Disorders of Muscles in Animals

General overview

Normal muscle, comprising many motor units, is dynamic, and its function and structure can be influenced by many diseases.

- Complete **paralysis**, **paresis**, or **ataxia** may be caused by primary muscular dysfunctions of infectious, toxic, or congenital origin.
- However, in most instances the primary disorder can be attributed to the **nervous system** eg;

I. **Tetanus:** Toxemia is caused by a specific neurotoxin produced by *Clostridium tetani* in necrotic tissue. Almost all mammals are susceptible, although dogs and cats are relatively more resistant.
II. **Equine rhinopneumonitis** (caused by EHV-1 and EHV-4): An acute febrile respiratory disease upon primary infection, characterized by rhinopharyngitis and tracheobronchitis.
III. **Canine distemper**: Canine distemper is a highly contagious, systemic, viral disease of dogs seen worldwide. Clinically, canine distemper is characterized by a diphasic fever, leukopenia, GI and respiratory catarrh, and frequently, pneumonic and neurologic complications.
IV. **Protozoal myelitis:** CNS infection of equids with either of the apicomplexan protozoa ***Sarcocystis neurona*** or *Neospora hughesi*]), with the muscular system simply representing the effector organ.

- Disorders that affect the **neuromuscular junction** can result in muscle fatigue, weakness, and paralysis. eg: **myasthenia gravis**, **hypocalcemia**, **hypermagnesemia**

- The neuromuscular junction can also be affected by **muscle-relaxing drugs** eg:

✓ **curare:** It paralyzes the motor nerves & is traditionally used by some Indian to poison their arrows and blowpipe darts
✓ **Succinylcholine:** a synthetic compound used as a short-acting muscle relaxant and local anesthetic
✓ **M99 (Morphine)**: certain antibiotics and toxins (eg, botulism, tetanus, venoms).

- Disorders primarily of the **muscle membrane** and, to some extent, of the actual muscle fibers are called myopathies. Muscle membrane disorders may be:

I. **Hereditary** (eg, myotonia congenita in goats)
II. **Acquired** (eg, vitamin E and selenium deficiencies, hypothyroidism, and hypokalemia).

- Myopathies involving the actual muscle fiber components include: **muscular dystrophy**, **polymyositis**, **eosinophilic myositis**, **white muscle disease**, **exertional rhabdomyolysis**.

- Trauma to muscles is common in horses and also occurs in other species.
- The trauma can be from external injury or from intense athletic activity, during which muscle tears and ruptures may occur.
- Fibrotic myopathy in the rearlimb of horses is a mechanical lameness caused by trauma and subsequent fibrosis or ossification of the muscle.

(White Muscle Disease, Stiff Lamb Disease, Nutritional Muscular Dystrophy)

Nutritional musculodystrophy (NMD) is an acute, degenerative disease of **cardiac and skeletal muscle** caused by a **dietary deficiency of selenium or vitamin E** in young, rapidly growing calves, lambs, and kids.

Etiology: Low blood levels of selenium and/or vitamin E due to:

- Dams have usually consumed selenium-deficient diets during gestation.
- Selenium deficiency appears to be more important than vitamin E in causing NMD.
- NMD occurs worldwide in areas where the soil (and therefore the derived grains and forage) is deficient in selenium, and storage conditions do not preserve vitamin E in forages.
- Vitamin E deficiency occurs most commonly when animals are fed poor-quality hay, straw, or root crops.

Pathogenesis:

- Both vitamin E and selenium have an important **antioxidant** function and protect cell membranes against damage from free radicals.
- Selenium is an essential component of five antioxidant selenoproteins, including glutathione peroxidase, and vitamin E acts as an antioxidant within lipid bilayers.
- **Muscle degeneration** is the result of oxidant damage to cell membranes and proteins, leading to a loss of cellular integrity.
- **Young**, **rapidly** growing animals usually are affected, although the disease has also been reported in yearling and adult cattle.

Clinical Findings:

- In such cases, the **clinical course** is frequently **short**, with **death** occurring commonly in <24 hours despite medical therapy.
- When **cardiac muscle** is primarily affected, animals may be found in respiratory distress, have cardiac arrhythmias, or be found **dead**.
- When **skeletal muscle** is primarily affected, signs of muscle **weakness**, **stiffness**, and **difficulty rising** are seen.
- Most affected animals are able to remain standing only for **short periods**, and **locomotor muscles** may be **firm** and **painful** on palpation.
- If the **respiratory muscles** are affected, the animal may show **respiratory distress** and evidence of increased **abdominal effort** when breathing.
- The muscles of the **tongue** may be involved, resulting in **dysphagia**.
- Animals with skeletal NMD often respond **favorably** to treatment and rest.
- Improvement is evident after a few days; within 3–5 days, animals can often **stand** and **walk**.

Post mortem lesions:

- **Bilaterally** symmetric **myodegeneration** is a consistent finding in NMD.
- Skeletal muscle degeneration is characterized by **pale discoloration** and a **dry appearance** of affected muscle, **white streaks in muscle** bundles, **calcification**, and **intramuscular edema**.
- The **white streaks** seen in **cardiac** and **skeletal muscle** bundles represent bands of **coagulation necrosis** or, in chronic cases, **fibrosis** and **calcification**.

- In **calves**, the **left ventricle and septum** are most frequently involved, but **both ventricles** are usually involved in **lambs**.
- Histologically, affected muscle fibers may be hypercontracted and fragmented, with some mineralization of muscle fibers and others undergoing macrophage infiltration.

Diagnosis:

- Beside the main clinical signs of this disease, supportive evidence of NMD includes increased levels of **Creatine Kinase** (CK), Aspartate Aminotransferase (**AST**), and Lactate dehydrogenase (**LDH**).
- Definitive diagnosis is based on demonstration of **low** whole **blood selenium** (normal range >0.1 ppm) or liver content (normal cattle 0.9–1.75 mcg/g of dry matter, sheep 0.9–3.5 mcg/g dry matter).
- The critical concentration of **vitamin E** (alpha-tocopherol) in plasma is **1.1–2** ppm in large animals.
- Vitamin E destroyed rapidly in plasma samples. Therefore, plasma samples for alpha-tocopherol analysis should be put on ice immediately, protected from light by wrapping in foil, and stored at –21°F (–29°C) if analysis is to be delayed.

Differential Diagnosis:

1. infectious diseases resulting in septicemia, pneumonia, and toxemia
2. cardiac anomalies caused by ionophore antibiotics and cardiotoxic agents found in plants (eg, oleander, senna, yew, white snakeroot, and gossypol toxicity from cottonseed)
3. diseases causing stiffness of gait, weakness, and recumbency with no change in mental status, including:
a. spinal cord compression
b. cerebellar disease
c. suppurative and nonsuppurative meningitis/myelitis
d. polyarthritis
e. neurotoxins such as organophosphates and tetanus
f. pelvic fractures
g. parasitic myositis
h. clostridial myositis
i. traumatic injuries

Treatment:

- The cardiac form of NMD is often acutely **fatal**, whereas the skeletal form may **respond** to injectable selenium products.
- The label dosage for **selenium is 0.055–0.067 mg/kg** (2.5–3 mg/45 kg), IM or SC.
- Dosage of these injectable products should not be greatly increased above that on the label to prevent an **inadvertent selenium toxicosis**.
- When using vitamin E/selenium combinations, the amount of vitamin E is insufficient for supplementation; it is present only as a preservative for the solution.
- Injectable vitamin E products that contain **300 and 500 IU vitamin E per mL** as d-alpha-tocopherol are available.
- Oral supplementation is the general approach to provide additional dietary levels of vit. E.
- Recommended levels of supplementation for calves range from **15 to 60 mg** of dl-alpha-tocopherol acetate per **kg of dry feed**.
- **Antibiotics** may be indicated to combat secondary pneumonia.

- Provision of adequate **energy intake** and attention to the fluid and electrolyte balance are critical if recovery is to be successful.

Prevention:

- Selenium can be incorporated into the total ration of ruminants and other species to a level of 0.3 ppm.
- In salt/mineral mixtures formulated for free-choice feeding, selenium can be incorporated at 90 ppm for sheep and 120 ppm for cattle.
- In certain areas or in herds, levels as high as 200 ppm selenium in salt/mineral mixtures may be necessary to maintain adequate selenium levels.
- The regulations limit the intake of supplemental selenium to 0.7 mg/head/day in sheep and 3 mg/head/day in cattle.
- Alternatively, individual animals can be supplemented by periodic (30- to 60-day intervals) injections of selenium/vitamin E preparations to help maintain body concentrations and assist in transplacental transfer of selenium.
- Feeding animals properly prepared and stored hay and grain or allowing access to high-quality, green forage should ensure adequate vitamin E intake.

Hypokalemic Myopathy

Etiology and Pathogenesis

- Hypokalemic myopathy in dairy cattle occurs when serum **potassium** concentrations are <2.0 mmol/L, producing severe signs of muscle weakness.
- Anorexia and enhanced potassium excretion due to the administration of one or more doses of **isoflupredone acetate** to **ketotic** cows are common causes of hypokalemia.
- Isoflupredone acetate has both glucocorticoid and mineralocorticoid activity, resulting in a decrease in mean plasma potassium concentration by 25% 2 days after a single injection (20 mg) and 46% in cows 3 days after two injections.

Clinical Findings:

Clinical signs of hypokalemic myopathy include:

- severe weakness
- Recumbency
- abnormal position of the head and neck
- rumen hypomotility or atony
- abnormal feces
- Anorexia
- tachycardia
- Cardiac arrhythmias are also common.

Diagnosis:

- Diagnosis is based on clinical signs combined with serum potassium of <2.0 mmol/L.
- Other common clinical chemistry abnormalities include **ketosis**, **metabolic alkalosis**, and increased serum **CK** and **AST** activities.
- Muscle biopsies reveal a **vacuolar myopathy**

Treatment and Prevention:

- ✓ Restoration of whole-body potassium balance can be difficult, and serum potassium concentrations do not necessarily reflect muscle potassium concentrations.

- ✓ Recommended supplementation includes potassium chloride given IV (16 g/l00 kg) and PO (26 g/100 kg) for approximately 5 days.
- ✓ Treatment should also be directed at resolving the primary cause of ketosis and anorexia as well as providing supportive care.
- ✓ Survival has been reported to be 22%–79%.

Equine exertional rhabdomyolysis (ER), Tying up, Azoturia, or Monday morning disease

ER is a syndrome that damages the muscle tissue in horses. It is usually due to overfeeding horse carbohydrates and appears to have a genetic link. ER occurs either sporadic or chronic.

Etiology

Beyond a highly probable **hereditary factor**, there does not seem to be a single cause that triggers ER in horses.

Exercise is seen in every case, but exercise is always **accompanied by another factor**. It is likely that several factors must act together in order to cause an ER.

The most common cause of ER is an imbalance between the animal's diet and his workload, especially when he has a high-grain diet.

Pathogenesis:

ER occurs when there is an inadequate flow of blood to the muscles of an exercising horse. The muscle cells, lacking in oxygen, begin to function **anaerobically** to produce the needed **ATP by anaerobic metabolism of the stored glycogen**. The anaerobic work creates a buildup of **waste products**, **acid**, and **heat**. This subsequently alters the cell by preventing the **cell's enzymes** from **functioning** and the **myofilaments** from efficiently contracting. The **cell membranes** may then be **damaged** if the horse is forced to continue work, which allows **muscle enzymes** and **myoglobin** to leak into the bloodstream.

A horse on a high-grain diet with little work collects more glycogen in its muscles than it can use efficiently when exercise begins, which is why horses on a high-grain diet are more likely to develop ER.

Proper conditioning can help prevent ER, as it promotes the growth of capillaries in muscles and the number of enzymes used for energy production in muscle cells. However, improvement in these areas can take several weeks. Thus, ER is more common in horses that are only worked sporadically or lightly, and in horses just beginning an exercise regimen.

A **common misconception** is that ER is caused by the buildup of lactic acid. Lactate is *not* a waste product for a cell, but a fuel, used when the cell's oxygen supply is insufficient. Lactate does not damage a cell, but is rather a byproduct of the true cause of cell damage: inadequate blood supply and altered cell function. Lactate naturally builds up in an exercising horse without harming the muscle cells, and is metabolized within an hour afterwards.

The pain is caused by the inadequate blood flow to the muscle tissue, the inflammation from the resulting cell damage, and the release of cell contents. Muscle spasms, caused by the lack of blood to the muscle tissue, are also painful.

Clinical Findings (Sporadic ER):

- A horse developing ER will usually begin showing signs right after the beginning of exercise, although for mild cases, signs may not be seen until after the horse is cooled out.

Signs of mild ER include: (the symptoms appear to be tiredness or lameness):
Reluctance to move, stiffness or shortened gait when the animal is forced to move, and muscle spasms or cramps, with hard, painful muscles (especially the **hindquarters**) when palpated.

Signs of a severe ER may include:
Reluctance to move, sweating, elevated heart and respiratory rates as a result of the pain, anxious expression, shifting of weight from side to side, standing hunched and tense, passing **reddish-brown urine**, dehydration, shock, and inability to rise.

- If signs of ER are seen, the horse should not be moved. Movement can cause further muscle damage. If the animal is far from the barn, it is best to trailer him back rather than move him.
- After a bout of ER, blood levels of CK and AST rise.

Disease Complication:

- Severe ER can lead to renal compromise due to **ischemia** and the combined **nephrotoxic effects** of myoglobinuria, dehydration, and NSAID therapy.
- The first priority in horses with hemoconcentration or myoglobinuria is to reestablish fluid balance and induce diuresis.
- In severely affected animals, regular monitoring of blood urea nitrogen (**BUN**) and/or CK is advised to assess the extent of renal damage.
- **Diuretics are contraindicated** in the absence of IV fluid therapy and are indicated if the horse is in oliguric renal failure

Diagnosis:
A diagnosis of ER is made on the basis of a horse with no previous history, or a brief history, of ER, signs of muscle cramping and stiffness after exercise, and moderate to marked increases in serum CK and AST.

Treatment:
Mild or moderate cases:

1. The horse should receive several days of **NSAIDs**, **rest**, and grain or pellets should be **withheld**.
2. To improve **blood flow** to the muscles and help to with muscle spasms, **heat therapy** and **Equine Massage** may be beneficial, as well as hand-walking if the horse is comfortable walking.
3. Turn-out in a pasture will encourage movement.
4. A horse should be moving normally within 12–36 hours after the attack.

Severe cases:

1. A horse may need **fluids**, especially if its urine is colored, the horse is receiving **NSAIDs**, or if he is dehydrated. Fluids will increase the production of urine that will in turn help flush out the excess, and potentially damaging, **myoglobin** from the kidneys and will reduce NSAID-produced kidney damage. Fluids should be **administered** until the urine is **clear**, which usually takes from a few hours to a few days.
2. **Vasodilators**, such as a**cepromazine**, can help improve blood flow to the muscles. However, caution should be taken as it can lower the animal's blood pressure and can cause collapse in a severely dehydrated horse.
3. **Vitamin E** is an anti-oxidant, and so may help prevent further cell degeneration in the affected muscles. However, vitamin E products must be used with caution if they also contain **selenium**.

4. Except to get a horse to **his stall**, a horse showing signs of severe ER should not be moved until he is comfortable enough to do so eagerly. This may take several days.
5. After this point, it is important to either hand-walk the horse a few times each day, or provides him with a few hours of turnout in a pasture or paddock.

- ❖ A horse **may be returned to work** after it is **no** longer showing **signs of ER**, and is **no** longer on **NSAIDs**—which can hide signs of another bout of ER.
- ❖ If **NSAIDs are needed** to keep the horse comfortable, or if the horse is reluctant to continue work, the animal **is not yet ready** for a return to his regular training program.
- ❖ **Blood tests** should reveal that the horse's **CK** concentration and **AST** levels are normal before the horse is returned to work.
- ❖ To begin bringing the horse back, he should be **exercised** at the walk and trot for 10–15 minutes at least once every day.
- ❖ **Grain** is **gradually reintroduced** as exercise resumes, but grain can contribute to the development of ER.

Prognosis:

Mild to moderate ER: prognosis is excellent

Severe ER: The prognosis is guarded due to degeneration and fibrosis of muscles.

Prevention:

Diet:

- ✓ Reducing any extra energy in a horse's diet is essential to maintaining a horse that has experienced ER.
- ✓ Decreasing carbohydrates and increasing the daily intake of hay or pasture can usually accomplish this.
- ✓ Grain may need to be **cut out** altogether and replaced by a substitute, such as **vegetable oil**, to meet the individual energy needs of the horse.
- ✓ Grain should be **reduced** or removed from a horse's ration on days when he **cannot be worked**.

Exercise:

Proper conditioning is very important in preventing ER. Beginning with a base of long, slow distance work will ensure that the horse has a foundation before proceeding on to more strenuous work. The horse should always have a 10-minute warm-up at the walk and trot before more strenuous work is begun, and should always have a proper cool down of 10 minutes.

It is best that a horse receive exercise every day, or possibly twice a day, to prevent the recurrence of ER.

Supplements and drugs:

- ✓ Adding **potassium** and **salt** to the diet may be beneficial to horses that suffer from recurrent bouts of ER.
- ✓ Horses in hard training may need a **vitamin E** supplement, as their requirements are higher than horses in more moderate work.
- ✓ The horse may also be deficient in selenium, and need a feed in supplement. Selenium can be dangerous if overfed, so it is best to have a blood test to confirm that the horse is in need of supplemental selenium.
- ✓ Drugs have been used with success include phenytoin, dantrolene, and dimethylglycine.
- ✓ Bicarbonate and NSAIDs are of no use in preventing ER