EXERTIONAL MOPATHIES

• severe muscle degeneration following strenuous exercise

• lesions similar to WMD, but mainly in major muscles with predominately type 2 fibers

• pathogenesis: altered energy metabolism, abnormal excitation-contraction coupling → mechanical stresses of excessive contraction → myofiber degeneration / necrosis

• with myofiber necrosis get leakage of enzymes (eg CK & AST) and myoglobin
Equine Exertional Rhabdomyolysis (= Azoturia = paralytic myoglobinuria)

- esp heavy horse breeds, with strenuous exercise after a long resting period &/or diet rich in CHO

- clinically see excess sweating, muscle weakness, reluctance to move, myoglobinuria

- in severe cases can see renal failure, recumbency and death

- postulated that these horses have an underlying polysaccharide storage myopathy
Equine Exertional Rhabdomyolysis

Gross Pathology:

- lumbar / gluteal muscles are swollen, edematous, pale to dark (myoglobin)
- kidneys also show dark discoloration (myoglobin staining)
- in horses that survive, affected muscles become pale and atrophic

Myoglobinuria in a horse with exertional myopathy. (Diseases and Disorders of the Horse, Saunders, 2003)
Equine Exertional Rhabdomyolysis

Fig 3-77 (Maxie) Equine exertional rhabdomyolysis. Affected muscle has pale areas as well as red-tinged zones. These gross findings do not aid in diagnosis of possible underlying causes.

Fig 5.42 Acute renal failure. Dark reddish discoloration / mottling of kidney due to severe myoglobinuria over a 3-day period. Knottenbelt and Pascoe's Color Atlas of Diseases and Disorders of the Horse, 2nd ed
Equine Exertional Rhabdomyolysis

Histopathology:

- acute cases show segmental degeneration / necrosis with little / no calcification

Fig 3-78 (Maxie) Transverse section of acutely necrotic myofibers in a horse with rhabdomyolysis. H&E stain.

Selective degeneration of fibers (left), probably type II fibers.

UGA College of Vet Med – Dept of Path
Tying Up (= Transient Exertional Rhabdomyolysis = setfast)

- mild, transient form of exertional rhabdomyolysis
- in lighter horse breeds; similar syndrome in racing greyhound dogs
- rarely produces visible myoglobinuria or gross muscle lesions
• acute and often fatal myopathy of many wild mammals and birds
• after chase, struggle or transport → extreme overexertion (+/- catecholamine release)
• grossly → pale edematous muscle or may have pale &/or hemorrhagic streaks
*Capture myopathy, Elk.* Extensive hemorrhages in muscles and subcutis of the distal hindlimb. Also, note detached tendon (arrow) likely the result of strenuous struggle during capture.

*Capture myopathy, white-tailed deer.* Some muscles of the rear leg show extensive pallor (indicative of degeneration & necrosis).
**TOXIC MYOPATHIES**

**Ionophore toxicosis**

- used in veterinary medicine as drug / feed supplement (e.g., monensin)
- act by altering membrane transport / permeability of electrolytes
- at excess levels cause degeneration / necrosis of skeletal and cardiac muscle
- **horses** are extremely susceptible to muscle damage at relatively low levels
Locally-extensive area of pallor in myocardium of horse indicative of muscle degeneration and necrosis due to monensin toxicity.

Fig 15-38 Ionophore toxicity, monensin, skeletal muscle, horse. The pale white to gray foci are areas of necrotic myofibers. Myocardium will often contain similar lesions.
Toxic plants and plant-origin toxins

- A variety of plants contain toxins that can cause degeneration / necrosis of muscle.
- Eg: Cassia (coffee senna), Gossypium spp (cottonseed contain gossypol), etc.
Seasonal pasture myopathy of horses

- extensive rhabdomyolysis with myoglobinuria in pastured horses following ingestion of seeds of box elder maple trees and sycamore maples in North America and Europe

- seeds contain hypoglycin A → multiple acyl-CoA dehydrogenase deficiency (MADD) → damages mitochondria / impairs lipid metabolism within skeletal and cardiac muscle

Fig 42-15  Box elder seeds that contain the toxin hypoglycin A, which causes seasonal pasture myopathy. Large Animal Internal Medicine, 5th Ed.
Masticatory myositis of dogs

- Immune-mediated, eosinophilic and atrophic myositis

- Early phase → repeated bouts of bilateral swelling & pain of the masseter and temporal muscle associated with eosinophilic myositis

- Over time see progressive destruction & atrophy of these muscles → atrophic myositis

- Pathogenesis → autoAb directed against type 2M myosin (isoform in masticatory muscles)

- A diagnostic test for 2M antibodies in serum is available
Masticatory Myositis

- Eosinophilic Myositis
  - Acute
    - Muscle Swelling
    - Eosinophilic Infiltrates
  - Chronic
- Atrophic Myositis
  - Chronic
    - Muscle Atrophy
    - Lymphocytic Infiltrates

Antibodies against II-M fibers
Head of a dog with the chronic (atrophic) form of masticatory myositis. Severe atrophy of masseter (m) and temporal (t) muscles.

Fig 3-84 (Maxie) Chronic masticatory myositis in a dog; severe atrophy of masticatory muscles.
Masticatory myositis of dogs

Histopathology:
- acutely see edema & extensive infiltration of eosinophils

Acute eosinophilic myositis.
Myofiber loss and expansion of endomysium with eosinophils.
Masticatory myositis of dogs

Histopathology:
- chronically see lymphocytes / plasma cells and myofibers become atrophic

Chronic lymphoplasmacytic myositis.

Above - Fig 3-85 (Maxie) Dense infiltrates of lymphocytes, including many plasma cells, separating myofibers in temporal muscle from a dog with masticatory myositis. This is a particularly florid lesion.

Right - In the chronic form, there is extensive loss of myofibers and inflammatory infiltrates; predominantly lymphocytes and plasma cells (latter marked with arrows). There has been some attempts at repair as shown by the presence of multinucleated myoblasts (asterisk).
Polymyositis of dogs

- rare condition in dogs; presumed autoimmune mediated by cytotoxic T cells
- all muscles affected (esp esophagus)
- sometimes masticatory muscle involvement dominates (but -ve for serum Ab to 2M myosin)
- histopath: degeneration / necrosis with infiltration of mostly lymphocytes & variable eosinophils

Fig 3-86 (Maxie) Polymyositis in a dog. There is a regenerating myotube as well as active inflammation consisting of eosinophils and lymphocytes.
Acquired myasthenia gravis

- rare disease of humans, dogs and cats
- NM junction disease causing weakness & severe muscular fatigue; often following mild exercise
- circulating Ab against motor end plate Ach receptors $\rightarrow$ reduction in receptor density
- some dogs / cats have thymomas $\rightarrow$ altered function $\rightarrow$ failure to remove self-recognizing clones
Acquired myasthenia gravis

Fig 35-13 The pathogenesis of myasthenia gravis. Destruction of acetylcholine receptors prevents effective neuromuscular transmission. Blockage of cholinesterase activity by anticholinesterase drugs permits acetylcholine to accumulate and so enhances neuromuscular transmission. *Veterinary Immunology*, 9th ed.
Acquired myasthenia gravis

- megaesophagus, dysphagia & aspiration pneumonia are common complications in dogs

Fig 9-13 (Zachary) Acute to subacute aspiration pneumonia, acute necrotizing bronchopneumonia, right lung, dog. The cranioventral portions of the lung are firm, hemorrhagic, & necrotic. The necrotic areas are gray-yellow-brown and are caused by gastric content, especially hydrochloric acid, discoloring, coagulating, and digesting proteins in the tissues of the bronchi, bronchioles, and alveoli. The red regions around the necrotic foci are areas of active hyperemia in acute inflammation. This dog had myasthenia gravis and aspirated stomach content secondary to an acquired megaesophagus (M).
Fig 12-16 Dermatomyositis. A 12-year-old Shetland sheepdog with chronic dermatomyositis. Skin is permanently scarred, and facial muscles are so atrophic, dog cannot blink, move its lips, or swallow. *Small Animal Dermatology, 7th ed.*

Fig 10-8 Familial Canine Dermatomyositis. Severe muscle atrophy on the lumbar musculature in an affected dog. The lateral processes of the vertebrae can be easily palpated. *Small Animal Dermatology, 3rd ed.*
INFECTIOUS MYOSITIS

- muscle is generally inhospitable for most bacteria (exceptions are Clostridia & Histophilus)
- a few viral agents cause muscle lesions (eg FMD, Bluetongue)

Death from FMD may result from the virus-induced damage to the developing cells of the myocardium of young calves, lambs, kids, and piglets before gross development of vesicles. The diseased heart may be soft and flaccid with white or greyish stripes (the so-called "tiger heart") or foci of necrosis, especially in the left ventricle and interventricular septum. (homepage.usask.ca/~vim458/virology)

Fig 3-94 (Maxie) Disseminated pale areas of myonecrosis in foot-and-mouth disease in a calf.
Blackleg

• an acute fatal emphysematous myositis of ruminants caused by *Clostridium chauvoei*

• characterized by the activation of latent spores in muscle

• pathogenesis:

  step 1: soil-containing spores → ingestion by host → spores from GIT to liver / muscle (latent)

  step 2: muscle injury / hemorrhage → changes local environment (↓ O₂ tension) → germination of spores in muscle → exotoxins → edema/myonecrosis → emphysema → generalized toxaemia → death (24 hrs)
Table 15-3 (Zachary)  **Clostridial Toxins Causing Muscle Damage**

<table>
<thead>
<tr>
<th>Toxin</th>
<th>Type</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-Toxin</td>
<td>Calcium-dependent phospholipase</td>
<td>Hydrolyzes membrane phospholipids</td>
</tr>
<tr>
<td>θ-Toxin</td>
<td>Oxygen-labile cytotoxin (perfringolysin-O)</td>
<td>RBC and WBC lysis</td>
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<tr>
<td></td>
<td></td>
<td>Induces platelet-activating factor leading to leukostasis and decreased tissue perfusion</td>
</tr>
<tr>
<td>κ-Toxin</td>
<td>Collagenase</td>
<td>Contributes to tissue lysis</td>
</tr>
<tr>
<td>μ-Toxin, γ-toxin</td>
<td>Hyaluronidases</td>
<td>Disruption of muscle integrity</td>
</tr>
<tr>
<td>ε-Toxin</td>
<td>Lipase</td>
<td>Lipid membrane lysis</td>
</tr>
</tbody>
</table>

*RBC, Red blood cell; WBC, white blood cell.*
Gross Pathology:

- can affect any striated muscle; but generally large muscle masses
- muscle lesions are red-black with emphysema (crepitation) & “rancid butter” smell
- mild interstitial and subcutaneous edema peripheral to primary lesion
- fibrin tags often found on the epicardial and pleural surfaces
- often see serosal hemorrhages, severe pulmonary edema & rapid post-mortem bloating
Blackleg

- animals often found dead without any clinical signs
- when animals ill, can see lameness, crepitation and swelling

Fig 12.64 Blackleg (*C. chauvoei*): massive left gluteal swelling in calf.

12.65 Blackleg: dark, necrotic, gluteal musculature (left), and normal (right)
Fig. 15-38 (Zachary) Blackleg, hemorrhagic-necrotizing myositis (Clostridium chauvoei), thigh muscle, cow.

A (top), The dark red areas are caused by hemorrhagic necrosis of the underlying muscle. These lesions are characteristic of blackleg.

B (left), Clostridium chauvoei can also produce substantial quantities of gas within infected tissues as shown here by the numerous (“pseudocystic”) spaces within hemorrhagic and necrotic muscle.
Fibrinous pericarditis and pulmonary edema often seen with blackleg infections. (Noah’s Arkive)

The myocardium may be involved alone or in combination with other muscles. (Noah’s Arkive)
**Blackleg**

**Histo:** segmental degeneration / necrosis, edema, emphysema; few PMN's & bacteria

Scattered segmental degeneration and necrosis with prominent Interstitial edema and mild inflammatory cell infiltration. (Noah's Arkive)

*Fig. 15-38C (Zachary) Blackleg, hemorrhagic-necrotizing myositis (Clostridium chauvoei), thigh muscle, cow.* Gram-positive bacilli are present in the serous exudate. Gram stain.
Blackleg

- lab Dx: submit formalin-fixed tissues for histopath and fresh tissues for FAT

Figure 16.3 Direct fluorescent antibody technique showing *C. chauvoei* in muscle tissue from a case of blackleg in a heifer. (×400). 
*Clinical Veterinary Microbiology*, 2nd ed.

**Fluorescent Antibody Test (FA test).** The positive fluorescence for *Clostridium chauvoei*. Remember to submit fresh (non-fixed) tissues for this confirmatory test.
Malignant Edema & Gas Gangrene

- an acute, often fatal wound infection by: *Cl. septicum, Cl. perfringens, Cl. novyi, Cl. sordelli, Cl. chauvoei*

- mostly ruminants, horses & swine → route of entry is always through a wound (spores in soil & feces)

- not all wounds contaminated with these organisms result in Malignant edema or Gas gangrene

- affected areas are cold on palpation (live animals) and can be crepitant (emphysema)

- animals show generalized signs of toxemia and finally prostration / death
Gross Pathology:

- lesions are locally extensive involving mostly connective tissue (subQ & fascia)
- severe edema, variable emphysema, hemorrhage, and discoloration of skin

Fig 42-2 Fasciotomy / myotomy incisions in gluteal region of 2-year-old Quarter Horse filly that developed clostridial myonecrosis secondary to vaccination at the site.  *Equine Infectious Diseases, 2nd ed.*
Severe edematous and to a lesser extent emphysematous expansion of the subcutaneous connective tissues (arrow). In addition, there may be hemorrhage (B). Skin generally remains intact (asterisk).

Fig 4-65 Clostridial infection. Well-delineated area of ulceration postnecrosis and slough. *Equine Dermatology*
Histopathology:

- predominately edema and cellulitis with minimal myositis
- definitive diagnosis also requires FA testing

Positive fluorescence of Clostridia in affected tissue.
## Overall differences between Blackleg & Malignant Edema

<table>
<thead>
<tr>
<th></th>
<th>Myositis</th>
<th>Cellulitis</th>
<th>Edema</th>
<th>Emphysema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blackleg</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>++++</td>
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<tr>
<td>Malignant Edema</td>
<td>+</td>
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