Untying Tying Up

with **Dr Paula Williams**
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Her clinical interests include diagnostic imaging, the investigation and management of musculoskeletal issues in the equine athlete, the equine foot, neonatology and internal medicine.

Tying Up is a syndrome and a term used to describe a group of common muscle disorders in the horse. It is one of the most misunderstood and controversial syndromes in the horse, with much speculation over its causes and mechanisms. The typical signs of a horse that is tying up are muscle fatigue, pain, cramping and reluctance to move. Other names that have been used include Monday morning disease, azoturia, myopathy, myositis and rhabdomyolysis. It is a condition that has been known throughout history and described in 19th-century literature. In a veterinary text from 1883, the clinical signs were described as "sweating and trembling, scarcely able to turn in the stall, the muscles of the back and loins in a state of spasm, tail quite stiff" - this is still a relevant description now!

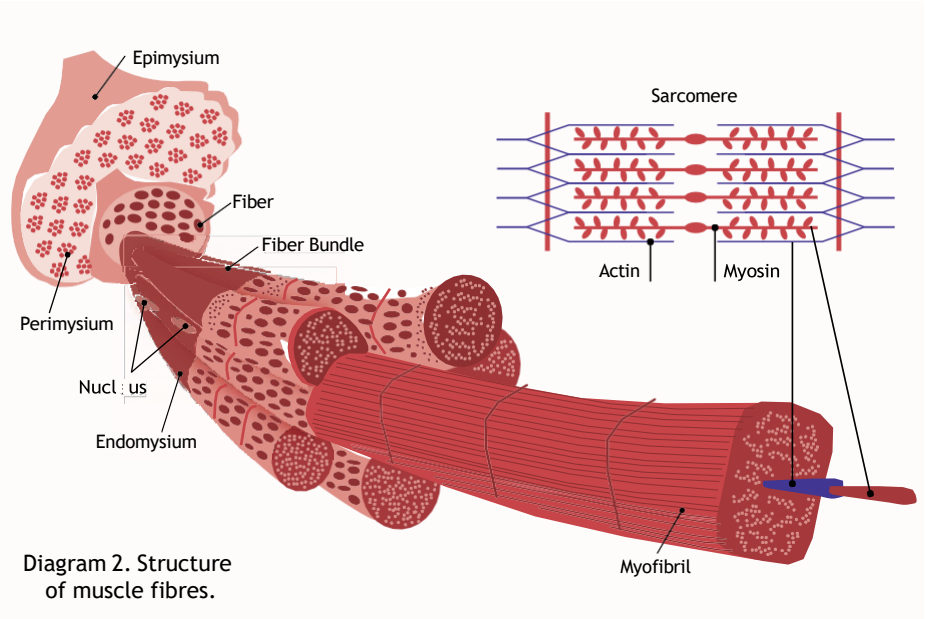

Diagram 2. Structure of muscle fibres.

Over the years, researchers have learned much about this condition, and we now understand that tying up is not one disease but several different ones. One of the key researchers is Dr Stephanie J Valberg, DVM, PhD, who has spent years researching this very interesting but frustrating condition.

Here, we are going to look at muscle anatomy and physiology, some of the different types of tying up, clinical signs and management.

Muscle anatomy and physiology

Horses are supreme athletes and, as a result, have developed a large muscle mass for their endeavours, be it speed, endurance, jumping, working cattle or elegant dressage movements. It is the muscles that create movement by pulling on the bones to operate the joints that allow their incredible feats. Minor or intermittent disruptions in muscle function can have major impacts on an equine athlete's performance.

Diagram 1 on next page shows the main muscle groups of the horse. **Fun fact:** there are approximately 700 muscles in the horse, the largest muscles of which are those of the back and the hindquarters.

Muscles are composed of groups of **muscle fibres** - essentially, within a muscle there are fibres that are stacked on top of one another and are all parallel. Within those fibres are smaller units called **myofibrils**, which are the functional units of muscles and are microscopic in size. Diagram 2 shows the muscle fibre structure. The myofibrils are composed of two main protein **filaments - actin** and **myosin** which lie against one another and interdigitate with each other with little finger-like projections from the actin molecule. The filaments slide back and forth during exercise to allow the muscle to stretch and shorten.

A **sarcomere** is the basic building block of myofibrils and is the cellular structure responsible for muscle fibre contraction. When the myofibrils are extended, the muscle is relaxed, and when they are interdigitated more, the muscle is contracted.

Without getting into the depths of molecular biology during muscle contraction, key molecules involved include **acetylcholine** (a neurotransmission chemical), **adenosine triphosphate (ATP) sodium** and **calcium**. **Glycogen** is the key molecule for the energy production required for muscle activity and is stored in the muscles at a higher concentration than that of people.

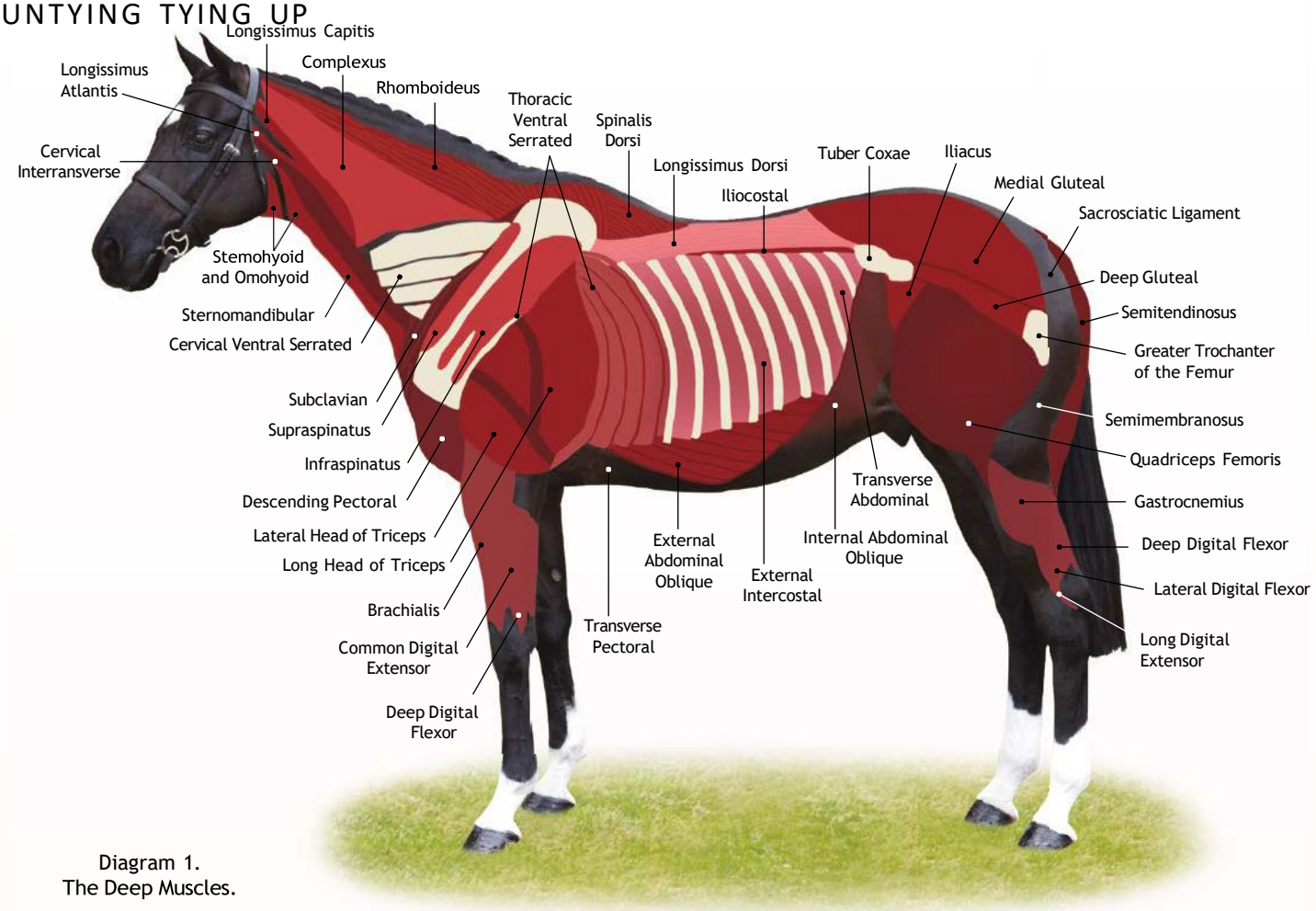

Diagram 1.
The Deep Muscles.

"The typical signs of a horse that is tying up are muscle fatigue, pain, cramping and reluctance to move."

What are the clinical signs of tying up?

The clinical signs are usually associated with exercise; they can vary in severity and include:

- Stiffness
- Pain
- Distress and anxiety
- Reluctance or refusal to move
- Swollen muscles
- Muscle fasciculations
- Sweating
- Increased respiratory rate
- Increased heart rate
- Mild cases may show poor performance
- Severe cases may result in:
  - Recumbency
  - Myoglobinuria – dark wine-coloured urine
  - Kidney failure

What type of horses are prone to tying up?

Usually horses that are in work and being exercised are prone to tying up – this includes racehorses, showjumpers, endurance horses, eventers, cutting and campdrafting horses and dressage horses. All breeds are susceptible, but certain types of tying up are more prevalent in Quarter Horses, Thoroughbreds, Arabs, Morgans, Warmbloods and Draft horses. Some of the conditions have been shown to have a genetic predisposition.

How is the diagnosis confirmed?

The diagnosis of tying up is based on history and clinical examination. Diagnostic tests that may be performed include:

- Blood samples – particularly biochemistry to evaluate the muscle enzymes **creatine kinase (CK)** and **aspartate transaminase (AST)** (See Table 1), electrolyte abnormalities and kidney function
- Urine samples to check for **myoglobin**
- Dietary analysis
- Exercise testing
- Genetic testing
- Muscle biopsy

The diagnostic tests utilised will depend upon the clinical case and the type of tying up that may be implicated.

Table 1.

Muscle Enzymes
➢ Creatine Kinase (CK) Short term muscle enzyme used an indicator of recent muscle tissue damage. It peaks at 6 – 12 hours. Levels over 400 IU / L are significant.
➢ Aspartate Transaminase (AST) This enzyme may remain elevated for days to weeks following an episode. Levels over 1000IU/L are significant.

What are the risk factors that may predispose to tying up?

There are many predisposing factors implicated in tying up, but generalised ones are:

- Dietary excess of soluble carbohydrates (high sugar diets)
- Frequency of exercise or change in exercise routine

- Stress
- Electrolyte disturbances
- Dehydration
- Travel
- Nervous horses

A look at the different types of tying up.

Exertional Rhabdomyolysis (ER) is the term currently in favour for this "tying up" group of conditions - **exertional** pertaining to exercise, and **rhabdomyolysis** referring to the changes that occur in the skeletal muscle (breakdown or necrosis of the muscle).

Sporadic Exertional Rhabdomyolysis
This case of tying up occurs as a singular episode (irregular or random). Usually, these horses have no previous history of tying up, and all breeds of horses are susceptible to this type. The most common causes are exercise levels that exceed the horse's state of training and dietary imbalances, particularly diets high in soluble carbohydrates and low forage. Other predisposing factors are infectious respiratory disease, exhaustion, dehydration, dietary deficiencies of sodium, vitamin E or selenium and calcium - phosphorous imbalances.

Once the horse has recovered, changes in management in terms of diet and exercise usually prevent this type of tying up from happening again.

Chronic Exertional Rhabdomyolysis
Some horses have repeat or recurrent episodes of tying up or rhabdomyolysis, even with light exercise. There have been 4 types of the chronic form identified (on the basis of muscle biopsies and genetic testing). These types of horses often don't respond well to prolonged rest.

1 Polysaccharide Storage Myopathies (PSSM)

A Type 1 Polysaccharide Storage Myopathy (Type 1 PSSM)
This occurs more frequently in Quarter Horse related breeds and also in Morgans and Draft horses. It is a genetic mutation in the glycogen synthase 1 (GYS 1) gene, and a diagnosis can be made by genetic testing of blood or hair samples.

These horses often develop signs of tying up from a young age with minimal exercise. Episodes are characterised by gait asymmetry, hindlimb stiffness and a tucked-up appearance; sometimes colic-like signs are seen. In other cases, there may be loss in muscle mass and weakness.

B Type 2 Polysaccharide Storage Myopathy (Type 2 PSSM)
This occurs in Arabs, Morgans, Thoroughbreds and Warmbloods; it may also be seen in Quarter Horses. A diagnosis is confirmed by a muscle biopsy and shows an abnormal pattern of glycogen storage. The horses show chronic episodes of muscle stiffness, soreness and muscle wastage.

2 Myofibrillar Myopathy

This is a newly recognised disorder in Arab and Warmblood horses. In Arab horses, it occurs more commonly in endurance horses and is characterised by muscle pain and stiffness. In Warmbloods, the most common signs are mild shifting lameness, exercise intolerance and loss of muscle mass.

3 Malignant Hyperthermia

This is caused by a genetic mutation in the skeletal muscle ryanodine receptor gene (RYR1). This mutation is responsible for both anaesthesia and non-anaesthesia-related causes of rhabdomyolysis in Quarter Horses. Some Quarter Horses have both malignant hyperthermia and PSSM, so they may show more severe clinical signs.

4 Recurrent Exertional Rhabdomyolysis (RER)

This occurs frequently in Thoroughbreds, Standardbreds and Arabs. The predisposing factors in this type appear to be high-stress environments and in horses with nervous temperaments. There appears to be abnormal regulation of intracellular calcium in the skeletal muscles.

What is the treatment for tying up?

The management and treatment very much depend on the severity of the episode and the underlying cause. Your veterinarian will instigate treatment appropriate to the individual case.

Acute case
- Exercise is stopped
- Horse moved to a stable or confined area
- Control pain and anxiety
  - Sedatives may be advised, such as acepromazine (ACP) and opioids
  - Nonsteroidal anti-inflammatory drugs (NSAIDs) such as phenylbutazone, flunixin or ketoprofen MAY be considered if there is no dehydration or kidney compromise.
- Intravenous fluid therapy may be initiated if there is evidence of renal compromise, myoglobinuria and in very severe cases.
- A hay-only diet with a vitamin and mineral balancer is advised in the initial stages.
- Rest with regular access to a paddock until the muscle enzymes have corrected
- Gradual reintroduction to work
- Long-term dietary adjustment

Chronic case
- Dietary modification – usually based on a forage diet with limiting grain (starch) and replacing it with a fat supplement.
- Exercise regimes adjusted according to the underlying condition
- Change environment and training for those with nervous temperaments and affected by stress (for example, minimising stable confinement, using turnout, exercising and feeding this horse before others, appropriate equine company and the judicious use of low-dose tranquilisers)
- Supplementation with amino acids such as cysteine, antioxidants such as Coenzyme Q10 and vitamin E
- Medications such as dantrolene and phenytoin may be considered, but long-term management with these is expensive

What should I do if my horse ties up when being exercised?

> Stop exercising the horse – do not force it to walk
> Move the horse to a stable or confined area
> Rug the horse if it is cool
> Provide water – small frequent sips to a hot horse or free access to a horse that has cooled down
> Remove concentrates – only allow hay
> Call your veterinarian
> Do not administer medications without the direction of your veterinarian

Summary

Tying up is an umbrella term for a group of diseases affecting the muscles of the horse – the current favoured term for this syndrome is exertional rhabdomyolyisis (ER). The syndrome has long been known about, but research on the three decades has discovered that there are different forms and causes. The clinical signs can vary in severity but are usually associated with exercise and include painful, cramping muscles, anxiety, reluctance to move, sweating and high respiratory and heart rates. The cases can be sporadic or chronic. If your horse ties up, then the key to preventing further muscle damage is to stop exercising the horse, put it in a confined area, and to call your veterinarian.