THE VETERINARY CLINICS Equine Practice

Vet Clin Equine 18 (2002) 469–490

# Exercise physiology of the older horse

Kenneth Harrington McKeever, MS, PhD, FACSM

*Equine Science Center, Department of Animal Science, Cook College, Rutgers–The State University of New Jersey, 84 Lipman Drive, New Brunswick, NJ 08901-8525, USA*

There is an increasing proportion of the equine population that is older than 20 years of age, with many of those animals performing various athletic activities well into their 20s [1,2]. As is the case with their human counterparts, older equine athletes that remain active continue to perform in athletic events for a variety of reasons, including genetics, better health care, and greatly improved nutritional management [1–7]. Many studies in human beings have reported the observation that the ability to perform strenuous work decreases with age, with much of the decline in aerobic capacity and anaerobic power attributed to the effects of aging on physiologic function [8–14]. Much debate exists in the literature as to how much of that decline is caused by physiologic aging versus disease processes related to inactivity [8–10,13,14]. The latter would result in a decline in function that may be preventable, because recently reported data from aged human beings demonstrate that dynamic and resistance exercise training forestalls or even reverses some of the decline in cardiopulmonary performance and muscle function [8–15]. This information would suggest that some of the decline in exercise capacity in older individuals is related to a general decline in physical activity rather than to aging per se [8–11]. These observations have led to a fine-tuning of exercise prescription for the older human athlete so as to prevent the adverse and potentially dangerous effects of excessive work [9–11]. The results are new and improved programs to promote fitness for the growing population of older adults [9–14,16–19]. Unfortunately, only limited data have been published regarding the exercise capacity of the aged horse [3,4,20–32].

*E-mail address:* mckeever@aesop.rutgers.edu (K.H. McKeever).

This work was supported by funds from the New Jersey Agricultural Experiment Station and the New Jersey State Special Equine Initiative.

The author dedicates this article to his father, Kenneth Francis McKeever, who passed away on October 28, 2001.


PII: S0749-0739(02)00029-9

The fact that more horses are living into their 20s has stimulated some research into the effects of age on normal equine physiology [1,2]. Nutritional studies have resulted in the development of complete rations specifically tailored to the unique nutritional needs of the older horse [5,7]. Other recently reported data demonstrate that insulin-like growth factor (IGF-I) concentrations decline with age in the horse [3]. Aging seems to alter metabolic control, immune function, and endocrine function in horses at rest and after exercise [3,6,20,21,23–25,30]. The older horse also undergoes significant changes in body composition [22,33]. Like their human counterparts, some older horses exhibit an obese phenotype, and some have a thin old mare appearance [22,33]. The thin phenotype has lower fat-free mass (FFM) (ie, muscle mass), a pattern that is also similar in aged human beings, whereas the obese phenotype has 50% more fat mass than their younger counterparts [22,33]. As is the case with other organ systems, however, the question remains as to whether this is caused by inactivity or aging [22,33]. Interestingly, like humans, horses exhibit a shift in muscle fiber type distribution away from a more aerobic profile that fits with their less active lifestyle and decline in aerobic capacity [22,33]. Functional studies have demonstrated that maximal heart rate ($HR_{max}$) and aerobic capacity seem to decline with age [4,20], an observation similar to the decrease in cardiovascular function seen in human beings [9–14]. Therefore, one would hypothesize that there would be a similar decline in aerobic capacity and the ability to perform work in the older horse; however, minimal data have been reported for the older horse.

As is the case with their human counterparts, older equine athletes (for the purpose of the present article, horses older 20 years of age) have the ability to continue to perform in athletic events. Unfortunately, some horse owners continue to train their older animals using exercise training protocols that, although appropriate for a younger or middle-aged animal, may not be appropriate for the older equine athlete. The present article reviews how aging affects the major physiologic systems that would be expected to alter exercise ability.

## Age-related changes in the cardiovascular response to exercise

A great deal of data has been generated on the effects of aging on cardiovascular function in healthy older human beings [8–14,17–19]. Aging seems to have profound effects on the cardiovascular system, producing decreases in $HR_{max}$; changes in baroreceptor sensitivity; decreased vascular compliance; and hypertension in species like rats, dogs, and human beings [8–14,17–19]. Both older people and horses exhibit a decline in maximal oxygen concentration ($Vo_{2max}$) and exercise capacity [4,8–14,17–20]. The decline in $HR_{max}$ may limit maximal cardiac output and thus $Vo_{2max}$ and the ability to perform exercise [4,8,10,12–14,20]. Data are mixed regarding the effect

of age on stroke volume, with some studies demonstrating a decline and others suggesting that fit aged human beings make up for the lower $HR_{max}$ by increasing stroke volume [8,12–14,20]. In extremely old individuals, however, there seems to be a decrease in both $HR_{max}$ and stroke volume that certainly results in a decline in maximal cardiac output in people [8,12–14,20].

Data are also mixed regarding the contribution of central and peripheral cardiovascular factors in the decline in exercise performance seen in horses, dogs, and human beings [4,8,10,12–14,20,34,35]. The maximal aerobic capacity of an individual is dependent on central and peripheral mechanisms, and the age-related decline in central cardiovascular function accounts for some of the observed decrease in $Vo_{2max}$. Decreased muscle mass, alterations in muscle capillary density, and decreased vascular compliance may also limit exercise capacity by limiting blood flow to working muscles [36]. Thus, some of the decline in aerobic capacity is also caused by changes in peripheral mechanisms affecting the ability to utilize oxygen. Most of these data have been extrapolated from submaximal studies, however, and the debate continues on whether age-related declines in cardiovascular capacity in human beings are dominated by central or peripheral mechanisms.

Older horses undergo a decline in maximal aerobic capacity similar to that seen in healthy older human beings. McKeever and Malinowski [4] demonstrated that submaximal oxygen consumption seems to be similar in young and old horses subjected to an incremental exercise test. $Vo_{2max}$ was significantly lower in unfit horses older than 20 years of age ($\sim$90 mL/kg/min) compared with unfit young horses younger than 10 years of age ($\sim$120 mL/kg/min), however. As expected, the amount of work needed to reach $Vo_{2max}$ was lower in the older horses [4]. That study also suggested that there was a decline in the capacity to tolerate high-intensity exercise, because older horses became fatigued at lower intensities compared with young animals [4]. This is the first study we are aware of to report differences in aerobic capacity, lactate levels, and exercise capacity in older horses compared with younger animals. These observations are similar to the well-documented aging-induced decreases seen in human beings [8,10,12–14]. In general, there are few studies of any kind pertaining to the aged horse [3,4,6,20,21,23–25,27–31]. Furthermore, most equine exercise physiology studies are focused on the athletic animal; thus, most researchers have used a younger group of animals representative of horses in competition. In terms of physiologic age, the older horses in the above-mentioned study were analogous to human beings ranging from 60 to 78 years of age [4]. That experiment demonstrated that compared with other species, even the older mare has a tremendous innate aerobic capacity [4]. To put the observed results in perspective, one can compare the results with those in studies of human beings. A recent study of moderately fit, healthy, postmenopausal women reported maximal aerobic capacities averaging 22 mL/kg/min [10,13]. Elite Olympic-caliber human athletes typically have maximal aerobic capacities

in the range of 60 to 80 mL/kg/min [9]. Elite fit horses have $Vo_{2max}$ rates higher than 145 mL/kg/min [4,32]. Older mares had an average mass-specific $Vo_{2max}$ of 90 mL/kg/min, well below that of their fit equine counterparts but, interestingly, still higher than levels reported for young, fit, elite human athletes [4]. One should note that although the average $Vo_{2max}$ for the younger horses was lower than that reported for elite horses, it was similar to previously published data collected from unfit Standardbred and Thoroughbred horses [32].

One benefit to having greater aerobic capacity in the younger horse may be a delay in the need to increase the rate of anaerobic glycolysis to fuel higher intensity exercise [4]. Younger horses had to work harder to reach the "anaerobic threshold," or the point where one observes the onset of blood lactate accumulation (OBLA), which is marked by a blood lactate concentration of 4 mmol/L [4]. At this point, there is a curvilinear increase in blood lactate concentration indicative that lactate production by the working muscles has exceeded lactate utilization throughout the rest of the body [4]. This variable is important, because the velocity to produce a blood lactate concentration of 4 mmol/L ($V_{LA4}$) coincides with changes in several important physiologic processes. Many researchers have observed that the respiratory exchange ratio (RER) usually exceeds 1.0 at this point and that there is a substantial change in ventilation [4]. This latter observation, called the ventilatory threshold, is a compensatory respiratory mechanism to maintain blood pH through the elimination of carbon dioxide from the body. The older horses reached the $V_{la4}$ at both a lower speed and a lower relative work intensity [4]. The observation that it took a lower relative work intensity to reach the anaerobic threshold coupled with a lower aerobic capacity and proportionally lower velocity at $Vo_{2max}$ in the older mares is another piece of evidence suggestive of possible central limitations on the ability to perform work [4]. The observation that the older mares were not able to run as long or as hard (maximum velocity [$V_{max}$]) before reaching fatigue would tend to suggest that the older mares also had a reduction in factors affecting the peripheral mechanism associated with general exercise tolerance.

A more recent study by Betros et al [20] attempted to find a break point in this decline in aerobic capacity by comparing young (average age of ~7 years), middle-aged (average age of ~15 years), and old (average age of 27 years) horses. That experiment also attempted to determine if there were age-related declines in $HR_{max}$ and if any of the changes in cardiovascular function were reversed with training [20]. The study found that there were no differences between young and middle-aged horses with regard to $HR_{max}$ ($218 \pm 2$ beats per minute [b/min] vs $213 \pm 3$ b/min), $Vo_{2max}$ ($116 \pm 3$ mL/kg/min vs $109 \pm 3$ mL/kg/min), maximal oxygen pulse ($OP_{max}$) ($0.55 \pm 0.01$ mL/kg/b vs $0.52 \pm 0.02$ mL/kg/b), velocity at $HR_{max}$ ($9.0 \pm 0.3$ m/s vs $9.3 \pm 0.2$ m/s), or velocity at $Vo_{2max}$ ($8.8 \pm 0.2$ m/s vs $8.8 \pm 0.2$ m/s) [20]. Old horses had a lower $HR_{max}$ ($193 \pm 3$ b/min), $Vo_{2max}$ ($95 \pm 2$ mL/kg/min), and $OP_{max}$

($0.43 \pm 0.01$ mL/kg/b) and reached them at lower velocities compared with young and middle-aged horses [20]. Training resulted in substantial improvements in $Vo_{2max}$ and $OP_{max}$ but did not alter $HR_{max}$ in all groups [20]. Posttraining measurements revealed no differences between the young and middle-aged horses [20]. Despite training-induced increases in aerobic capacity, the old horses still had substantially lower values than the other groups [20]. Two important findings of that study were the report of an age-related decline in $HR_{max}$ and maximal stroke volume in the horse [20] and the observation that training can partially reverse some of the decline in cardiovascular function in the older horse [20]. The first observation may be important, because many horse owners use heart rate monitoring to judge the physiologic intensity of the work that their horses are performing. The second suggests that older horses can still benefit from exercise.

In the horse, the fact that the decline in $HR_{max}$ seems to contribute to the decline in $Vo_{2max}$ is similar to changes seen with aging in human beings [12]. The decrease in $HR_{max}$ with age is thought to result from several mechanisms, including aging-induced changes in the number of pacemaker cells in the sinoatrial node (SA), increases in the elastic and collagenous tissue in all parts of the conduction system, and the deposition of adipose tissue around the SA node [12]. In human beings, aging seems to affect autonomic tone as well, and there seems to be a downregulation of sensitivity to the sympathetic nervous system, which appears to influence the ability to increase heart rate during exercise [12]. The horse seems to use similar autonomic mechanisms to control heart rate, and indirect evidence suggests that the horse may also undergo aging-induced changes in the neuroendocrine control of cardiovascular function [4,32,37]. Functionally, this decrease in central cardiovascular capacity may not only affect maximal aerobic capacity but alter thermoregulatory capacity.

## Age-related changes in thermoregulation and fluid and electrolyte balance

A limited amount of data has been reported comparing the thermoregulatory responses of older and younger men and women during exercise in the heat [38]. It has been concluded that age influences thermoregulatory function during exercise [38,39]. Other experiments in human beings have determined that the ability to dissipate heat during exercise in hot and humid environments declines with increasing age [38]. Suggested reasons for this age-related decline in the ability to thermoregulate properly during exercise in human beings include lower cardiovascular capacity as a result of the age-related decrease in cardiac output, alterations in mechanisms associated with the control of skin blood flow, and a possible state of hypohydration in the elderly [38]. Data are mixed on the role of each of these factors alone and in combination in exercising older human beings [38]. In research performed specifically in human beings, lower stroke volumes and cardiac outputs have been seen in older men compared with younger men during

upright exercise. These differences are also present when skin venous pooling is augmented by the imposition of an additional heat stress [38]. In studies of older men and women, it has been demonstrated that older individuals have lower cardiac outputs than younger subjects even though they are exercising at the same absolute low-intensity workload [18,38].

Although there are numerous papers that examining thermoregulation in young horses [27,40,41], this author is aware of only limited data addressing the effects of age on the thermoregulatory response to exercise in the horse [29]. McKeever and co-workers [29] exercised young and old horses at the same submaximal absolute work intensity of 1625 W until they reached a core body temperature of 40°C. Old horses reached a core temperature of 40°C in almost half the time required by the younger mares [29]. The heart rates of the older mares were also substantially higher than the heart rates of the younger mares at 40°C [29]. Interestingly, both groups had similar heart rates and core temperatures by 10 minutes after exercise [29]. It was suggested that older mares were not able to thermoregulate as effectively as younger mares during exercise. The higher heart rate seen in the older mares suggests that their hearts had to work harder to muster sufficient cardiac output to accommodate the combined exercising demand of increased blood flow to the organs and muscles as well as to the skin for thermoregulation [29]. Even with the more rapid heart rate, older horses were still unable to dissipate the heat generated from exercise as quickly as younger mares, leading to a faster increase in core temperature after the onset of exercise. Interestingly, both groups had similar core temperatures and heart rates 10 minutes after exercise [29]. The authors interpreted this to suggest that the old mares could handle the demands of thermoregulation alone but not the combined demands of exercise and thermoregulation [29]. Unfortunately, the study was only descriptive and could not address potential mechanisms involved in this apparent age-related decrease in thermoregulatory ability during exercise [29]. Data from human studies may shed light on reasons for the apparent impairment of thermoregulation, however. During exercise, delivery of oxygen to active muscle involves a local decrease in vascular resistance, which, in turn, creates a challenge to blood flow delivery that is met by increases in cardiac output and adjustments in vascular resistance in nonactive tissues [38]. Increasing cardiac output during exercise helps to meet the dual demand for increased blood flow to working muscle and skin, especially when coupled with the redistribution of blood flow from visceral organs to augment perfusion of skin and active muscle vascular beds [38]. In human beings, an inadequate ability to increase cardiac output to support maximal skin blood flow sufficiently often leads to a compromise of an elderly person's ability to dissipate heat and defend against hyperthermia [38]. It could be suggested that the shorter time taken by older horses to reach 40°C during exercise and an almost 30% higher mean heart rate at 40°C indicates that older horses may have had a decrease in maximal cardiac output with age, leading to compromised thermoregulatory ability

during exercise. That speculation is supported by the apparent decline in $HR_{max}$ and stroke volume as reported by Betros et al [20].

Another suggested reason for the decline in the ability to thermoregulate effectively may be associated with age-related alterations in fluid and electrolyte balance. Older human beings commonly have lower total body water, plasma volume, and reserves of fluid for sweating [10,38]. Data are mixed, however, as to whether older people are chronically hypohydrated [38]. Interestingly, in the study comparing older horses and younger horses mentioned previously, markers of fluid status suggested that there were fluid shifts of a similar magnitude in young and old horses [38]. Another study revealed that older horses have a substantially lower pre-exercise plasma volume compared with younger animals [28]. Thus, although the relative reduction in plasma volume during exercise was similar, the older horses started off with a significantly lower absolute amount of vascular fluid volume in reserve to facilitate cardiovascular and thermoregulatory stability.

An additional observation was that the sweat rate was higher in the old horses [29] and that the older horses could not thermoregulate as well. This could have been caused by their potentially lower cardiac output or by alterations in skin blood flow. Although skin blood flow was not measured in the horse, studies in human beings have demonstrated an impaired skin blood flow response to exercise in older individuals [37,42,43]. The inability to keep cool despite an increased sweat rate in the older horse would be consistent with an impairment of skin blood flow as observed in human beings. Although it is pure speculation, the mechanism for an age-related decline in skin blood flow during exercise could involve alterations in the sensitivity of neuroendocrine mechanisms affecting vascular tone. This is an area currently being investigated in human beings and would be supported by age-related differences in the endocrine response to exercise in the horse [30].

The horse's athletic capacity can be considered elite among mammalian species, but its ability to dissipate heat during exercise is limited because of a relatively small surface area–to-mass ratio [26]. During high work intensities, the rate of heat production of the horse can exceed basal levels by 40- to 60-fold [26]. If the excess metabolic heat generated during exercise is not dissipated, life-threatening elevations in body temperature may develop, and the horse's athletic performance is adversely affected [26]. The adverse effects of hyperthermia on the health and performance of horses can develop during all exercise intensities and weather conditions. Failure to dissipate metabolic heat can cause a continuous and excessive rise in internal body temperature [10,26]. If heat loss mechanisms are impaired by aging, the only way that a horse would be able to decrease its body temperature is to decrease the rate of heat gain by decreasing the intensity of the exertion [26]. Recognizing that older horses have a decreased ability to thermoregulate during exercise may lead to improved monitoring practices for heat stress and a decreased occurrence of exercise-induced hyperthermia during equine athletic activities. The increased susceptibility of older horses to

overheating exemplified by this study should enable veterinarians, owners, and riders of horses to identify certain horses as being more likely than others to develop hyperthermia during exercise so that exercise regimens and athletic events can be designed to prevent heat stress. For example, age classes could be implemented in athletic competitions such that the duration of the race and length of the course designated for each class are shortened as the age of the horses increases. Additionally, the frequency of veterinarian checks that are required during equine athletic events could be based on age, such that more veterinarian checks are mandatory for older horses. Improved methods for preventing heat stress should decrease the occurrence of exercise-induced hyperthermia during equine athletic events.

## Aging-induced changes in respiratory function that may affect exercise

The literature contains many articles suggesting that factors affecting lung health can have a cumulative effect in the horse [44]. Over a lifetime, older horses can be exposed to more pathogens and allergens, which ultimately can lead to small airway disease [44]. Conditions like hyperreactive airway disease and chronic obstructive pulmonary disease are more prevalent in older animals [44]. It is highly likely that those disease processes cause a decrement in respiratory function during exertion [44]. Unfortunately, this author cannot find any published studies of the effects of aging by itself on the respiratory response to exercise in healthy older horses. In human beings, however, aging seems to have a significant effect on lung function during exercise [45].

A recent review by Dempsey and Seals [8] suggests that there are several alterations in pulmonary function that limit respiratory capacity. First, an examination of flow/volume loops suggests that an expiratory flow limitation occurs at lower work intensities in older individuals [8]. The decrease in the end-expiratory lung volume that is seen in human beings during exercise is also altered in older individuals [8]. These investigators suggest that elastic recoil of the lung is altered with aging, which affects expiratory flow rates [8]. Interestingly, older individuals also seem to have a greater dead space, which affects the dead space–to–tidal volume ratio [8]. They also report that in older human beings, the work of breathing is increased during exertion. Lastly, they report that lung hemodynamics are affected by aging-induced decreases in arteriolar compliance, which, in turn, may lead to capillary stress failure [8]. The latter may have implications for the horse, because capillary stress fractures are part of the etiology of exercise-induced pulmonary hemorrhage [8]. Furthermore, Dempsey and Seals [8] report that despite all of these age-related changes in lung physiology, ''alveolar to arterial gas exchange and pulmonary vascular hemodynamics are only slightly modified by aging.'' Many investigators have suggested that the normal equine lung is not built large enough to handle the demands of high

intensity. It would be interesting to determine if similar patterns of aging-induced change are present in the horse [44].

## Effects of age on body composition and muscle fiber type

Another measure that may have an important bearing on the ability to perform exercise is a horse's body composition and, more importantly, total FFM [46–48]. Older human beings exhibit substantial decreases in muscle mass and, in many cases, increases in fat mass, which affects their ability to perform exercise [14,49–51]. Data from recent work in horses suggest that they may undergo similar aging-induced changes [22,24,33]. The predominant component of a horse's FFM is muscle mass, and a recent study has documented the strong correlation between FFM and performance in elite Standardbred horses [46]. this author is aware of only one study that has attempted to examine the effect of age on body composition in the horse [22,33]. In that study, it was found that there were differences between old and young mares in total body weight, rump fat thickness, percentage of body fat, and fat weight [22,33]. Old mares had greater FFM or lean body weight than the young mares [22,33]. That study found that old horses could be divided into two groups by appearance [22,33]. Some horses were either extremely lean or extremely fat [22,33]. The "skinny" old mares had significantly smaller rump fat thickness, lower percentage of body fat, and less fat weight than both the fat old mares and the young mares [22,33]. The skinny old mares had significantly less body weight than the fat old mares but not compared with the young mares [22,33]. They also had greater lean body weight than the young mares, but there was no significant difference in this parameter when compared with the old fat mares [22,33]. In turn, the old fat group had a significantly larger rump fat thickness, percentage of body fat, and fat weight when compared with the young mares [22,24,33]. These data suggest that as mature horses gain weight, they gain fat mass at a rate faster than FFM. This is indicated by an increase in the percentage of fat per given body weight. A larger fat mass may be detrimental to performance [48] and may lead to other complications in older horses like insulin resistance [24].

These morphometric differences in horses may result from some of the same factors at play in aged human beings [14,49–51]. For instance, aged horses exhibit similar clinical metabolic and endocrine disorders as those seen in aged human beings, including hyperinsulinemia and hyperglycemia, pituitary and thyroid adenomas, Cushing's disease, and decreased somatotropin (ST) concentrations [24]. Aged horses also exhibit decreases in nutrient absorption and utilization, and research has come up with new diet formulations to address those age-related alterations in nutrition [5–7,24]. Also, as discussed below, new data suggest that endocrine control of glucose metabolism after exercise is altered in the old horse, suggesting a need for new strategies to meet the metabolic demand of exercise in the active old horse [24].

Although old horses seem to retain muscle mass, one must ask whether that is functional muscle mass. That question can only be addressed by looking at muscle fiber profiles, enzyme concentrations, and substrate concentrations. There are many studies that have documented muscle fiber type, enzymatic activity, and substrate storage and utilization patterns in the horse [52–59]. Only a few studies have examined peripheral changes associated with aging in the horse, however, and those studies have focused on changes in fiber type associated with aging [22,33,56]. This authors is aware of only two papers that have attempted to present data grouped by age [22,33,56]. Rivero et al [55] examined muscle fiber type distribution in a number of horses; however, the mean age of the oldest age group in that study was only 15 years, an age when many horses are still in their prime athletically and physiologically analogous to human beings in their 40s. Conversely, a more recent study compared young and extremely old horses [22,33]. The major finding of that study was that older horses had a change in muscle fiber type distribution compared with young horses [22,33]. The results of a gel electrophoresis analysis of muscle biopsy samples showed that the aged mares had fewer type I and type IIA fibers than the young mares. Type I fibers represented approximately 8% of the fiber population in the old mares versus approximately 12% in young horses [22,33]. Type IIA fibers represented approximately 28% of the fiber population in the old mares versus approximately 36% in the young mares [22,33]. Old horses had more type IIX fibers than young horses (65% vs 52%) [22,33]. On a functional level, the authors suggested that the older horses had a switch in fiber type population away from that which would be favorable to endurance exercise. It was further suggested that those observations may partially explain the decrease in maximal aerobic capacity documented in other studies [4]. The documented change in muscle fiber profile is similar to the change observed in disuse atrophy models, such as hind limb suspension in rats and space flight models in human beings, Rhesus monkeys, and rats [14,60–64].

On a cellular level, aging seems to alter muscle structure and function significantly [20,33,56,65–68]. Studies in rats and human beings demonstrate that connective tissue content in the muscle is altered, with evidence of significant amounts of collagen [14,69,70]. These changes would tend to interfere with normal contractile function. Other studies have reported conflicting results regarding skeletal muscle blood capillarity in aged human beings, with some indicating no change with age and some demonstrating a significant age-related decline [36]. Blood flow has been reported to be lower in older men, however [10,35]. Oxidative capacity also declines with age in old human beings and other animals [20,33,66,67]. Glucose utilization seems to be altered in older human beings, possibly through changes in GLUT-4 activity, insulin insensitivity, and alterations in insulin-regulated glucose transporter [10,69,71]. Finally, glycogen depletion/repletion patterns in skeletal muscle seem to be altered by age in rats and human beings [36,69,70,72]. Unfortunately, no data have been published that have examined the effect of

exercise on muscle enzyme concentrations or glycogen depletion and repletion patterns in the old horse. Aging-induced alterations in those metabolic control mechanisms may be important, because they certainly would affect both the ability to exercise and to recover from exercise.

## Age-related alterations in the endocrine response to exercise

Exercise involves the integration of multiple organ systems that communicate via neural and endocrine pathways. Human beings undergo substantial alterations in neural control mechanisms, with primary alterations in sympathetic nervous system responsiveness [10,19,50,73,74]. No such information exists for the horse. Aging also alters the endocrine response to exercise, with reported changes in hormones associated with the control of cardiovascular function, stress hormones, and endocrine/paracrine factors related to the control of metabolic function and substrate utilization [10,19,73,74].

### *Cardiovascular and renal hormones*

A recent study reported the effect of aging on four of the hormones related to the control of cardiovascular function in the horse. McKeever and Malinowski [30] reported similar resting concentrations of the various hormones involved in the control of cardiovascular and renal function, including atrial natriuretic peptide (ANP), arginine vasopressin (AVP), plasma renin activity (PRA), aldosterone (ALDO), and endothelin-1 (ET-1) healthy old and young horses. Similar observations have been reported for normal healthy human beings and other species [38,75]. Old and young horses had directionally similar exercise-induced alterations in PRA, ANP, AVP, and ALDO [30]. The major finding of this investigation was an age-related change in the magnitude of the response to exertion [30]. Although old horses had different concentrations of these hormones, the observed concentrations were still within the range of normal for maximally exercised horses and other species [32,38,75].

Interestingly, plasma concentrations of the vasoconstrictor ET-1 [76] were not affected by exercise in either group of horses, a phenomenon previously reported for young horses [27] and human beings [77]. These data suggest that although aging may alter the control of cardiovascular function in the exercising horse, it does not produce the pronounced alterations that one would see in an exercising individual with a compromised cardiovascular system. Such is the case in studies of age-matched individuals with heart failure or hypertension [19,78–80]. Age-related differences in PRA and the plasma concentrations of ANP, AVP, and ALDO reflect differences in sensitivity in the regulation of blood pressure and blood flow during exertion. Younger horses were observed to have greater plasma concentrations of the vasodilator ANP. Functionally, this ANP-induced vasodilation would aid in

the redistribution of blood flow during exercise [32,75]. ANP also inhibits PRA and the production and release of antagonistic hormones like AVP and ALDO [32,75]. Thus, greater concentrations of plasma ANP in younger animals may enhance the ability to vasodilate blood vessels in the periphery, especially in the working muscles.

McKeever and Malinowski [32] also reported that older horses had greater PRA at speeds eliciting $Vo_{2max}$. This change may be physiologically important, because it is well recognized that exercise-induced increases in the plasma renin–angiotensin cascade are an important part of the defense of blood pressure during exercise and fluid and electrolyte balance after exercise. Increases in circulating plasma angiotensin I and II aid in vasoconstriction in nonobligate tissues, which is part of the redistribution of blood flow [32,75]. Furthermore, increases in PRA and angiotensin also act to stimulate thirst and cause an increase in the synthesis and release of aldosterone [32,75]. Mediation of this neuroendocrine defense of blood pressure involves the integrative actions of both the low- and high-pressure baroreceptors [32,75]. Aging seems to alter baroreceptor sensitivity and the normal feedback loop that integrates cardiovascular control [19]. One might speculate that reported differences in ANP and PRA may reflect an age-related difference in baroreceptor sensitivity to the challenge of exercise. Such differences may also reflect differences in autonomic control and input from the sympathetic nervous system and other stimuli that affect the control of central and peripheral cardiovascular function. This may be important, because increases in renal sympathetic nerve activity and stimulation of the juxtaglomerular apparatus are the primary stimuli for renin release during exertion. A recent study in human beings suggests that aging-induced changes in PRA may also affect renal function and may indirectly contribute to possible alterations in skin blood flow [38,43]. The latter speculated aging-induced change could be important because it could potentially alter the ability to thermoregulate in human beings. It would also be important to horses because they are the only other athletic species that sweats to thermoregulate [32]. Any age-related difference in blood volume, $HR_{max}$, and vascular tone may also influence the integrative neuroendocrine defense of blood pressure.

Surprisingly, younger horses seem to have a greater vasopressin response during exercise. Vasopressin functions independent of the renin angiotensin system in the defense of blood volume and blood pressure during exercise. Plasma AVP concentration increases when the cardiopulmonary baroreceptors sense that cardiac filling pressure is inadequate, when the high-pressure baroreceptors sense that mean arterial blood pressure is too low, or when hypothalamic osmoreceptors sense that plasma osmolality is too high [32,75]. Vasopressin causes vasoconstriction in nonobligate tissues during exercise. It also facilitates the uptake of water and electrolytes from the large intestine, another important action during exercise [32,75]. Post-exercise AVP causes retention of solute-free water by the kidney and stimulates thirst and drinking [32,75]. Studies are needed to explore the role of aging in these

latter functions, because some studies suggest that aged human beings do not drink as much and many times are hypohydrated [38]. Suppression of thirst and drinking is an important consideration for those concerned with postevent care of the horse.

*Growth hormone*

It is well recognized that older horses have lower plasma concentrations of the thyroid hormones, ST, and IGF-I compared with young animals, suggesting an age-related decline in the somatotropic axis in horses similar to that observed in other mammalian species [3,25]. This may be linked to aging-induced changes, including decreases in cardiopulmonary function, decreased aerobic and exercise capacity, decreased immune function, impaired nutrient utilization, decreased nitrogen retention, and decreased lean body mass [3,25]. Similar changes have been observed in other species, and comparative physiologic data from rats, dogs, and human beings [9,10, 14,36] have shown that there is a causal relation between plasma concentrations of ST and what has been termed the *aging phenotype*.

Recent experiments have demonstrated the efficacy of recombinant human ST treatment in preventing or retarding functional decline in geriatric human beings [81]. Chronic ST administration seems to increase strength and the ability to perform a battery of weight-lifting exercises in aged male human beings [81]. Research has also been conducted on the efficacy of chronic recombinant equine ST therapy in geriatric horses [32,82]. Researchers conducting those studies have asked "quality of life" questions similar to those posed in experiments performed using aged human beings [9,10,14]. Although it was shown that recombinant equine ST therapy increased nitrogen retention and improved the appearance of geriatric horses [3,25], experiments that focused on the effects of equine ST therapy on aerobic capacity and markers of performance failed to demonstrate any improvement as a result of chronic administration of recombinant equine ST to aged horses [31]. The authors also examined the effects of equine ST therapy on markers of anaerobic power, such as maximal velocity during the incremental exercise test, total time to fatigue, peak blood lactate concentrations, and work rate expressed in watts. As with aerobic capacity, data from our unfit geriatric horses indicate that equine ST therapy does not alter lactate tolerance or cause an increase in maximal power that one would associate with an increase in muscular strength. This does not detract from previously published information demonstrating that equine ST therapy improves nitrogen retention, body composition, and overall appearance, however [25].

Another objective of the previous study was to examine the effect of equine ST therapy administration on the prevention of muscle damage [31]. The authors used measurement of plasma creatinine kinase (CK) and aspartate aminotransferase (AST) concentrations before and after exercise as markers of muscle damage based on data from papers demonstrating that

the plasma concentrations of these enzymes increase slightly with the mild muscle damage caused by overexertion [31]. At that time, no data had been published examining the effects of maximal exertion on muscle integrity or markers of muscle damage in aged horses, and the authors were concerned that the exercise tests would induce some muscular remodeling and a concomitant elevation in postexertional concentrations of CK and AST consistent with mild overtraining. They also speculated that equine ST therapy administration might have a protective effect on exercise-induced muscle damage if any occurred. Amazingly, there were no exercise-induced alterations in CK or AST concentrations in the old mares after high-intensity exertion [31]. The authors thus speculated that muscles in the unfit aged horse, unlike the aged human being, seemed to be amazingly resilient [31].

*Endorphin and cortisol: the "stress" hormones*

Endorphins and cortisol have been used as markers of the degree of physiologic stress during exercise [23,82]. The release of these two hormones is a normal response to exercise; however, the direction and magnitude of their response differentiate between what one can consider a normal response to the physiologic challenge of exertion and a true stress response. Increases in these hormones are linked to duration and intensity, and their release may provide protection from the physiologic challenge of exertion [23,82]. β-Endorphin functions as a natural opiate, forestalling the central mechanisms that would induce fatigue [23,82]. Cortisol functions as a metabolic hormone during exercise, influencing glucose metabolism [23,82]. After exercise, cortisol exerts a degree of anti-inflammatory and immunosuppressive activity, possibly aiding in the repair of tissue altered by exertion and protecting against the inflammation associated with overexertion.

This author is aware of only one study that has examined the effects of age and training on the release of these hormones in response to acute exercise [23]. That experiment attempted to determine whether training and age affected plasma β-endorphin, cortisol, and immune function responses to acute exercise in unfit Standardbred mares [23]. Unfortunately, β-endorphin and cortisol were measured at rest and at 5, 10, 20, 40, 60, and 120 minutes after graded exercise test (GXT) but not during exercise. The authors reported that cortisol rose by 5 minutes after GXT in young and middle-aged mares before and after training [23]. There was no rise in cortisol the old mares after GXT, however, either before or after training [23]. Pretraining β-endorphin concentrations increased by 5 minutes of exercise in all mares [23]. Training enhanced the β-endorphin response to acute exercise in all three groups; however, the peak concentration for the older mares occurred later than the peak seen in the other groups [23].

*Metabolic hormones and the control glucose homeostasis*

It is well recognized that age substantially alters metabolic function in human beings [43,69,70,72–74,83–85]. Aging is frequently associated with

glucose intolerance and insulin resistance in people and horses [7,84,86]. Participation in regular exercise activity may elicit a number of favorable responses that contribute to healthy aging [84]. This author is aware of only one study that has attempted to examine the effects of aging and training on the glucose and insulin responses after acute exertion in horses [23]. The primary finding of that study was that old horses required greater concentrations of insulin to manage their response to an oral glucose tolerance test [23]. The authors also reported that there was an age-related effect on the glucose and insulin responses to acute exercise both before and after 12 weeks of exercise training [23]. Interestingly, 12 weeks of exercise training resulted in a post-GXT increase in insulin in all age groups [23]. The authors concluded that the resultant hyperinsulinemia occurring after exertion after exercise training may have been related to an increased need for glycogen repletion in the muscle after exercise [23]. Interestingly, this posttraining response was highest in the oldest horses, quite possibly because of a greater need to replenish muscle glycogen [23]. They also reported that exercise training altered the insulin responses more in the old horses and that it did not affect the glucose response in any of the age groups of horses, regardless of age [23]. This was interpreted to suggest an improvement in insulin sensitivity in the older animals [23]. The exact mechanisms to explain the age-related difference in glucose and insulin metabolism are unknown, but published papers from studies in rats and human beings suggest that they may be related to differences in fuel utilization, mitochondria respiration rates, and skeletal muscle content of GLUT-4 transporters [35,66,67,70,87].

## Alterations in the immune response to exercise

Studies in human beings have demonstrated that aging alters the immune response in general and, more importantly, the immune response to the challenge of exercise [88,89]. Few data have been published on the immune response to acute exercise in older human beings [88,89]. One study demonstrated that there was no difference in natural killer cell activity in young and old subjects after acute exercise [88]. Studies in mice have shown that lymphocyte proliferative ability is suppressed after endurance exercise; however, exercise training seems to exert a beneficial adaptation [88,89].

Two studies have reported on the effect of aging on the immune response to acute exertion in horses [21,23]. Horohov and co-workers [21] reported that there were differences in the immune system of young and old horses both before and after exertion. Old horses exhibited lower proliferative responses to mitogens, suggesting an age-related alteration in T-cell–mediated function and in immunosenescence [21]. Interestingly, acute exercise caused a decrease in the lymphoproliferation response in the younger horses but not in the old mares [21]. The authors suggested that the lower cortisol response to exertion in the old horses compared with the young horses may explain the differences in the immune response between the groups [21].

A more recent experiment examined the effects of aging and training by measuring immune responses to a graded exercise test performed before and after 12 weeks of training at 60% $HR_{max}$ in young, middle-aged, and old mares [23]. The authors measured leukocyte cell number, CD4+ and CD8+ cell subsets, and the lymphoproliferative response to mitogenic challenge, and they found significant aging and training effects [23]. The older horses had lower monocyte counts after the posttraining GXT [23]. Lymphocyte numbers rose in all mares after exercise, with age having an effect as evidenced by different levels in the middle-aged and old mares [23]. Interestingly, the CD4+ lymphocytes were more numerous at rest in old and middle-aged mares compared with younger mares [23]. Furthermore, age had a profound effect, with a reduction in the number of CD4+ lymphocytes seen in the old and middle-aged horses but not in the young horses after the pretraining GXT [23]. A reduction was seen in all group after the posttraining GXT [23]. It was also stated that age had no effect on resting CD8+ lymphocytes and that training resulted in an increase in all groups [23]. Age and training also seemed to alter the lymphocyte proliferative response, again suggesting a degree of immunosenescence [23]. Together, these studies suggest that special preventive care may be needed for the older athletic horse.

## Renal, gastrointestinal, and other systems

Research in human beings has suggested that many of the observed changes in renal function seen with aging are not inevitable and are the combined effect of pathologic changes coupled with the aging process. This author is aware of only limited data on the effect of age on the renal response to acute exercise in human beings [38,43,90]. Those studies have primarily focused on the effect of aging on the normal reduction in blood flow seen with acute exertion [38,43,90]. Functionally, older individuals have smaller reductions in renal blood flow and smaller increases in skin blood flow compared with younger individuals [38,43,90]. This may alter renal function as well as thermoregulatory capacity, because the redistribution of blood flow away from nonobligate tissues toward working muscles and skin is an important response to exertion [38,43,90]. No work has been performed in the horse; however, a reduction in skin blood flow would alter the ability to thermoregulate and may explain some of the differences in thermoregulatory capacity reported in older horses. Aging-induced alterations in renal sympathetic nerve activity and the plasma renin–angiotensin cascade may play a role in the change in blood flow distribution in human beings. This hypothesized mechanism may play a role in the horse as well, because the horse is the only species other than human beings that sweats to thermoregulate during exercise, and, as mentioned previously, the older horse has an altered PRA response to exertion. More work is also needed to determine if aging alters mechanisms affecting the glomerular filtration rate and tubular function during exercise and afterward. The latter may

be important, because long-term control of total body water, plasma volume, and fluid and electrolyte balance seems to be altered in human beings and horses.

Other systems altered with age in other species include the gastrointestinal tract and bones and ligaments as well as the integumentary system [10]. Changes in the gastrointestinal tract ranging from the wearing down of teeth to decreased absorptive capability influence the uptake of water and nutrients and have the potential to alter the ability to perform exercise. Bone pathologic changes ranging from osteoarthritis to demineralization certainly can alter the ability to perform exercise in old horses. Changes in the skin have the potential to alter sweating and thermoregulation. Unfortunately, this author is unaware of any data on the effects of age on the these systems in the horse.

## Summary

Surveys indicate that up to 15% of the equine population in the United States is older than 20 years of age, with many of these animals performing various athletic activities well into their 20s [1,84]. As is the case with their human counterparts, these geriatric equine athletes have the ability to continue to perform in athletic events. Unfortunately, many horse owners continue to train their active older animals using exercise training protocols that, although appropriate for a younger animal, may not be appropriate for the older equine athlete. Studies in aged human beings have led to a fine-tuning of exercise prescription for the older human athlete so as to prevent the adverse and potentially dangerous effects of excessive work. Published results have led to new and improved programs to promote fitness for the growing population of older adults. Unfortunately, limited data exist regarding the exercise capacity of the aged horse. Future studies on the effects of aging on exercise capacity in equine athletes need to take a few major directions. One question to be answered is at what age does physiologic function first begin to decline in the horse? In human beings, this age varies with training, but noticeable changes in aerobic capacity are first seen in 40- to 50-year-olds. Second, data are needed to determine what levels of exercise enhance the health and well-being of the older horse without harm. Lastly, studies are needed to determine the physiologic mechanisms associated with the onset of aging-induced decreases in physiologic function in the horse. The ultimate goal of all these studies should be to adjust exercise levels to meet the needs of the growing population of athletically active older equine athletes.

## Acknowledgment

The author thanks Jennifer McKeever, Charles Kearns, and Mary Beth Gordon for their help in editing the manuscript.

## References

[1] Hintz HF. Nutrition of the geriatric horse. In: Proceedings of the Cornell Nutrition Conference, Cornell University. Ithaca (NY): Cornell University 1995. p. 195–8.
[2] Rich GA. Nutritional and managerial considerations of the aged equine. In: Proceedings of Advanced Equine Management Short Course, Colorado State University. Fort Collins (CO): Colorado State University 1989. p. 121–3.
[3] Malinowski K, Christensen RA, Hafs HD, Scanes CG. Age and breed differences in thyroid hormones, insulin-like growth factor-I and IGF binding proteins in horses. J Anim Sci 1996;74:1936–42.
[4] McKeever KH, Malinowski K. Exercise capacity in young and geriatric female horses. Am J Vet Res 1997;58:1468–72.
[5] Ralston SL, Breuer LH. Field evaluation of a feed formulated for geriatric horses. J Equine Vet Sci 1996;16:334–8.
[6] Ralston SL, Nockels CF, Squires EL. Differences in diagnostic test results and hematologic data between aged and young horses. Am J Vet Res 1988;49:1387–92.
[7] Ralston SL. Effect of soluble carbohydrate content of pelleted diets on post prandial glucose and insulin profiles in horses. Pferdeheilkunde 1992;49:112–5.
[8] Dempsey JA, Seals DR. Aging, exercise, and cardiopulmonary function. In: Lamb DR, Gisolfi CV, Nadel E, editors. Perspectives in exercise and sports medicine. Exercise in older adults. Carmel, IN: Cooper Publishing; 1995. p. 237–304.
[9] Haskell WL, Phillips WT. Exercise training, fitness, health, and longevity. In: Lamb DR, Gisolfi CV, Nadel E, editors. Perspectives in exercise and sports medicine, vol. 8. Exercise in older adults. Carmel (IN): Cooper Publishing; 1995. p. 11–52.
[10] Holloszy JO, Kohrt WM. Excercise. In: Masoro EJ, editor. Handbook of physiology, section 11. Aging. New York: Oxford University Press; 1995. p. 633–6.
[11] Holloszy JO. Exercise, health, and aging: a need for more information. Med Sci Sports Exerc 1993;15:1–5.
[12] Lakatta EG. Cardiovascular system. In: Masoro EJ, editor. Handbook of physiology, section 11. Aging. New York: Oxford University Press; 1995. p. 413–74.
[13] Raven PB, Mitchell JH. Effect of aging on the cardiovascular response to dynamic and static exercise. In: Westfeldt ML, editor. The aging heart: its function and response to stress. New York: Raven Press; 1980. p. 269–96.
[14] Stamford BA. Exercise and the elderly. In: Pandolf KB, editors. Exercise and sport science review, vol. 16. New York: Macmillan Publishing Company; 1998. p. 341–80.
[15] Ekelund LG, Haskell WL, Johnson JL, Wholey FS, Criqui ML, Sheps DS. Physical fitness in the prevention of cardiovascular mortality in asymptomatic North American men. N Engl J Med 1988;319:1379–84.
[16] Ready AE, Naimark B, Ducas J, Sawatzky JV, et al. Influence of walking volume on health benefits in women post-menopause. Med Sci Sports Exerc 1996;28:1097–105.
[17] Seals DR, Reiling MJ. Effect of regular exercise on 24-hour arterial blood pressure in older hypertensive humans. Hypertension 1991;18:583–92.
[18] Seals DR, Hagberg JM, Hurley BF, Ehsani AA, Hollozy JO. Endurance training in older men and women: I. Cardiovascular responses to exercise. J Appl Physiol 1984;57:1024–9.
[19] Seals DR. Influence of aging on autonomic-circulatory control at rest and during exercise in humans. In: Gisolfi CV, Lamb DR, Nadel E, editors. Perspective in exercise science and sports medicine, vol. 6. Exercise, heat, and thermoregulation. Dubuque (IA): WC Brown; 1993. p. 257–97.
[20] Betros CL, McKeever KH, Kearns CF, Malinowski K. Effects of aging and training on maximal heart rate and $Vo_{2max}$. Equine Vet J Suppl 2002;34:100–5.
[21] Horohov DW, Dimock AN, Gurinalda PD, Folsom RW, Malinowski K, McKeever KH. Effects of exercise on the immune response of young and old horses. Am J Vet Res 1999;60:643–7.

[22] Lehnhard RA, McKeever KH, Kearns CF, Beekley MD. Aging-related changes in fat free mass and myosin heavy chain in Standardbred mares. Vet J (in press).
[23] Malinowski K, Shock E, Roegner V, Rochelle P, Kearns CF, Guirnalda P, et al. Age and exercise training alter plasma β-endorphin, cortisol, and immune parameters in horses. J Anim Sci 2002;80(Suppl 1):156.
[24] Malinowski K, Betros CL, Flora L, Kearns CF, McKeever KH. Effect of training on age-related changes in plasma insulin and glucose. Equine Vet J Suppl 2002;34:147–53.
[25] Malinowski K, Christensen RA, Konopka A, Scanes CG, Hafs HD. Feed intake, body weight, body condition score, musculation, and immunocompetence in aged mares given equine somatotropin. J Anim Sci 1997;75:2727–33.
[26] McConaghy F. Thermoregulation. In: Hodgson DR, Rose RJ (editors). The athletic horse: principles and practice of equine sports medicine. Philadelphia: WB Saunders; 1994. p. 181–91.
[27] McKeever KH, Kearns CF, Antas LA. Endothelin response to exercise in horses. Vet J 2002;164:41–9.
[28] McKeever KH, Kearns CF. Aging-induced alterations in plasma volume in horses [abstract]. Med Sci Sports Exerc 2001;33(Suppl):S257.
[29] McKeever KH, Eaton TL, Geiser S, Kearns CF. Thermoregulation in old and young horses during exercise [abstract]. Med Sci Sports Exerc 2000;32(Suppl):S156.
[30] McKeever KH, Malinowski K. Endocrine response to exercise in young and old horses. Equine Vet J Suppl 1999;30:561–6.
[31] McKeever KH, Malinowski K, Christensen R, Hafs HD. Chronic equine somatotropin administration does not affect aerobic capacity or indices of exercise performance in geriatric horses. Vet J 1998;155:19–25.
[32] McKeever KH, Hinchcliff KW. Neuroendocrine control of blood volume, blood pressure, and cardiovascular function in horses. Equine Vet J Suppl 1995;18:77–81.
[33] Lehnhard RA, McKeever KH, Kearns CF, Ideus JM, Brown JB, Beekley MD. Myosin heavy chain is different in old versus young Standardbred mares [abstract]. Med Sci Sports Exerc 2001;33(Suppl):S13.
[34] Haidet GC, Parsons D. Reduced exercise capacity in senescent beagles: an evaluation of the periphery. Am J Physiol 1991;260:H173–82.
[35] Meridith CN, Frontera WR, Fisher EC, Hughes VA, Herland JC, Edwards J, et al. Peripheral effects of endurance training in young and old subjects. J Appl Physiol 1989;66:2844–9.
[36] White T. Skeletal muscle structure and function in older mammals. In: Lamb DR, Gisolfi CV, Nadel E, editors. Perspectives in exercise and sports medicine, vol. 8. Exercise in older adults. Carmel, IN: Cooper Publishing; 1995. p. 115–74.
[37] Goetz TE, Manohar M. Isoproterenol-induced maximal heart rate in normothermic and hyperthermic horses. Am J Vet Res 1990;51:743–6.
[38] Kenney WL. Body Fluid and temperature regulation as a function of age. In: Lamb DR, Gisolfi CV, Nadel E, editors. Perspectives in exercise and sports medicine, vol. 8. Exercise in older adults. Carmel, IN: WB Saunders; 1995. p. 305–51.
[39] Armstrong CG, Kenney WL. Effects of age and acclimation on responses to passive heat exposure. J Appl Physiol 1993;75:2162–7.
[40] Geor RJ, McCutcheon LJ, Ecker GL, Lindinger MI. Thermal and cardiorespiratory responses of horses to submaximal exercise under hot and humid conditions. Equine Vet J Suppl 1995;20:125–32.
[41] Naylor J, Bayly WM, Gollnick PD, Brengelmann GL, Hodgson DR. Effects of dehydration on thermoregulatory responses of horses during low-intensity exercise. J Appl Physiol 1993;75:994–1000.
[42] Ho CW, Beard JL, Farrell PA, Minson CT, Kenney WL. Age, fitness, and regional blood flow during exercise in the heat. J Appl Physiol 1997;82:1126–35.
[43] Kenney WL, Zappe DH. Effect of age on renal blood flow during exercise. Aging (Milano) 1994;6:293–302.

[44] Lekeux P, Art T. The respiratory system: anatomy, physiology, and adaptations to exercise and training. In: Hodgson DR, Rose RJ, editors. The athletic horse: principles and practice of equine sports medicine. Philadelphia: WB Saunders; 1994. p. 79–128.
[45] Davies CTM, Thomas DO, White MJ. Mechanical properties of young and elderly muscle. Acta Med Scand Suppl 1988;711:219–26.
[46] Kearns CF, McKeever KH, Kumagai K, Abe T. Fat-free mass is related to one mile performance in elite Standardbred horses. Vet J 2002;163:260–6.
[47] Kearns CF, McKeever KH, John-Alder H, Abe T, Brechue W. Body composition and other predictors of maximal oxygen uptake. Equine Vet J Suppl 2002;34:485–90.
[48] Kearns CF, McKeever KH, Abe T. Overview of horse body composition and muscle architecture implications for performance. Vet J (in press).
[49] Forbes GB, Reina JC. Adult lean body mass declines with age: some longitudinal observations. Metab Clin. Exp 1970;19:653–63.
[50] Kohrt WM, Spina RJ, Ehsani AA, Cryer PE, Holloszy JO. Effects of age, adiposity, and fitness level on plasma catecholamine responses to standing and exercise. J Appl Physiol 1993;75:1828–35.
[51] Kohrt WM, Malley MT, Dalsky GP, Holloszy JO. Body composition of healthy sedentary and trained, young and older men and women. Med Sci Sports Exerc 1992;24:832–83.
[52] Essen-Gustavsson B, Lindholm A. Muscle fibre characteristics of active and inactive Standardbred horses. Equine Vet J Suppl 1985;17:434–8.
[53] Gunn HM. Relative increase in areas of muscle fibre types in horses during growth. Equine Vet J Suppl 1995;18:209–13.
[54] Guy PS, Snow DH. The effect of training and detraining on muscle composition in the horse. J Physiol 1977;269:33–51.
[55] Rivero JLL, Galisteo AM, Aguer E, Miro F. Skeletal muscle histochemistry in male and female Andalusian and Arabian horses of different ages. Res Vet Sci 1993;54:160–9.
[56] Roneus M, Lindholm A. Muscle characteristics in Thoroughbreds of different ages and sexes. Equine Vet J 1991;23:207–10.
[57] Snow DH, Billeter R, Jenny E. Myosin types in equine skeletal muscle fibres. Res Vet Sci 1981;30:381–2.
[58] Snow DH, Guy PS. Muscle fibre type composition of a number of limb muscles in different types of horses. Res Vet Sci 1980;28:137–44.
[59] van den Hoven R, Wensing TH, Breukink HJ, Meijer AEFH, Kruip TAM. Variation in fiber types in the triceps brachii, longissimus dorsi, gluteus medius, and biceps femoris of horses. Am J Vet Res 1985;46:939–41.
[60] Desplanches D, Mayet MH, Sempore B, Flandrois R. Structural and functional responses to prolonged hindlimb suspension in rat muscle. J Appl Physiol 1987;63:558–63.
[61] Eddinger TJ, Moss RL, Cassens RG. Fiber number and type composition in extensor digitorum longus, soleus, and diaphragm muscles with aging in Fisher 344 rats. J Histochem Cytochem 1985;33:1033–41.
[62] Edgerton VR, Zhou MY, Ohira Y, Klitgaard H, Jiang B, Bell G, et al. Human fiber size and enzymatic properties after 5 and 11 days of spaceflight. J Appl Physiol 1995;78:1733–9.
[63] Haida N, Fowler Jr WM, Abresch RT, Larson DB, Sharman RB, Taylor RG, et al. Effect of hind-limb suspension on young and adult skeletal muscle. I. Normal mice. Exp Neurol 1989;103:68–76.
[64] Riley DA. Review of primary spaceflight-induced and secondary reloading-induced changes in slow antigravity muscles of rats. Adv Space Res 1998;21:1073–5.
[65] Andersen JL, Terzis G, Kryger A. Increase in the degree of coexpression of myosin heavy chain isoforms in skeletal muscle fibers of the very old. Muscle Nerve 1999;22: 449–54.
[66] Coggan AR, Abduljalil AM, Swanson SC, Earle MS, Farris JW, Mendenhall LA, et al. Muscle metabolism during exercise in young and older untrained and endurance trained men. J Appl Physiol 1993;75:2125–33.

[67] Coggan AR, Spina RJ, King DJ, Rogers MA, Brown PM, Nemeth PM, et al. Histochemical and enzymatic characteristics of the gastrocnemius muscle of young and elderly men and women. J Gerontol B Psychol Sci Soc Sci 1992;47:71–6.
[68] Frontera WR, Hughes VA, Fielding RA, Fiatarone MA, Evans WJ, Roubenoff R. Aging of skeletal muscle: a 12-yr longitudinal study. J Appl Physiol 2000;88:1321–6.
[69] Cartee GD. Influence of age on skeletal muscle glucose transport and glycogen metabolism. Med Sci Sports Exerc 1994;26:577–85.
[70] Cartee GD, Farrar RP. Exercise training induces glycogen sparing during exercise by old rats. J Appl Physiol 1988;64:259–65.
[71] Tankersley CG, Smolander J, Kenney WL, Fortney SM. Sweating and skin blood flow during exercise: effects of age and maximal oxygen uptake. J Appl Physiol 1991;71:236–42.
[72] Kurokawa T, Ozaki N, Sato E, Ishibahi S. Rapid decrease of glycogen concentration in the hearts of senescence-accelerated mice during aging. Mech Aging Dev 1997;97:227–36.
[73] Hoffman BB, Chang H, Farahbakhsh ZT, Reaven GM. Age-related decrement in hormone-stimulated lipolysis. Am J Physiol 1994;247:E772–7.
[74] Lonnqvist F, Nyberg H, Wahrenberg H, Arner P. Catecholamine-induced lipolysis in adipose tissue of the elderly. J Clin Invest 1990;85:1614–21.
[75] Rubany GM, Shepherd JT. Hypothetical role of endothelin in the control of the cardiovascular system. In: Rubanyi GM, editor. Endothelin. New York: Oxford University Press; 1992. p. 258–71.
[76] Wade CE, Freund BJ, Claybaugh JR. Fluid and electrolyte homeostasis during and following exercise: hormonal and non-hormonal factors. In: Claybaugh JR, Wade CE, editors. Hormonal regulation of fluid and electrolytes. New York: Plenum Press; 1989. p. 1–44.
[77] Maeda S, Miyauchi T, Waku T, et al. Plasma endothelin-1 level in athletes after exercise in a hot environment: exercise-induced dehydration contributes to increases in plasma endothelin-1. Life Sci 1996;58:1259–68.
[78] Hornig B, Maier V, Drexler H. Physical training improves endothelial function in patients with chronic heart failure. Circulation 1996;93:210–4.
[79] Predel HG, Meyer-Lehnert H, Backer A, et al. Plasma concentrations of endothelin in patients with abnormal vascular reactivity: effects of ergometric exercise and acute saline loading. Life Sci 1990;47:1837–43.
[80] Wilson JR, Mancini DM, Dunkman WB. Exertional fatigue due to skeletal muscle dysfunction in patients with heart failure. Circulation 1993;87:470–5.
[81] Yarasheski KE. Growth hormone effects on metabolism, body composition muscle mass, and strength. In: Holloszy JO, editor. Exercise and sport science reviews. Philadelphia: Williams & Wilkins; 1994. p. 285–312.
[82] Mehl ML, Schott HC, Sarkar DK, et al. Effects of exercise intensity on plasma β-endorphin concentrations in horses. Am J Vet Res 2000;61:969–73.
[83] Freestone JF, Shoemaker K, Bessin R, Wolfsheimer JK. Insulin and glucose response following oral glucose administration in well-conditioned ponies. Equine Vet J Suppl 1992; 11:13–7.
[84] Reaven GM. Insulin resistance and aging: modulation by obesity and physical activity. In: Lamb DR, Gisolfi CV, Nadel E, editors. Perspectives in excercise and sports medicine, vol. 8. Excercise in older adults. Carmel, IN: Cooper Publishing; 1995; p.395–428.
[85] Sial S, Coggan AR, Carroll R, Goodwin J, Klien S. Fat and carbohydrate metabolism during exercise in elderly and young subjects. Am J Physiol 1996;271:E983–9.
[86] Williams CA, Kronfeld DS, Staniar WB, Harris PA. Plasma glucose and insulin responses of Thoroughbred mares fed a meal high in starch and sugar or fat and fiber. J Anim Sci 2001;79:2196–2201.
[87] Terada S, Yokozeki T, Kawanaka K, Ogawa K, Higuchi M, Ezaki O, et al. Effects of high-intensity swimming training on GLUT-4 and glucose transport activity in rat skeletal muscle. J Appl Physiol 2001;90:2019–24.

[88] Fiatarone MA, Morley JE, Bloom ET, Benton D, Soloman GF, Makinodan T. The effect of exercise on natural killer cell activity in young and old subjects. J Gerontol 1989; 44:M37–45.
[89] Nieman DC. Immune function. In: Lamb DR, Gisolfi CV, Nadel E, editors. Perspectives in exercise and sports medicine, vol. 8. Exercise in older adults. Carmel, IN: Cooper Publishing; 1995; p. 435–61.
[90] Farquhar WB, Kenney WL. Age and renal prostaglandin inhibition during exercise and heat stress. J Appl Physiol 1999;86:1936–43.