The Physiology of Fatigue in Horses During Exercise

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What is Fatigue?

Dictionary definitions of fatigue include:

- *Temporary loss of strength and energy resulting from hard physical or mental work; "growing fatigue was apparent from the decline in the execution of their athletic skills"*

- *Feeling of tiredness or weariness usually associated with performance decrements*

- *Fatigue means mental or physical tiredness, usually caused by prolonged or intense activity, but also possibly caused by disease, lack of adequate nutrition or other anomalous factors*

- *A feeling of tiredness or weariness resulting in a decreased capacity for physical and mental work*

- *A condition that results when the body cannot provide enough energy for the muscles to perform a task*

- *Physical weariness resulting from exertion*

However, the use of the word fatigue in relation to exercise has very specific meanings. The term fatigue covers a wide range of manifestations ranging from:

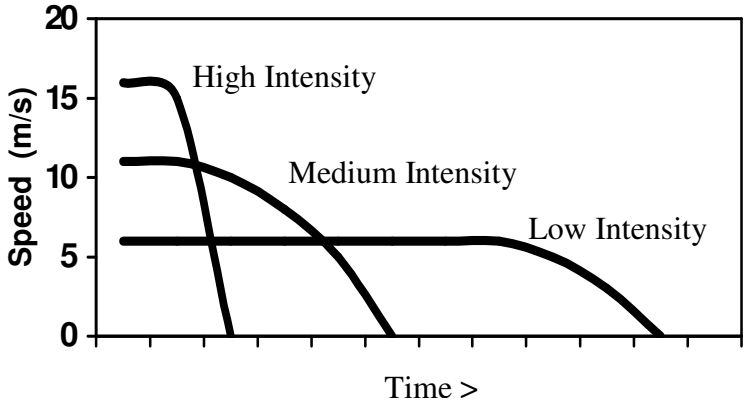
- *the horse that will not move another step*
- *the endurance horse at the end of a 100 mile race that shows great reluctance to trot*
- *the racehorse that has slowed in the last 100-200 meters of a race, but when passing the post is still travelling in excess of 16 m/s.*
- *the horse that slows down when galloping at steeplechase pace, but when given a few strides at a slightly slower pace, is able to return to the original faster pace*
- *the horse that is able to maintain its pace at gallop in a jump race, but when it comes to the next fence is unable to recruit enough muscle fibres to execute a jump to clear the obstacle*

All these animals are experiencing fatigue, but the underlying mechanisms and the consequences for each will be very different. To reiterate this point, at the end of the 100 metres, the human sprinters will all be slowing down and will be experiencing fatigue. At the end of the marathon, the human runner will be fatigued. However, given a days rest, the human sprinter may be able to reproduce his form from the previous day. The marathon runner would not. In addition, the sensation of fatigue experienced by each of these types of athletes would also be very different.

At a practical level in sport we use the term fatigue to describe the sensations of tiredness and the accompanying decrease in athletic performance. This applies equally to humans and horses. We can therefore use the following definition in relation to exercise:

Fatigue refers to the inability to continue exercise at a given intensity

In general terms, the higher the intensity of exercise, the earlier the onset of fatigue.



Causes of Fatigue

Fatigue could result from the failure of one enzyme system, one cell, one organ or one body system. This is turn can place an excessive burden on other body systems as they try to compensate.

There are a number of different areas that have been studied to try and understand the mechanisms of fatigue:

(1) Fatigue of the energy generating systems within and external to muscles

(2) Accumulation of metabolic by-products & failure of the muscular contractile mechanism

(3) Disturbances to homeostasis

(4) Central or peripheral nervous system

Fatigue is still poorly understood, however it is clear none of these areas can explain all the different aspects of fatigue that are recognised. For example, although at the end of an endurance ride a dramatic reduction in muscle glycogen concentration may occur, fatigue can arise when muscle glycogen concentrations are still high, for example in show-jumping.

A number of factors are known to influence the onset of fatigue, including

(1) Intensity, duration and pattern of exercise
(2) Fitness
(3) Age
(4) Body condition
(5) Environmental conditions
    a. Heat or heat and humidity
    b. Cold
    c. Pollution
    d. Altitude

(1) Depletion of Energy Stores as a Cause of Fatigue

Energy from high-energy intermediate ATP supports almost all cellular based active processes, including muscle contraction. However the amount of ATP stored in the muscles is low and will only support exercise for several seconds of muscular activity. When ATP is broken down to ADP it must be regenerated back to ATP. There are four different ways to regenerate ATP from ADP. These are:

- Transfer of a phosphate from another high energy intermediate within cells known as phosphocreatine (PCr)
- Rapid breakdown of intramuscular glycogen to lactic acid
- Aerobic breakdown of muscle glycogen or blood glucose
- Aerobic breakdown of muscle tryglycerides (fats) to free fatty acids (FFA) or uptake of FFA from blood

ATP Replenishment from Phosphocreatine (PCr)

The transfer of a phosphate from PCr to ADP to regenerate ATP is catalysed by the enzyme creatine kinase (CK). This process is very rapid, but the stores of PCr are limited and can only support contractions for a few seconds (See Table 1). Two ADP's can be used to generate one ATP and one AMP, a reaction catalysed by the enzyme myokinase. Neither the rephosphorylation of ADP by PCr nor the production of ATP from 2 x ADP requires oxygen and hence these processes are often referred to as anaerobic energy production.

ATP Replenishment from Glycogen Breakdown to Lactic Acid

The second form of anaerobic energy generation is the rapid breakdown of intramuscular energy stores of glycogen to lactic acid. Accumulation of lactic acid within muscles and the associated reduction in muscle pH are believed to play a role in the development of fatigue (see later). Paradoxically, production of lactic acid is essential for fast exercise. It's also essential to produce energy by this route at the onset of exercise before the aerobic systems have come up to speed (See Table 1). Human sprinters have the capacity to generate much higher blood lactate concentrations than human endurance athletes. The same is true of racehorses *versus* endurance horses. Without the ability to produce lactic acid, we could not change pace or accelerate rapidly. Whilst this energy pathway is described as anaerobic, that does not mean that lactic acid is only produced when there is no oxygen present. It simply means that it will function whether or not oxygen is available.

ATP Replenishment from Aerobic Metabolism of Muscle Glycogen or Blood Glucose
The complete aerobic breakdown (oxidation) of glycogen or blood glucose to carbon dioxide and water takes place in both the cytoplasm of the cell (which does not require oxygen and produces a small amount of ATP) and in the mitochondria. It is within the mitochondria that the oxygen is used and the majority of ATP is regenerated. This process is much more efficient at regenerating ATP from ADP, but is slower than the anaerobic pathways described above (and see Table 1). This route of energy production is fundamental to endurance exercise. Around 90% of the total body stores of glycogen are stored within the muscles, with the majority of the remainder being stored in the liver.

ATP Replenishment from Aerobic Metabolism of Fat
The aerobic metabolism or oxidation of tryglycerides (fat) to regenerate ATP from ADP also requires oxygen and takes place primarily within mitochondria. It also generates carbon dioxide and water as the end products. In contrast to glycogen, intramuscular tryglycerides account for only around 10% of the total body stores, with the remainder being found in adipose tissue and subcutaneous fat depots. Tryglycerides must be broken down to liberate FFA before they can be metabolised further. FFA are then transported in the blood from sites of fat deposits to be taken up by working muscles.

Table 1. Sources of energy for use by muscles during exercise.

	Max Power (mmol ATP/kg/s)	Time to reach Max Power	O_2 Requirement (mmol O_2/ATP)	Work time to fatigue
Anaerobic ATP	11.2	< 1s	0	seconds
PCr	8.6	< 1s	0	seconds
CHO > Lactate	5.2	< 5s	0	minutes
Aerobic				
CHO > CO_2 + H_2O	2.7	3 minutes	0.167	hours
FFA > CO_2 + H_2O	1.4	30 minutes	0.177	days!!

Depletion of Energy Stores as a Cause of Fatigue in Endurance Exercise
At the end of endurance rides it has been shown using muscle biopsies that many muscle fibres are completely depleted of glycogen. If these fibres are still functioning, they will have to do so by taking up blood glucose or exclusively using fat. Whilst it is possible to deplete muscle glycogen stores, it is almost impossible to deplete stores of fat in a single bout of exercise; even a thin endurance horse is estimated to have enough fat to complete 5 x 100 mile rides. In addition to depletion of muscle glycogen stores, horses at the end of competitive 100 mile rides often exhibit low plasma glucose concentrations (<2.5 mmol/l), indicating marked depletion of liver glycogen stores. Repletion of muscle and liver glycogen in horses may take 24-48h. Depletion of brain glycogen has also been shown to occur in association with prolonged

exercise. This has been suggested to be involved in central fatigue. However, the brain appears to be able to restore glycogen much more rapidly than liver or muscle.

Depletion of muscle glycogen and its effects on performance are well recognised in human sport and is referred to as "hitting the wall". When this point is reached, the athlete is obtaining the majority of the energy from the aerobic metabolism of fat. As glycogen concentrations are very low or exhausted in some fibres, the athlete is limited as to the maximum speed they can run at and will be unable to accelerate if another runner approaches from behind. The same scenario undoubtedly occurs in endurance horses.

(2) Accumulation of Metabolic By-Products as a Cause of Fatigue

Lactic Acid Accumulation
Associated with moderate to high intensity exercise. Not likely to be an important factor in fatigue in the endurance horse.

PCr Depletion and Accumulation of Phosphate Ions
Associated with moderate to high intensity exercise. Not likely to be an important factor in fatigue in the endurance horse.

Calcium
Calcium is intimately involved in linking nerve impulses to muscle activity. This is known as excitation-contraction coupling and involves calcium release by the sarcoplasmic reticulum (SR). Calcium lost from the SR during excitation-contraction coupling may be taken up by mitochondria, interfering with their function. In addition, the ability of the SR to release calcium may be reduced, resulting in a less powerful contraction. The uptake of calcium by mitochondria also reduces their efficiency for regenerating ATP. Fatigue caused by alterations in intracellular (intramuscular) calcium homeostasis may be an important factor in fatigue in prolonged exercise, such as endurance.

Oxygen Depletion/Delivery
Oxygen must continually diffuse from the capillaries into the muscle to support continued mitochondrial ATP replenishment. Changes in oxygen demand by the muscle or supply from the circulation can be buffered by intramuscular myoglobin, but this is only sufficient for seconds as opposed to minutes. A mismatch between oxygen supply and demand predominantly occurs at the start of exercise, during strenuous exercise or exercise at altitude, and results in increased lactic acid production.

(3) Disturbances to Homeostasis
Both the ability to exercise and the ability to exercise for a prolonged duration requires the integration of many different body systems. Thus, single or multiple factors can cause fatigue to occur. Some of the factors that may be involved in maintaining homeostasis during exercise include:

- Electrolyte concentrations and their compartmentalisation
- Concentrations of glucose in blood, muscle and other tissues (e.g. brain)
- Concentrations of FFA

- Blood and plasma volume
- Muscle and systemic pH and osmolality
- Temperature (especially muscle and brain)
- Hormone concentrations

There is no compelling evidence to suggest that the ability to perform prolonged endurance exercise is limited by cardiac muscle fatigue. In people free of heart disease it is rare to find signs of ischaemia (on the basis of changes in ECG) during or following exercise.

(4) Central or Peripheral (Neuromuscular) Nervous System Fatigue

It is possible to have muscular fatigue when the function of the muscle itself is not impaired as there are many functional levels between the CNS and the muscle that can be impaired. Painful afferent inputs from muscles and joints may have a negative effect on an animal's willingness to continue to exercise. The brain receives a number of different inputs during exercise and these can all affect its physiological response:

- Pain
- Breathlessness
- External stimulation (e.g. crowd, use of a whip, rider's voice)

It is believed that one of the effects of training may be to reduce the impact of painful or unpleasant afferent inputs to the CNS i.e. after training the horse may be able to tolerate a higher level of physiological "discomfort" and so have a greater potential to perform at a level that will result in a greater amount of tissue injury.

Fatigue In The Endurance Horse

Fatigue in equine endurance competition is most likely to occur due to:

- Depletion of muscle, liver and possibly brain glycogen
- Dehydration and electrolyte imbalance

Depletion of muscle and liver glycogen is a consequence of prolonged endurance exercise but the rate or extent of depletion may be increased by:

- Insufficient or inappropriate warm-up
- Constant change in pace
- Rapid accelerations
- Competing in extreme environmental conditions
- Horses with low aerobic capacity
- Horses with high proportions of IIB muscle fibres

Dehydration, electrolyte and acid-base disturbance can occur in any endurance horse even in thermally unchallenging conditions if food and fluid intake are reduced. However, the risk is greatly increased for prolonged exercise in hot or hot and humid

environmental conditions. This may be compounded by other factors that serve to increase exercise "intensity", such as soft ground and hilly terrain.

Indicators of Fatigue in the Endurance Horse

Ataxia, Stumbling, Unwillingness to Exercise
This may be a sign of low blood glucose, electrolyte and acid-base disturbance hyperthermia, hypovolaemia and/or muscle weakness. These are probably best characterised and quantified by clinical observation.

Hypoglycaemia
Plasma glucose concentrations in endurance horses may fall as low as 2.5 mmol/l following a competitive 100 mile race ride.

EMG
There are changes in the electromyographic output of muscle that have been shown to be associated with the development of fatigue in human and other animal models, but not in horses to the best of the authors knowledge.

Dehydration
Dehydration may be associated with electrolyte and acid-base disturbance. Most studies suggest that exercise performance may be compromised above a loss of ~5% bodyweight in horses. Dehydration and hypovolaemia will be reflected in increases in heart rate at rest and during exercise.

Synchronous Diaphragmatic Flutter (SDF or "thumps")
SDF is an indication of dehydration and/or marked acid-base and electrolyte disturbance. Whilst SDF alone may not cause fatigue or even be deleterious *per se*, it is an indicator of a failure to maintain homeostasis and should be considered as an indication to terminate exercise.

ECG
Changes in the ECG of a horse may also be a reflection of marked acid-base and electrolyte disturbance. There appears to be little data on changes in the equine ECG following endurance exercise.

Summary

Fatigue during or following prolonged exercise is a complex entity, but in the endurance horse is most likely related to muscle and liver glycogen depletion, low plasma glucose concentration, hypovolaemia and electrolyte and acid-base disturbance. At present, in addition to a clinical examination, the only objective physiological variable that can be measured in the vet-gate is heart rate. Whilst an accurate assessment of the degree of dehydration would likely be informative, at present the accuracy or sensitivity of the skin-pinch test is unknown. Assessment of blood glucose concentration in the latter stages of a race as an aid to determining how fatigued an animal also warrants investigation.