Chapter 8

Skeletal Muscles

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Perspective on Visible Changes

Normal skeletal muscle is organised around the functional myofibre with its satellite cells. Its gross appearance is a combination of genotype (eg volume/mass viz double muscling), of activity (eg disuse atrophy or body-building hypertrophy) and of general metabolic and nutritional state viz catabolism vs anabolism (eg BCS2 prime lamb vs BCS5 fat lamb). This allows for a huge "normal" variation in volume/mass relationships which are critical to any determination and appreciation/description of abnormality (pathology). They are also best appreciated in the live animal!!

Myofibre type and its relationship to particular anatomical function(s) also has a significant influence on muscle texture and normal appearance. Type II fibre predominant muscles are fast twitch/periodic high activity in function (glycolytic) and structure with often looser texture. Hence the M. semi-membranosus or M biceps brachii are low in fascia, highly end tendoned and paler red in colour (less myoglobin, less highly vascularised). M. semi-tendinosus in race horses has 80-95% Type II fibre content.

Predominant Type 1 fibre muscles are constant load bearing, higher in fascia, less dense in glycolytic myofibre mass and generally darker and more red (myoglobin and constantly vascularised) eg vastus intermedius, Triceps Brachii, Anconeus, Tensor fascia lata, masseter muscles in ruminants. Diaphragmatic muscles in cattle are 80-95% Type 1 fibres.

Mixed fibre type muscles have intermediate features in respect to the multiple range of functions, degree of fascial anatomy, range of fibrous texture, and colour from vascularisation. They are of course the most common neck, trunk and pectoral/pelvic girdle suspensory muscles.

Muscle colour is determined by haemoglobin (vascularisation) and myofibre myoglobin (red/brownness eg "pink" Chicken vs "red" meat). Pathology may be indicated by pronounced redness eg haemorrhage, darkening/blackening eg haemorrhage with myonecrosis or varying shades of pallor eg anaemia or whiteness eg subacute to chronic myonecrosis. Massive peracute myonecrosis without haemorrhage may be virtually imperceptible to the naked eye in terms of colour change. In contrast focal or multifocal fibrotic or caseous/calcareous lesions may be highly visible eg Cysticercus ovis cysts, but of relatively minor consequence to the animal as a whole. Myositis will largely be visualised

because of inflammatory/vascular features eg eosinophilic myositis – green tinged due to eosinophils.

Muscles may undergo alteration of colour during rigor mortis and putrefaction. In a well-fed animal which dies suddenly, the muscles become pale (fish-fleshed) probably due to the leaching of myoglobin by postmortem lactic acidosis. Onset of rigor is long-delayed (>12 hours). If glycogen is depleted eg chronic disease or malnutrition, the muscles become unusually dark after death and rigor is slight or absent.

The myofibre has a very homogeneous response to damage irrespective of cause. Therefore later stages of various afflictions eg chronic myopathies are difficult to distinguish grossly or microscopically. The myofibre microscopic repair sequence involves calcification, phagocytosis, satellite cell proliferation and myoblastic regenerative repair, characterised by basophilic myofibrillar replacement/regeneration. The ability of the body to rapidly repair the damaged segment(s) of a myofibre without apparent complication to the remainder of the fibre is without parallel in other cells of the body. Thus lytic (metabolic), toxic and nutritional degenerative myopathies are frequently sub-gross and sub-lethal/sub-clinical in presentation. Hence the use of muscle biopsy and clinical pathology (Ca^{2+}, Mg^{2+}, K^{+}, Na^{+}, CK (creatinekinase) and AST (asportate amino-transferase, glucose and lactic acid [muscle PH]) as essential tools for incrimination and discrimination of muscular involvement and likely clinical recovery.

Myodystrophies characteristically have no effective regenerative myofibre response and show progressive fibre abnormalities eg internal nuclei, fibre size changes, peripheral sarcoplasmic masses or storage vacuolations etc. The pathogenesis though distinct will result in medium to end stage endomysial and perimysial fibrosis, fatty replacement and volume atrophy of the muscle fibres. Grossly this equates to pallor, whole muscle atrophy (shrinkage) and fibrosis which is not vastly different to scarring resulting from inflammatory necrosis or vascular crisis/ischaemia. Clearly pale, shrunken muscles should be interpreted cautiously as to cause until microscopic evidence is available.

My experience suggests that the muscular system can pose nearly as many challenges to the gross pathologist as do the more vital organs eg liver, kidney. However, its size, scope of functions, decentralised locations(s) and low profile ("it's just the meat off the bones") condemn the muscles to being constantly overlooked or misinterpreted. This occurs despite its critical role in conditions common to grazing ruminants such as toxic and nutritional myodegeneration and inflammation eg blackleg (*Clostridium chauvoei* infection). In the latter, secluded sites of gas gangrene such as psoas muscles, tongue, deep gluteals and even diaphragm should not be overlooked.

Lesions in the skeletal musculature may be congenital/developmental or acquired, focal or diffuse, bilaterally symmetrical or unilateral and have the usual range of aetiologic influences which will be covered in detail viz

1. Inflammatory disorders
2. Degenerative disorders
3. Neoplastic disorders
4. Metabolic/toxic disorders
5. Developmental (Genetic) disorders

Finally, muscle is the most valuable, economic carcase attribute, whilst bruising of and dark-cutting in meat producing ruminant animals are the greatest economic and quality burdens to the red-meat producing industries. The veterinary profession must focus on keeping muscles normal for the sake of its industry clients.

Inflammatory Disorders

Acute haemorrhage/bruising/trauma – sterile
eg contusions, trucking injuries, injections.

Acute inflammation – Clostridial myositis
a. gas gangrene, malignant oedema/cellulitis
   eg Clostridium septicum
b. peracute/acute deep myositis/blackleg
   eg Clostridium chauvoei in cattle and sheep (See Seddon *et al* [1931])

Acute to chronic inflammation/focal necrosis/trauma – non-sterile
eg penetrating grass seeds; lead shot, bullet wounds, dog bites, irritant foreign substance injections such as Vitamin E – Dickson J *et al* (1986). AVJ. 63 : 231-233.

Abscessation/suppurative myositis – bacterial
eg Actinomyces pyogenes in cattle
a. Corynebacterium pseudo-tuberculosis in sheep and goats.

Chronic fibro-granulomatous inflammation
eg Roeckl's granuloma; skin mycobacteriosis.

Eosinophilic myositis
– principally caused by the degeneration of sarcocystis species.

Protozoan myositis including
a. Sarcosporidiosis eg S. cruzi in cattle, S. ovi-canis in sheep, S. capracanis in goats
b. Foetal neosporosis
c. Toxoplasmosis

Viral myositis
– associated with microvascular (ischaemic/thrombotic) pathology in
a. Ephemeral fever
b. Bluetongue infection in sheep

c. Ibaraki Disease in cattle in Japan
d. EHD of deer in USA
e. Foot and Mouth Disease - myocarditis – myositis in young calves/lambs and pigs (not EMC virus)

Viral arthrogryposis with myopathy in pre-term ruminants

a. Arbovirus induced including Akabane, Aino, Chuzan viruses
b. Pestivirus induced in sheep and cattle
c. Cache Vally viral arthrogryposis and encephalopathy in sheep in USA – (presumptive arboviral).
   See Edwards JF *et al* (1989) Vet. Pathol. 26 : 33-39

Parasitic myositis especially cysticercosis

a. Cysticercus bovis (Taenia saginata)
b. Cysticercus ovis (Taenia ovis)
c. Cysticercus Tarandi (Taenia krabbei)
   Larval forms in reindeer, gazelle, moose and other wild ruminants. Primary hosts are wild carnivores in temporal and arctic zones
d. Screw-worm fly myiasis
e. Elaphostrongylus cervi in Red Deer (Cervus elaphus)
   Encephalomyelitis, ganglio-neuritis (larval stages) and myositis (adult worms).
   See Handeland *et al* (2000) J. of Parasitology 86 : 1061-1066

Degenerative (Misuse) Disorders

Cachectic atrophy

– muscle texture soft, dark and sticky. Type II fibres depleted preferentially

Disuse atrophy due to pain

– preferential atrophy of Type 1 fibres; maintenance or hypertrophy of Type II fibres eg hip dislocation-uncorrected.

Degeneration atrophy

– common in congenital dysplasias eg cord lesions and birth trauma. Results in muscle paralysis and loss of mass. There is masking of fibre Type differences and presence of small fibres.

Vascular myodegeneration

a. Ischaemic (pressure) myonecrosis
   6-12 hour critical period in cattle (less in horse) before irreversibility. Severe end-stage acute myonecrosis. Thigh muscles of downer cows especially.
b. Iliac thrombosis in calves, under 6 months of age. Bacterial thrombo-embolism resulting in acute to chronic segmental necrosis or acute coagulation necrosis of whole fibres. Morley PS *et al* (1996). JAVMA 209 : 130

Myofibre hypertrophy
– this may be a normal physiologic response eg in trained racing animals. Compensatory hypertrophy occurs due to a defect/deficiency of fibres in an area eg chronic post-natal partial denervation atrophy.

Pigmentation of muscle
a. Melanosis – congenital in calves, low prevalence similar to hepatic melanosis melanin not in myofibres.
b. Yellow/lipid (xanthomatosis). Old age related (up to 0.5%) but 10-25% in aged Ayrshire cows. Pigmented phagolysosomes within the myofibres.

Steatosis
– Fatty replacement of muscle fibres – may be sequel of failed repair following acute degeneration or terminal dystrophic pathology.

Neoplastic Disorders

Rhabdomyosarcoma
– primary tumours of striated muscle are rare but very malignant. They appear in limb, neck or head muscles as hard, pink-grey, spherical masses deep in the muscle. Haemorrhage and necrosis is common. There is vigorous local invasion and metastases occur to many organs and may become confluent but retain nodularity.

Metaplastic Rhabdomyosarcoma
– those tumours arising in sites where no striated muscle is normally found eg lungs of lamb. Less likely to metastasise and are better differentiated.

Secondary Tumours
– these can involve muscle especially lymphoid and melanotic tumours.

Comment: Slaughter of aged animals in ruminant flocks/herds with normal management will mitigate against the appearance of most tumours, including muscle tumours. U-V induced skin tumours and intestinal adenocarcinomas appear to be honourable exceptions.

Metabolic/Toxic Disorders

"Dark-cutting" meat
– most important re dollars

Exertional Rhabdomyolysis
– physiologic myolysis vs pathologic myolysis
(See Bartsch *et al* 1977)
a. Transport myopathy/Honda disease
b. Azoturia draft oxen/horses (Typing-up)

c. Capture plus chase and capture myolysis in domestic and wild ruminants. Gro ssly oedema, haemorrhagic streaking, pallor and/or indistinct pale streaks may be seen.

Haemoglobinuria (brown urine) is a key clue

Nutritional myodegeneration

– usually sub-acute not myolytic, no visible haemoglobinuria

a. northern hemisphere "Spring turn-out" disease
b. complex myofibre homiostasis involving
    - Selenium – cytosolic GSHPx anti-oxidant
    - Alpha-tocopherol – cell membrane anti-oxidant
    - Polyunsaturated fatty acids – membrane structure/stability vs peroxidation
    - Prostroglandin/arachidonic acid biochemistry?

C. Not simple deficiency diseases. (*See highlighted references)

Phytotoxic nutritional degenerative myopathy

a. Australia due to
    - *Ixiolaena brevicompta* (Plains Plover Daisy) – NSW/QLD
    - *Cassia occidentalis* (Coffee Senna) – NT, QLD
    - *Malva parviflora* (Marshmellow) – WA, NSW
b. Worldwide due to
    - *Thermopsis Montana* – USA Colarado
    - *Geigeria ornativa* – South Africa
    - *Karninskia humboldtiana* (Coyotilla) - USA
c. Enzootic calcinosis of muscle caused by
    - *Solanum malagoxylon*
    - *Tricetum* spp
    - *Cestrum* spp

Toxic myopathies

a. Monensin toxicity and potentiated (Macrolide anti-biotic) Monensin toxicity
b. Maduramicin (ionophore anti-biotic) toxicity
c. Lasalocid toxicity
d. Inorganic toxins – Selenium, iron, thallium, sulphur and cobalt have caused natural muscle disease in animals

Developmental (Genetic) Disorders/Muscular Dystrophies

These conditions can be congenital (infantile) or of early (juvenile) or delayed (adult) post-natal onset. Time of onset is usually a correlate of genotype defect variation eg Human Pompe's Disease.

Information can be sourced at the University of Sydney OnLine Mendelian Inheritance in Animals (OMIA) Database at – http://www.angis.su.oz.au/databases/BIRX/omia
Currently lists 1995 disorders/defects in 13 animal species.

CPOMD Merino myopathy
– see McGavin *et al* (1969) in Queensland, Christie (1962) in Victoria and Dent *et al* (1979) in Western Australia. A Type 1 fibre Dystrophy. Must examine grossly the *M. vastus intermedius*!

Pompe's Disease in Brahman and Shorthorn Cattle and Corriedale Sheep
– generalised clinical weakness and pallor in skeletal muscles in some animals. (See Edwards & Richards [1979], O,Sullivan *et al* [1981] and Reichmann *et al* [1993]).

Genotyping technology based on DNA from tail hairs is now available at EMAI Camden (Dennis *et al* 1999, 2001 & 2002)

Bovine Myasthenia gravis in South Africa
(See Thompson PN 1998)

Hanging head lambs in Suffolk and Border Leicester sheep in United Kingdom
– cervical myodystrophies in lambs.

Arthrogryposis multiplex congenita (AMC) eg acorn calves.

Arthrogryposis and palatoschisis in Charolais, Friesian, Swedish and Danish Red cattle.

Multifocal symmetrical encephalomyelopathy (MSE) in Simmental calves.

Progressive degenerative myeloencephalopathy in Brown Swiss cattle.

Congenital myopathy in Braunvieh X Brown Swiss calves.

Diaphragm and intercostal muscular dystrophy in Meuse-Rhine-Yssel breed adult cattle in the Netherlands.

Congenital clefts of diaphragm

Congenital muscular hyperplasia in cattle and sheep (1 flock) (double-muscling).

Limb-girdle dystrophy in humans and ? in Brahman cattle.

Heritable myotonia in Angora goats (fainting goats).
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