

Exertional rhabdomyolysis---excruciatingly specific details of what's happening at the cellular level.

The complete pathophysiology (Why It Happens) of exertional rhabdomyolysis (most commonly called "tying up") is still not completely understood. Currently, the conditions that are known to be factors in causing tying up are

1. resting a conditioned horse on a full-grain diet, followed by exercise ("Monday morning disease");
2. whole-body potassium depletion;
3. selenium deficiency;
4. an unaccustomed level of exercise;
5. postviral infections, particularly rhino;
6. intoxications with ionophores (a substance which increases cellular permeability to a specific ion, which would in turn disrupt the electrical potential of the cell), blister beetle, mercury, coffee bean (cassia) or gossypol from raw cottonseed.

Other factors which have been suggested as being contributory are hypothyroidism, some high-performance lines of horses, nervous horses, fillies, shock, laminitis, tetanus, neural injury, estrus, hyperestrogenism (resulting from possibly a granulosa cell tumor), cold damp weather, heavy muscling, and low-sodium rations. Electrolyte depletion, especially calcium, magnesium and chloride may also cause muscle cramps, which are sometimes referred to as slow-onset rhabdomyolysis; or synchronous diaphragmatic flutter, commonly called "thumps". These are related syndromes, but not exactly the same as the syndrome described here, which is most accurately described as acute rhabdomyolysis.

One of the current hypotheses is that when a conditioned horse is not worked and kept on full feed high in soluble carbohydrates (such as grain), the horse will accumulate carbohydrates in the muscles. If there is a sudden demand for work, the body cannot adequately remove the rapidly accumulating lactic acid in the muscles. This in turn causes vasospasms and ischemia---which means essentially that the surrounding blood vessels "clamp down" so that the lactic acid waste product cannot be removed. As a result, intracellular pH drops, the muscle cell is disrupted and you get the hard, crampy muscles you see when a horse ties up.

Other theories of the biochemical mechanism is that there is a deficiency of the high-energy phosphates in muscle cells following maximal, anaerobic exertion, and/or a depletion of muscle glycogen after prolonged, slow (endurance-type) exercise. High body temperatures and electrolyte imbalances/depletions are also probably contributing causes, and certainly major factors in endurance horses that tie up during competitions.

Unless you're a biochemist, all of these different theories essentially boil down to the same net effect---the ion pumps (ie, sodium/potassium, calcium/magnesium and calcium/ATPase) in the membrane surrounding the muscle cell which move substrates in and out of the cell are disrupted, and so the interior environment of the muscle cells either cannot get rid of waste products of metabolism, OR has too much of a metabolic substrate to be able to function, OR can't get enough of a metabolic substrate to be able to function. And so the muscle cell simply

shuts down. When muscle cells shut down, they don't do so in the relaxed position, they freeze up in the contracted position, which is why you get those rock-hard muscles. Biochemically, it's not all that different from rigor mortis.

The effect on kidneys comes in when the connective tissue (the sarcolemma) surrounding and enclosing the muscle cell is disrupted, releasing the contents of the muscle cell into the bloodstream. There are lots of different proteins and substrates and whatnot in a muscle cell, but the important one for this particular discussion is myoglobin. Myoglobin is a protein pigment which is responsible for oxygen transport in the muscle cell. Hemoglobin transports oxygen in the bloodstream, myoglobin transports oxygen in the muscle cell. When myoglobin is released from a disrupted muscle cell into the bloodstream, it travels to the kidneys and is filtered out. In being filtered out of the bloodstream (and keep in mind, there's probably a lot of it from the kidney's point of view), it causes (or CAN cause) kidney damage or even total renal failure by overwhelming and clogging up the kidney tubules and restricting the blood (and therefore oxygen) supply to the kidney tissue. This effect will be worsened if the animal is hypovolemic, meaning he's dehydrated and therefore has a decreased total plasma volume. A decreased plasma volume means that in turn the blood is thicker and that the heart must work harder to circulate. And this in turn means that less oxygen is delivered to the muscles and organs, fewer substrates, less waste product removed, and so on. A vicious cycle sort of thing.

So while myoglobin does not directly damage the kidneys, in great enough concentration it will cause damage indirectly by clogging them up and creating what is called myoglobinuric nephrosis and possibly renal failure. It's also the myoglobin being filtered out that shows up as very dark urine. The dark urine itself is not what you have to worry about---what you DO have to worry about is the fact that myoglobin in the urine means that significant muscle disruption and damage has occurred in the system, and that the kidneys are being overwhelmed with a whole lot of waste product to try and get rid of. Needless to say, this is serious s**t from the physiological point of view. However, dark urine doesn't always mean myoglobinuria. Dark urine can be caused by other things as well. But if your horse is dehydrated, won't move and is standing there hunched up and miserable and the urine looks a lot like coffee---you've got problems.

Some of the other things a veterinarian will look for in a suspected tying-up horse are elevated enzymes in the blood plasma, specifically CK (creatinine kinase) and AST (aspartate aminotransferase). AST is also referred to as SGOT, but both refer to the same enzyme. There are other things the vet will look for as well, like creatinine, urea, electrolytes and so on, but enzyme levels are at the top of the list. CK and AST are both enzymes contained in the muscle cell (as well as other types of cells) which are released into the blood when the muscle cell is disrupted. Therefore, if the enzyme levels are elevated in the blood panel, it must mean that tissue cells somewhere are being (or were being) damaged. The tricky part in diagnosis is figuring out where tissue damage is occurring---AST occurs in both muscle and liver cells, so elevated levels could mean problems in either muscle OR liver (and for that matter, AST levels can also be elevated by certain drugs or toxins). CK levels will indicate muscle damage, while other elevated enzymes in the blood panel will indicate liver damage. And to make things even more confusing, there are various isoforms of yet another enzyme, LDH (lactate dehydrogenase) which will indicate whether muscle damage occurring is from skeletal or cardiac (heart) muscle.

The elevation in CK will be detectable within a few hours of the onset of clinical symptoms, peak within 24 hours and decline fairly quickly. CK's half-life is six hours, meaning that half of the amount remaining is removed within six hours. Hence, 50% is gone within 6 hours, 75% is gone within 12 hrs, 87.5% is gone within 18 hrs, 93.75% is removed within 24 hrs, and so on. The concept of "half-lives" doesn't refer only to enzymes, by the way, the same general idea applies to drug half-lives, isotope half-life, etc etc (just a little extra trivia for you)(I know, riveting.)

The rise in levels of AST will peak approximately 24 hours after the onset of the clinical signs of tying up, and decline much more slowly---AST has a half-life of about 14 days, so with significant muscle damage, it'll be awhile before levels are really back to normal. The relative levels of these two enzymes, among other things, are what a DVM will look at in determining the extent of damage, whether damage is still occurring and how long ago the initial damage occurred. For example, if a horse transport company delivers a horse doing a good impersonation of a piece of granite, and swears the horse must have injured himself last week before they ever laid eyes on him...but the blood analysis shows screaming CK levels (indicating recent muscle damage) and relatively low AST levels (also indicating recent damage), then the transport companies arguments can be classified under the heading of I Don't Think So Chuckles.

References:

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