and matrix proteins. Collectively, the constellation of adipose tissue-derived secreted products has been referred to as adipokines (or adipocytokines). In excess of 100 different adipokines have been described that impart physiological relevance to lipid and glucose homeostasis, inflammation, hemostasis, osteogenesis, hematopoiesis, complement activities, reproduction, angiogenesis, blood pressure, and feeding behavior. It is the secretion of inappropriate quantities of adipokines over time that represents the basic pathophysiological foundation of many (if not most) of the health consequences of
Some adipokines are secreted in sufficient quantities that they exert a whole-body (endocrine) influence, whereas others exert their influence locally within the adipose tissue itself or in adjacent tissues and structures (paracrine and autocrine effects). Little is known of the functional significance of many of the adipokines, many of which likely exert their actions locally within the adipose tissue itself.\(^52,53\)

A complete discussion of the (presently) known adipokines is beyond the scope of this manuscript; however, there has been substantial interest in some specific adipokines. Many adipokines affect and modulate the immune system with a net effect leading to a state of chronic systemic inflammation. An incomplete list of adipokines that are known to affect inflammation should include interleukin-6 (IL-6), tumor necrosis factor-α (TNFα), IL-1β, IL-8, IL-18, leptin, adiponectin, resistin, plasminogen activator inhibitor-1 (PAI-1), and macrophage migration-inhibition factor.\(^45\) Plasma-leptin concentration is correlated with the overall adiposity of the body (higher plasma leptin levels are detected in obese individuals).\(^29\) Although several diverse functions have been attributed to leptin, an important function is its ability to signal within the central nervous system (CNS) to inhibit appetite (regulated through neuropeptide Y) in the face of developing obesity. That appetite is not necessarily suppressed suggests that interference with leptin signaling may play a role in the development of obesity in some individuals with elevated plasma-leptin concentrations. This phenomenon has been referred to as “leptin resistance.”\(^54\)

It has been suggested that leptin resistance is the most common cause of metabolic syndrome and obesity in other species and that, if an individual lives long enough, most people eventually develop leptin resistance in time.\(^54\)

Whereas leptin is secreted by adipocytes in adipose tissue, TNFα is secreted by macrophages that inhabit some adipose tissues, notably visceral adipose tissue.\(^49\) IL-6 is secreted by both adipocytes and macrophages.\(^45\) That visceral adipose tissue is inhabited by immune cells (macrophages) and, therefore, acts as a source of inflammatory mediators is both surprising and important from the perspective of linking visceral obesity with a higher risk of cardiovascular disease.\(^49\) A satisfactory explanation for the incursion of macrophages into visceral adipose tissue as it expands during a state of protracted positive energy balance is currently lacking but represents an area of active investigation.

Accordingly, obesity has been recognized as a pro-inflammatory condition.\(^8,45\) For example, TNFα is a pro-inflammatory cytokine produced by both non-adipose and adipose tissues. Elevated secretion of TNFα in the obese individual contributes to the development of IR, increased lipolysis, and increased procoagulant activity (all of which are important components of metabolic syndrome). Insulin resistance results from the inhibition of tyrosine-kinase phosphorylation of the insulin receptor by TNFα, which leads to defective insulin signaling.\(^54\)

Therefore, obesity may act to promote IR through several different mechanisms, including both the release of excessive quantities of non-esterified fatty acids and the elaboration of endocrinological mediators.\(^45,50,56\)

Local adipose tissue-derived TNFα has been implicated in the pathogenesis of thyroid-associated ophthalmopathies (paracrine influence from orbital adipose tissue)\(^57,58\) and in Crohn’s disease (paracrine influence from mesenteric adipose tissue).\(^59\)

Another excellent example of the potential role of local adipose tissue on an underlying organ is the situation in the subepicardial adipose tissue in immediate proximity to the left anterior descending (LAD) branch of the coronary artery. It has been known since 1933 that this adipose tissue site is important for local energy supply (very high capacity for free fatty-acid release and uptake).\(^60\) More recently, it has been shown that it is that part of the LAD branch that courses through the epicardial adipose tissue in which the most severe atherosclerotic lesions develop.\(^60\) The implication is that it is the proximity of this specific adipose repository that is directly responsible, thorough paracrine influence, for the development of atherosclerosis.\(^48\)

Therefore, the classic paradigm that adipose tissue is a benign connective tissue that acts to store energy in the form of triglycerides is being aggressively reevaluated.

IL-6 has also been strongly implicated in the pathogenesis of vascular disease and diabetes.\(^61\)

This adipokine is produced to a much greater extent by visceral compared with SC adipose tissue.\(^52\)

A central role for IL-6 in the pathogenesis of obesity-associated cardiovascular disease is based on the fact that it stimulates increased fibrinogen and C-reactive protein synthesis by the liver, it reduces HDL cholesterol, it promotes platelet aggregability, and it induces the expression of adhesion molecules by endothelial cells.\(^52\) The circulating concentration of PAI-1 is closely associated with visceral obesity; increased PAI-1 has been linked to both risk of thrombosis and development of IR.\(^53\)

Therefore, the long-term presence of adipose tissue exerts endocrinopathic (e.g., IR and activation of inflammation) and local (paracrine) effects on organs and tissues throughout the body. Conceptually, adipose tissue has been transformed from a passive energy-storage organ to an endocrinologically significant gland.\(^62\)

As noted above, although there has been a historic tendency to attribute much (most) of the adverse health effects of visceral obesity to IR, other important metabolic abnormalities, including hypertension, dyslipidemia, and glucose dysregulation, have been recognized as playing an important role. Among these has been the recognition that upregulated inflammation is also an important component of the pathophysiological perturbations that
link the development and persistence of obesity with risk for cardiovascular disease. That obesity leads to the production of many different adipokines with inescapable consequences for the health of the individual has led to remarkable growth in the field of adipobiology in the past few years with potential impact in both the basic and the applied aspects of the discipline. Identification of therapeutic strategies that effectively reduce the ratio of proinflammatory, insulin-desensitizing adipokines to anti-inflammatory, insulin-sensitizing adipokines represents a major goal of adipobiological research aimed at the treatment of obesity.

6. The Cellular and Molecular Basis of Insulin Resistance

Hyperglycemia attributable to IR could theoretically be caused by the disruption of the normal function of several different organs: pancreatic beta-cell secretion failure, enhanced hepatic gluconeogenesis, and reduced insulin-driven glucose uptake by skeletal muscle (and adipose tissue). In fact, virtually all of the IR observed in human diabetic patients has been attributed to defective insulin-stimulated muscle glycogen synthesis, which precedes the pancreatic and hepatic abnormalities by decades (Fig. 1). Although disruption of any of these steps could potentially lead to defective insulin-stimulated muscle glycogen synthesis, it is the first step that is defective in human IR. Specifically, almost all of the reduction in insulin-stimulated muscle glycogen synthesis during IR results from defective insulin-stimulated GLUT-4 mobilization.

Although it has long been recognized that a degree of hyperlipemia is correlated with IR in human patients (before the development of overt diabetes), there exists a much stronger correlation between the presence of intramyocellular lipid and IR. Whereas it had been previously suggested that an increased intramyocellular lipid led to IR as a result of inhibited pyruvate dehydrogenase and glycogen-synthase activities, it is now known that fatty acids in skeletal muscle directly inhibit insulin activation of glucose-transport activity (Fig. 2). In the healthy state, insulin-receptor binding leads to phosphorylation of insulin receptor substrate-1 (IRS-1), causing it to bind and activate phosphatidylinositol 3-kinase. Increased phospha-

Fig. 1. The pathway of muscle glycogen synthesis. GLUT 4 = glucose transporter 4; UDP = uridine 5’-diphosphate.

Fig. 2. The mechanism of fatty acid-induced insulin resistance in muscle. GLUT 4 = glucose transporter 4; IRS = insulin-receptor substrate; PI 3-kinase = phosphatidylinositol 3-kinase; nPKC = novel protein kinase C. Adapted from: Petersen and Shulman, 2006.
tideinositol 3-kinase activity leads to increased GLUT-4 activity and increased glucose uptake.72 Heightened intramyocellular lipid interferes with insulin-activated IRS-1-associated phosphatidylinositol 3-kinase activity and effectively inhibits GLUT-4 mobilization (Fig. 2). Specifically, intramyocellular lipid activates a protein kinase C that serves to inhibit insulin-stimulated IRS-1 tyrosine phosphorylation. The net result of increased intramyocellular lipid is blunting of insulin-driven GLUT-4 mobilization and IR (at the level of the skeletal muscle).

Therefore, it is not obesity per se that leads to IR; IR is more specifically mediated by the accumulation of lipid within skeletal muscle fibers.

7. Obesity and Glucocorticoids

Although obesity is commonly attributed to a simple protracted state of positive energy balance, glucocorticoids also cause expansion of adipose tissues in the body.32,33,73 Both a “moon face” and “buffalo hump,” manifestations of expanded SC adipose tissue, are phenotypical characteristics of individuals under the influence of excessive glucocorticoid action and Cushing’s syndromes. Moreover, expansion of the visceral adipose tissue as a result of the action of excess glucocorticoids contributes to the “pot-bellied” appearance in affected individuals. Specific circumstances under which individuals might be influenced by the action of excess glucocorticoids include Cushing’s syndromes, the administration of synthetic glucocorticoids for therapeutic purposes, and stress.

Visceral adipose tissue, to a greater extent than SC adipose tissue, is characterized by the expression of 11β-hydroxysteroid dehydrogenase-1 (11β-HSD1), an enzyme that acts to convert circulating cortisol (inactive glucocorticoid) to cortisol (active glucocorticoid).73,74 The implication of the presence of 11β-HSD1 in visceral adipose tissue is that cortisol is actively generated by this tissue; if present in sufficient quantity (as in the obese state), locally generated cortisol will both stimulate further local adipogenesis and contribute to IR.73,74 In this context, visceral obesity is associated with local paracrine actions of cortisol, and the circulating plasma concentration of cortisol is not elevated. The importance of 11β-HSD1 in visceral adipose tissue is underscored by the observation that 11β-HSD1 knockout mice can be fed (positive energy balance) to develop obesity, but these mice do not develop diabetes.75 Conversely, transgenic overexpression of 11β-HSD1 in mice led to rapid acquisition of visceral obesity, leptin resistance, and IR compared with controls.76 Increased levels of both free fatty acids and active glucocorticoids were present in the hepatic portal circulation of transgenic mice.76 Glucocorticoids exert a pronounced influence on the development of obesity and the attendant metabolic syndrome.32,33 It is reasonable to conclude that genes encoding 11β-HSD1 contribute to the inheritance of thriftiness.

8. Brain and Metabolic Syndrome

Neural mechanisms are also important in terms of communication between the adipose tissue and the brain. Although the brain clearly receives afferent information pertaining to the state of energy balance and peripheral metabolism in the form of circulating hormones (leptin and insulin) and macronutrients (long-chain fatty acids and glucose), there exists an important neuronal network that serves to connect the CNS with peripheral metabolic processes.77,78 Interestingly, visceral adipose tissue, the pancreas, and the liver share a common neural connection with the brain that is distinct and separate from the neuronal connections between the SC adipose tissue and the brain.79 In fact, the anatomic organization of the autonomic outflow to the important metabolic organs (visceral adipose tissue, pancreas, and liver) has not been studied extensively until recently.

Recent compelling data suggest that compartment-specific autonomic innervation likely plays a role in linking pancreatic insulin hypersecretion and hepatic IR with increased metabolic activity in the visceral but not SC adipose tissue.79 However, it has been known for some time that there exists demonstrable dysfunction in the autonomic nervous system in association with IR.80 Leptin has been reported to stimulate sympathetic nerve activity through activation of hypothalamic melanocortin-4 receptors.81 It has been suggested that neurons within the paraventricular nucleus are important for connecting the energy-balance regulatory system with the autonomic nervous system.82,83 It has been previously suggested that obesity and IR represent risk factors for the development of PPID in horses and ponies.84 It is intriguing to ponder the possibility that chronic hyperleptinemia might contribute to the pathophysiology of PPID by virtue of its actions in the paraventricular nucleus.

The question as to whether the autonomic nervous system plays a role in the pathogenesis of the metabolic syndrome (and causes IR) has not been answered. That said, it has been suggested that perturbations in the balance between the parasympathetic and the sympathetic components of the autonomic nervous system could promote the risk of developing IR.79 There is a rich bidirectional neural communication between the CNS and peripheral organs. It is becoming clear that the brain plays a critical role in the metabolic syndrome; hypothalamic responses to energy fluxes in the body result in alterations in both efferent neuronal activity and the production of pituitary hormones. When stimulated, not only does the brain affect peripheral metabolism through hormones released through the hypothalamic-pituitary axis, it also exerts tissue-specific modifications through changes in the parasympathetic and sympathetic outputs.
Accumulation of lipid in the liver as a result of IR is signaled to the brain using the nucleus tractus solitarius through vagal afferents. Moreover, adipose tissue is innervated by both sympathetic nerves that act to stimulate lipolysis (releasing glycerol and free fatty acids) and by parasympathetic nerves that promote insulin sensitivity. Parasympathetic innervation is important for the maintenance of insulin sensitivity. All of the parasympathetic nerves that regulate hormonal control of IR pass through the cervical vagus and its hepatic branch; transection at any of these sites leads to functional elimination of all hepatic parasympathetic input regulating insulin sensitivity. Insulin resistance is associated with attenuation of parasympathetic activity. Recent work has shown that stimulation of the vagal nerve will lead to weight loss.

9. Reactive Oxygen Species and Oxidative Stress
Reactive oxygen species (ROSs) have been implicated in the pathogenesis of diabetes-associated vascular dysfunction. Diabetic endotheliopathy has been attributed to increased production of superoxide by the mitochondrial electron-transport chain. Nitrotyrosine and 8-hydroxydeoxyguanosine are markers of oxidative stress that are increased under the influence of higher than normal levels of glucose. Interestingly, intermittently high glucose (as occurs in insulin-resistant states) tends to cause greater endothelial-cell dysfunction than a constant high-glucose situation. Hyperglycemia is regarded as the initiating factor for diabetic microvascular dysfunction, and oxidative stress has been proposed as the unifying factor for the damaging effect of hyperglycemia. Increasing evidence points to the role of acute hyperglycemia in the genesis of oxidative stress. Therefore, glucose fluctuations are specifically dangerous for endothelial cells, and it is the generation of ROSs that mediate this process.

Recently, there has been substantial interest in the implications of oxidative stress on equine health, especially from the perspectives of laminitis and PPID (equine Cushing’s disease). It is possible that the development of IR in obese horses could lead to the development of a proinflammatory state throughout the vasculature, which is the case in the human metabolic syndrome. By so doing, IR may, in turn, promote the risk of laminitis. The equine hoof-lamellar microvasculature is extremely sensitive to vasoconstrictors. Therefore, it might be uniquely susceptible to compromise, which results from the endocrinological circumstances that potentiate vascular smooth-muscle contractions in the horse.

Although ongoing research continues to provide new information pertaining to obesity and its attendant health risks in humans, much less is known about the implications of obesity in the equine species. Several equine conditions have been linked to obesity including laminitis, IR, hyperlipemia, infertility, and exercise intolerance; however, the extent to which obesity and IR truly lead to laminitis is deserving of further investigation. Several different plausible explanations have been proposed to explain the risk of laminitis that is associated with IR in horses and ponies, but a satisfactory answer still requires further work.

Recently, we showed that the equine hoof-lamellar interface is endowed with 11β-HSD1 and that the activity of this enzyme is higher in tissues acquired from laminitic horses (compared with non-laminitic controls). This implies that (through the action of cortisol) local glucocorticoid receptors are being activated. The pathophysiological significance of elevated 11β-HSD1 in the equine hoof and its relationship, if any, to 11β-HSD1 in the visceral adipose tissue of obese horses remains to be elucidated. Our team has recently cloned the equine 11β-HSD isotypes, and we are continuing to work on characterizing a role for 11β-HSD1 in regards to both laminitis and obesity.

10. Problems With Portliness—Denial and Objectivity
As is the case with both the human species and other companion animals under veterinary care, horses are commonly allowed to develop obesity. The tendency to accept an obese phenotype as representative of the healthy state can often be traced back to the perceptions of owners, trainers, and veterinarians. As is the case in humans, obesity arises in horses and ponies as a result of both physical inactivity and feeding practices. It is recommended that greater attention should be paid to the physical condition of ostensibly healthy horses presented for veterinary attention. There clearly exists a need for objective criteria by which horses might be “scored” in terms of whole-body adiposity.

In the human field, the “body-mass index” (BMI) has found utility in this respect; more recently, it has been suggested that simply measuring the circumference of the individual’s waist is an excellent indicator of visceral adiposity. In the equine field, various methods have been recommended for the purpose of assessing the relative adiposity of equine patients, including body condition score, equine BMI, and use of B-mode ultrasonography to assess rump fat thickness near the tail head.

11. Take Home Messages

- There is an expanding understanding that obesity represents a significant health hazard for many species; the extent to which obesity is deleterious to the health of horses and ponies is not completely understood.
- Although the traditional paradigm has regarded adipose tissue as a benign repository of stored energy, it is now being recognized as an important component of the metabolic syndrome. It is becoming clear that adipose tissue produces bioactive substances that influence insulin sensitivity and cause vascular injury.
Identification of therapeutic strategies that effectively reduce the ratio of pro-inflammatory, insulin-desensitizing adipokines to anti-inflammatory, insulin-sensitizing adipokines represents a major goal of adipobiological research aimed at the treatment of obesity in the human field.

The importance of better understanding obesity and its health implications to the equine patient is deserving of further investigation.

Although obesity has been linked to heightened risk for laminitis and PPID, there is clearly a need for better clarification of these relationships.

The authors are grateful to Shi-Xin Li for help with preparation of the figures.

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