Changing Patterns of Nutritional Myodegeneration (White Muscle Disease) in Cattle and Sheep in the Period 1975-1985 in Great Britain

R. Bradley*, P. H. Anderson *and* J. W. Wilesmith*****
*Departments of *Pathology, **Biochemistry and*
****Epidemiology*
Central Veterinary Laboratory
New Haw, Weybridge, KT15 3NB, UK

Abstract

Nutritional myodegeneration of ruminants (WMD) is an acute, non-progressive myopathy affecting skeletal or cardiac muscle or both. Myodegeneration is a non-specific lesion but is predominantly associated with nutritional deficiencies of vitamin E and/or selenium in combination with environmental stress.

Incidents of WMD diagnosed at Veterinary Investigation Centres have been recorded on a computer data base (Veterinary Investigation Diagnosis Analysis II) since 1975.

Analyses of these data have indicated:—

a) A variable annual incidence in cattle and sheep but with a rise in incidence from 1976 to 1979 and a decline since 1980, the latter probably due to successful preventative treatment.
b) A consistent increase in incidence in spring which is more prolonged for sheep than cattle.
c) For cattle, a variation in the month of peak incidence related to the spring weather, but no broad geographical variation in the month of peak incidence was apparent in any year.

The gross, histological and ultrastructural lesions in the heart and skeletal muscle are illustrated.

Introduction

So-called nutritional myodegeneration (White Muscle Disease = WMD) has been reported tc be the most common and certainly the most economically important animal myopathy (Hadlow, 1973). Though affecting a wide species range this report is concerned only with the disease in cattle and sheep. Fifteen years ago the typical acute, non-progressive disease was recognised principally in young calves and lambs, particularly those on a milk diet. Factors associated with the clinical and pathological expression of WMD were deficiencies of vitamin E and selenium, excessive dietary polyunsaturated fatty acids (PUFA's) or legumes and unaccustomed muscular activity and other stresses (Hadlow, 1973).

Incidents of farm animal disease in Great Britain are frequently referred by practitioners for investigation by State veterinarians (VIO's) in Investigation Centres (VIC's) situated throughout the country (Fig 1). Samples from live animals, necropsy specimens and carcases are submitted to the VIC's and a proportion of specimens is sent to Weybridge for further pathological and biochemical examination and report.

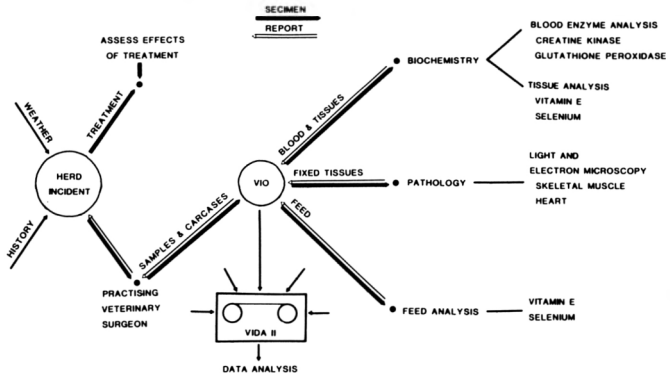

FIGURE 1. Network for investigation, report and analysis.

The data obtained from these examinations have enabled us to investigate the epidemiology of WMD from 1975 to 1985 in both cattle and sheep. In cattle we have been able to relate the pathological findings to the clinical syndromes whereas for both species explanatory hypotheses for the seasonal, geographical and annual patterns of disease occurrence are put forward.

Materials and Methods

The source of data was the VIDA II computer bank which records all diagnoses made in VIC's (Hall *et al* 1980). Data originated from VIC's investigating herd and flock disease incidents in Great Britain in the period January 1975 to December 1985. Analysis of data was undertaken on the basis of age, date of specimen submission, geographical location and diagnosis.

The source of pathological material was from animals involved in a proportion of these incidents. Field specimens of skeletal and cardiac muscle were fixed in phosphate-buffered, neutral, 10% formalin and prepared for histological and sometimes ultrastructural examination by standard methods.

Some incidents, particularly those involving yearling and adult cattle or sudden death in calves were more extensively investigated with regard to history, clinical signs, skeletal muscle enzyme histochemistry, biochemical findings (blood

**Present address: The Home Office, Queen Anne's Gate, London SW1H 9AT.

enzyme analysis for creatine kinase and gluthathione peroxidase and tissue levels of vitamin E and selenium), feed analysis for vitamin E and selenium and weather reports at the time of and immediately preceeding the onset of disease. The effects of treatment and prophylaxis were noted.

Results

Cattle

The annual incidence has been variable (Fig 2). High

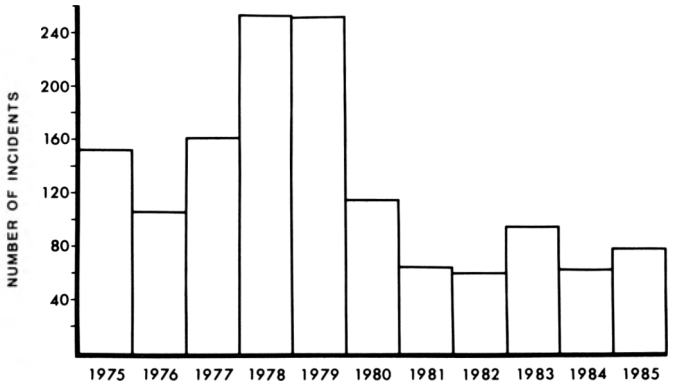

FIGURE 2. Number of herd incidents by year of WMD in cattle in Great Britain 1975-1985.

incidence years are related to poor springs and hence later turn out to pasture. Such weather conditions mean that in-wintered cattle have a longer period of conserved food than in years with good springs. Since 1980 the annual incidence has declined most likely as a result of the institution of effective preventive measures, appropriate, prompt and successful

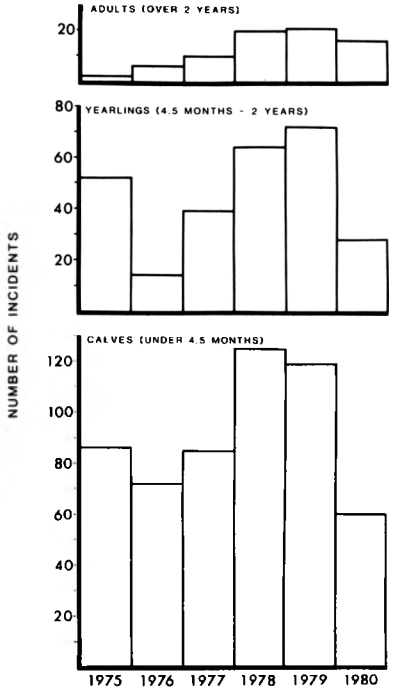

FIGURE 3. Number of herd incidents of WMD in cattle of three age groups diagnosed between 1975-1980 in Great Britain.

treatment or reduced reporting. From 1976 to 1979 incidence increased and the increase was greater in adults and yearlings than in calves (Fig 3). Calves have the highest and adults the lowest incidence.

In weaned calves and yearlings disease risk is increased in the spring. April and May are the months of peak rise (Fig 4). No major difference in the monthly distribution of incidents occurred between the periods 1975-1979 and 1980-1985 (Fig 5).

There is a between year variation in the month of peak rise (Fig 6). This is probably due to climatic factors affecting herbage growth which determines when in-wintered cattle are turned to pasture and when supplementary feeding is stopped.

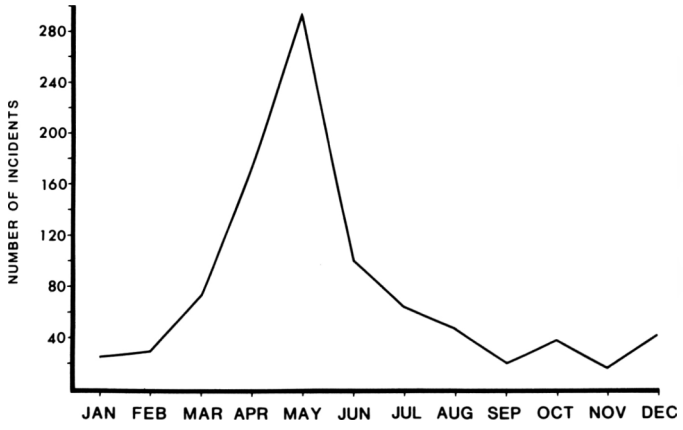

FIGURE 4. Number of herd incidents by month of WMD in cattle in Great Britain 1975-1979.

The months of peak incidence for calves and yearlings are coincident in the Spring, the time when animals are turned to pasture (Fig 7). The seasonal difference cannot be accounted for by the number of animals at risk.

Precipitating factors resulting in WMD in cattle deficient in vitamin E and selenium include turning out to pasture with inclement weather following unexpectedly. Also spring grass is seasonally rich in PUFA's (McMurray and McEldowney 1977).

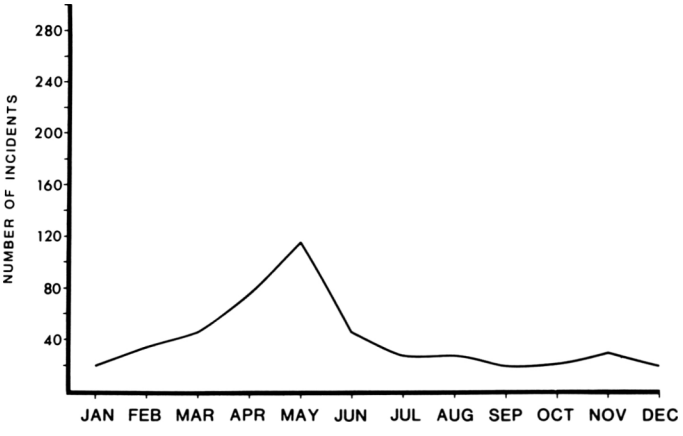

FIGURE 5. Number of herd incidents by month of WMD in cattle in Great Britain 1980-1985.

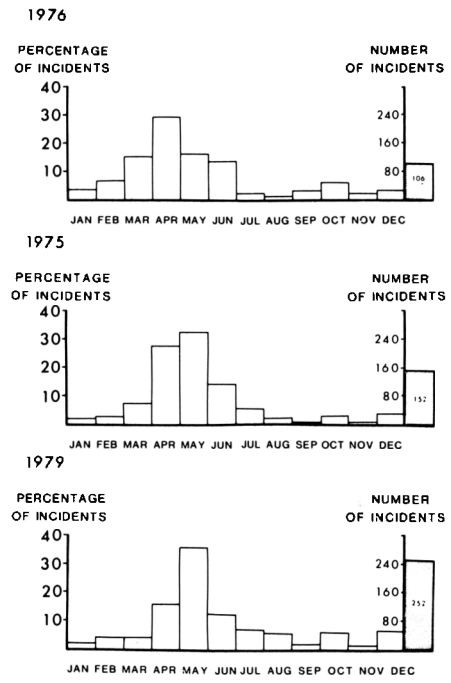

FIGURE 6. Yearly variation in month of peak incidence of WMD in Great Britain.

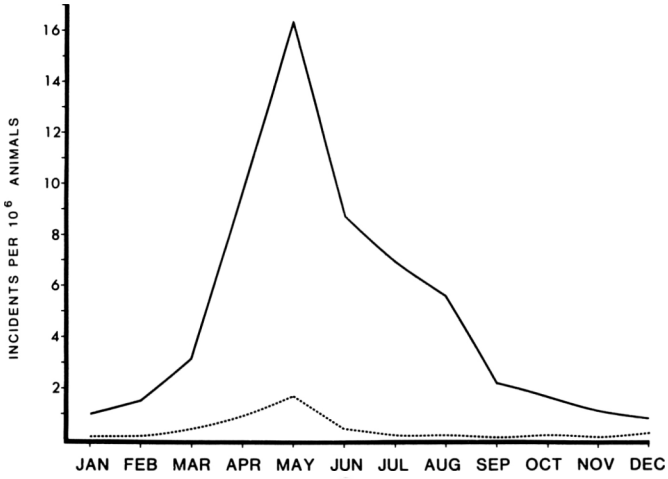

FIGURE 7. Monthly incidences (relative) of WMD in calves (<137 days) (solid line) and yearlings (137 days — 2 years) (dotted line).

When the incidence of WMD in Scotland and in English southern counties is compared (Fig 8), the month of peak incidence is the same despite the facts that the Scottish climate is harsher, spring grass growth is later and the period of inclement spring weather persists longer. Reasons for this anomaly may be that animals in problem herds in Scotland are turned out at the same time as those in southern England, the animals are better acclimatised to the more severe weather conditions before turnout and the local Scottish breeds may be better adapted to the environment.

Sheep

As with cattle the annual incidence has been variable (Fig 9) and the decline in incidence since 1979 is considered to be due to increased awareness which leads to the increased use of preventive and treatment measures by injection and the increased selenium status of pregnant ewes and hence offspring due to the use of selenium supplements. The annual incidence of disease in lambs up to one month old and in lambs one to six months old is broadly similar (Fig 10).

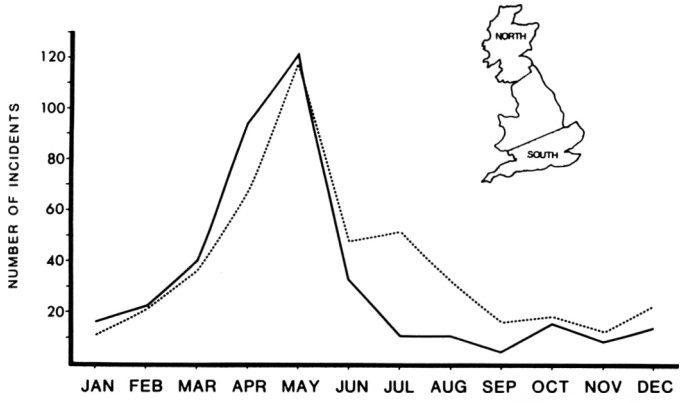

FIGURE 8. Cumulative total of WMD incidents in cattle by month for northern VIC's (Scotland) (solid line) and Southern VIC's (South of a line joining Cardigan and Kings Lynn) (dotted line) 1975-1984.

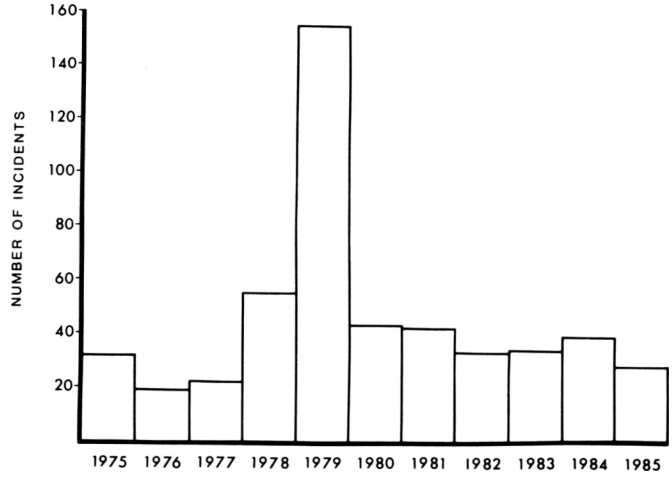

FIGURE 9. Number of flock incidents by year of WMD in sheep in Great Britain 1975-1985.

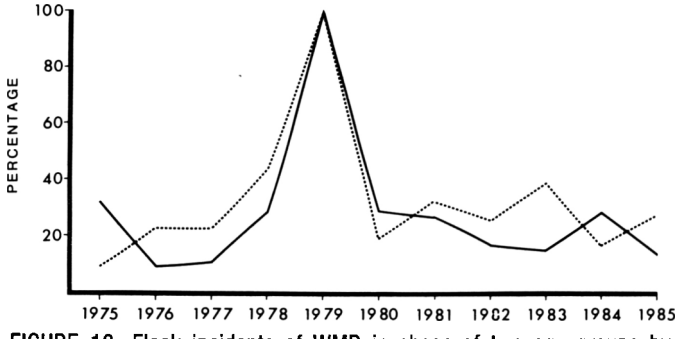

FIGURE 10. Flock incidents of WMD in sheep of two age groups by year 1975-1985 expressed as a percentage of the incidence in the peak year of incidence (1979 = 100%). (<31 days = solid line, 31-180 days = dotted line).

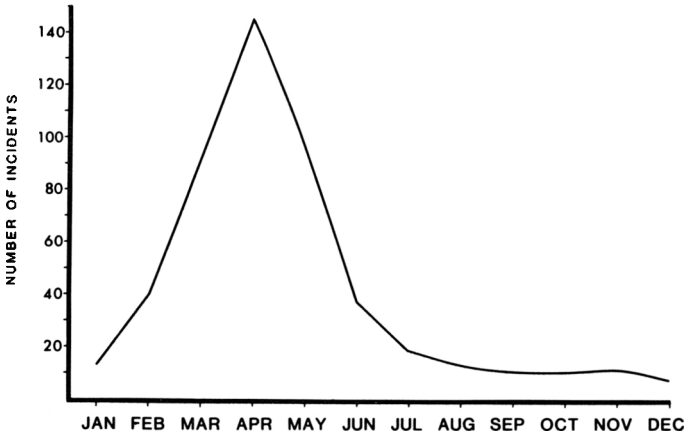

FIGURE 11. Cumulative totals of flock incidents of WMD in sheep in Great Britain 1975-1985.

As with cattle peak incidence occurs in the spring but the period of peak incidence is longer which we suggest is due partly to the long lambing period (Fig 11).

Clinical and pathological features in cattle and sheep

In calves there are three clinical forms. Dyspnoea associated with degeneration of the cardiac and/or the respiratory muscles; locomotor and postural disease associated with skeletal myodegeneration; sudden death associated with peracute myocardial necrosis (Bradley *et al* 1981).

In yearlings and adults the presenting signs are usually locomotor or postural disorder (Fig 12 and 13) accompanied sometimes with myoglobinuria (Fig 14) Allen *et al* 1975. In dairy cows the disease occurs around parturition and the clinical signs resemble those of milk fever (hypocalcaemia) but affected animals do not respond to conventional milk fever therapy (Gitter *et al* 1978).

In sheep congenital disease can occur but is rare and fatal. Disease usually presents as a flock problem in lambs.

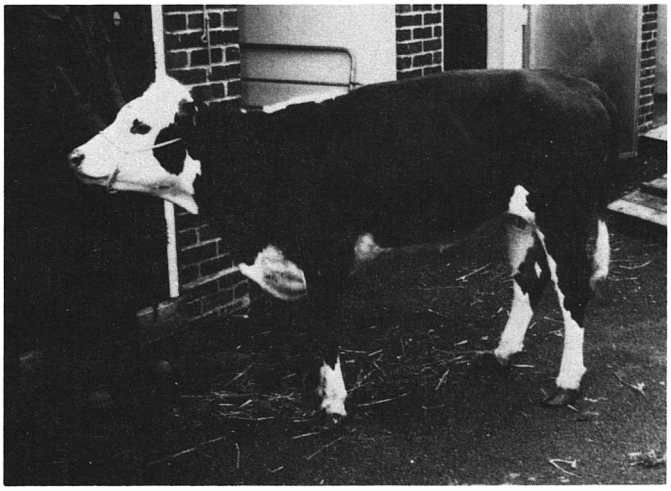

FIGURE 12. Yearling (A) with skeletal myodegeneration. Highest plasma creatine kinase (CK) 40,190 iu/1 at 30°C. Myoglobinuria positive. Note arched back and straight hind limbs.

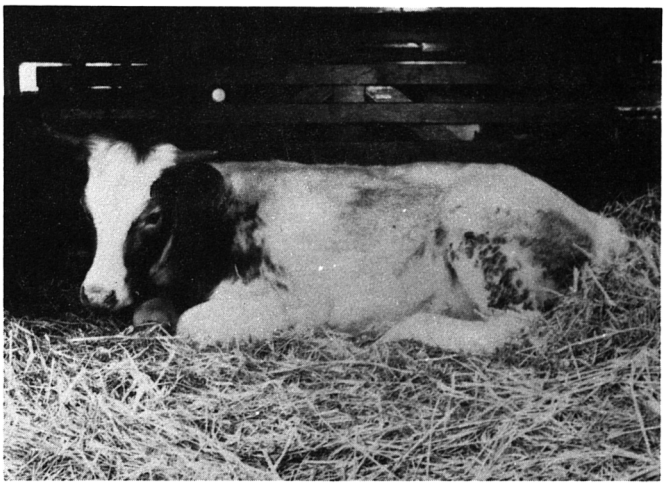

FIGURE 13. Yearling (B) with skeletal myodegeneration. Highest plasma CK 72,340 iu at 30°C. Myoglobinuria positive. Unable to stand due to severe myodegeneration of postural muscles of the limbs, abdominal and superficial back muscles.

Symptoms include sudden death, severe respiratory distress in the absence of significant respiratory pathogens or locomotor disease often presenting as 'Stiff lamb disease.'

In skeletal muscles sub-acute gross lesions if extensive enough are recognised by their bilateral symmetry and:—

a) focal or multifocal lenticular areas of pale muscle.
b) variably-sized pale pink or creamy white spots or streaks sometimes arranged with a ladder-like appearance (Fig 15).
c) whole muscles (Fig 16) or large portions of them (Fig 17) converted into a homogenous mass of firm creamy white material resembling uncooked chicken flesh. Mineralisation may occur and be detectable grossly in any lesion.

In cardiac muscle sub-acute lesions of similar colour and consistency are found typically in the sub-endacordial or sub-epicardial myocardium of the ventricles of predominantly the left side in cattle and right in sheep (Fig 18).

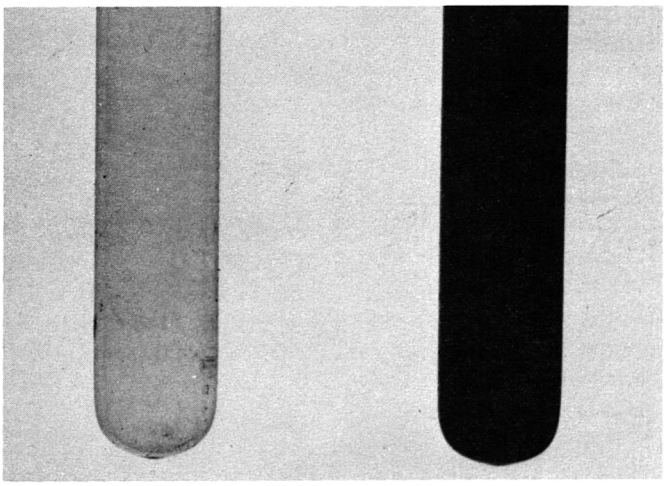

FIGURE 14. Urine from yearling B (Figure 13) (right) contrasted with that from a healthy control (left).

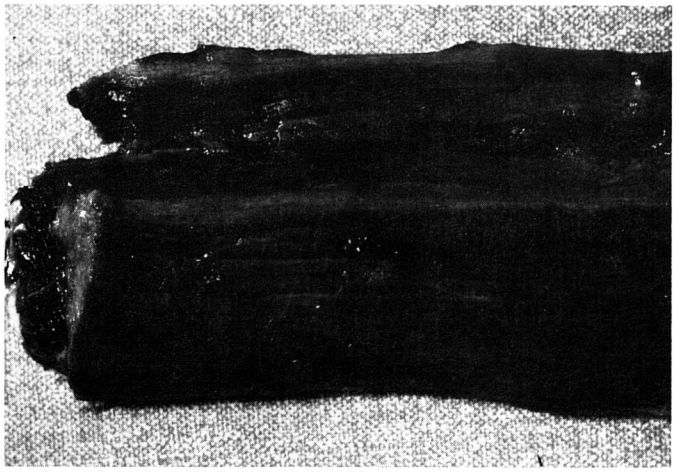

FIGURE 15. M. obliquus abdominis internus from yearling B (Figure 13). White streaks of myodegeneration some with a banded or ladder-like appearance oriented parallel to myofibre direction.

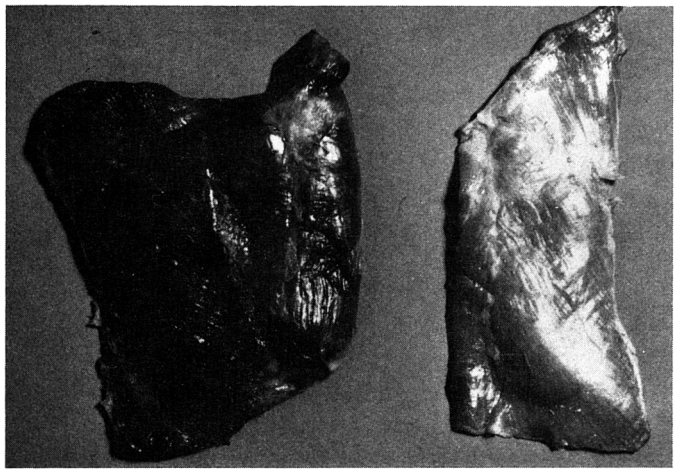

FIGURE 16. Ovine M. biceps femoris. Left healthy control, right affected.

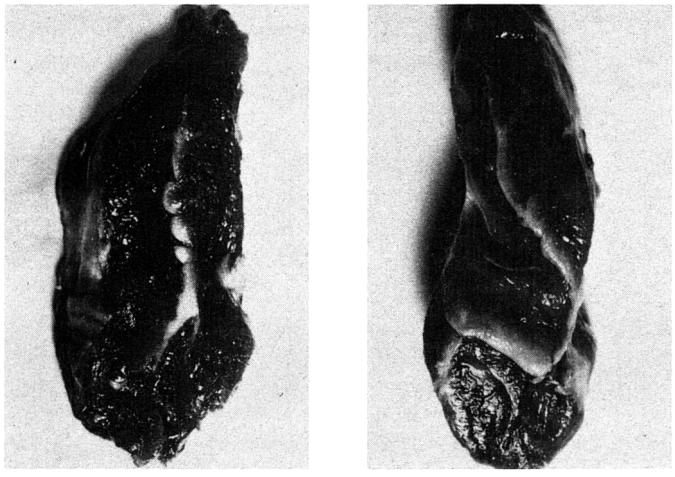

FIGURE 17. M. ulnaris lateralis, cut transversely. Healthy control left variable pallor coincident with areas of myodegeneration (right).

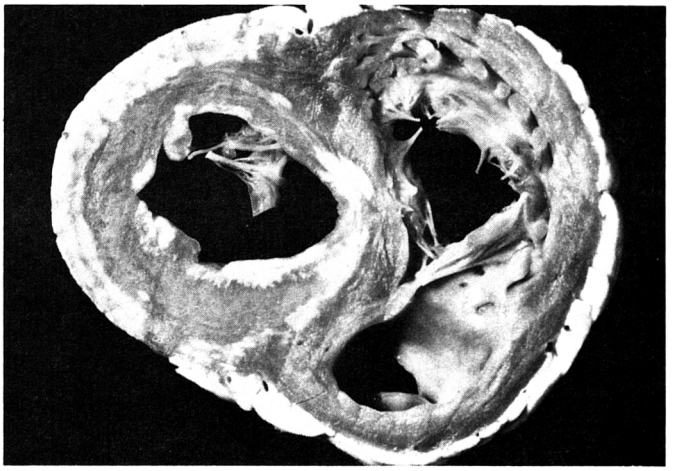

FIGURE 18. Bovine heart. Severe sub-acute sub-endocardial and sub-epicardial myodegeneration of left ventricle (fixed specimen).

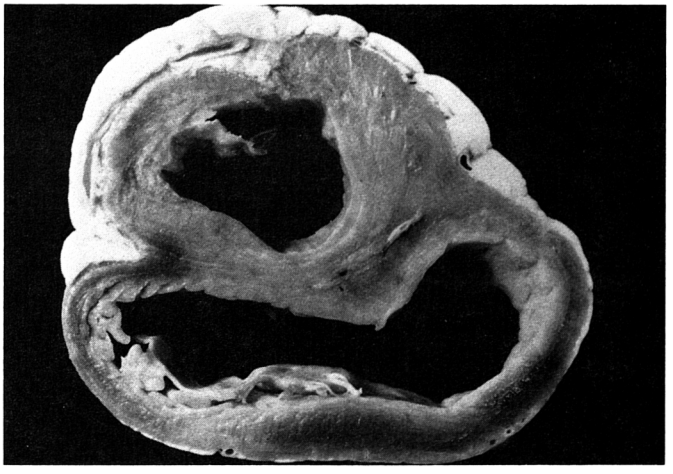

FIGURE 19. Heart from a calf dying suddenly. Variable myocardial pallor (fixed specimen).

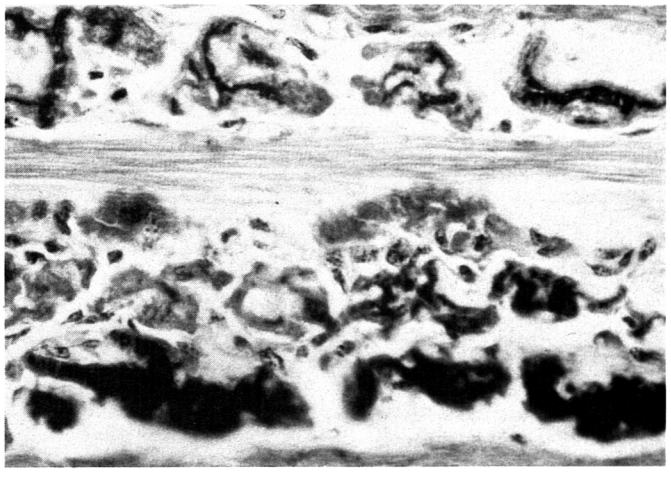

FIGURE 20. Early skeletal myodegeneration with floccular change. Martius scarlet blue (MSB).

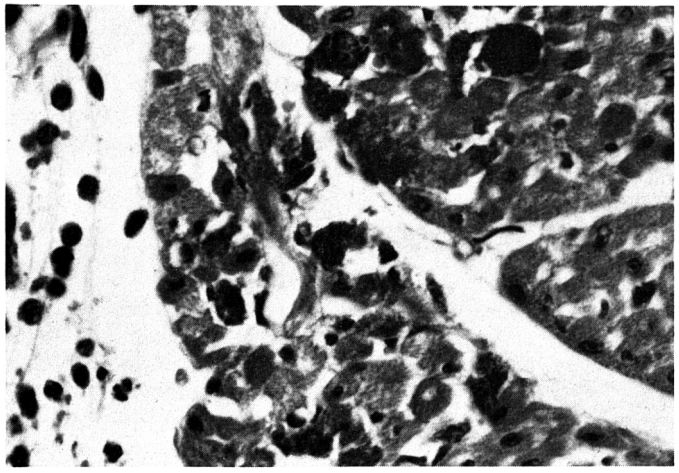

FIGURE 21. Granular change in myocardium. Hyaline, eosinophilic myocytes with pyknotic nuclei, mild phagocyte invasion. Haematoxylin and Eosin (HE)

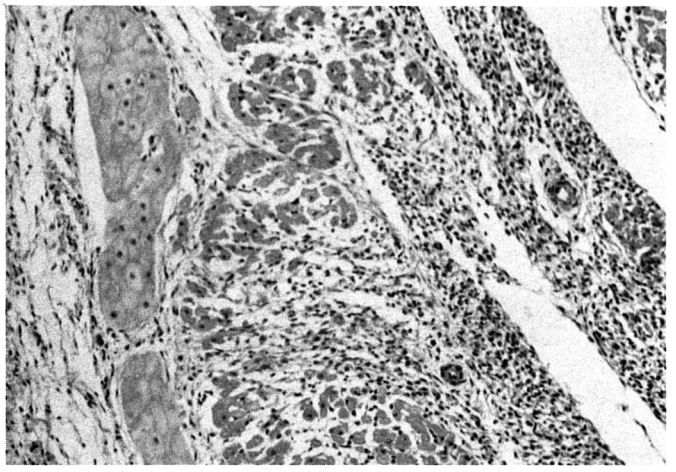

FIGURE 24. Sub-endocardial myodegeneration, phagocytosis, connective tissue collapse and fibroblast invasion. Purkinje fibres have resisted the degenerative process. HE

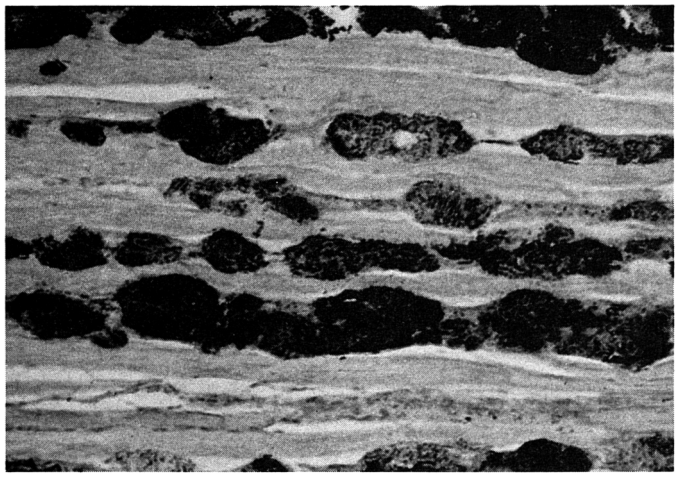

FIGURE 22. Skeletal myodegeneration. Cellular calcification. von Kossa

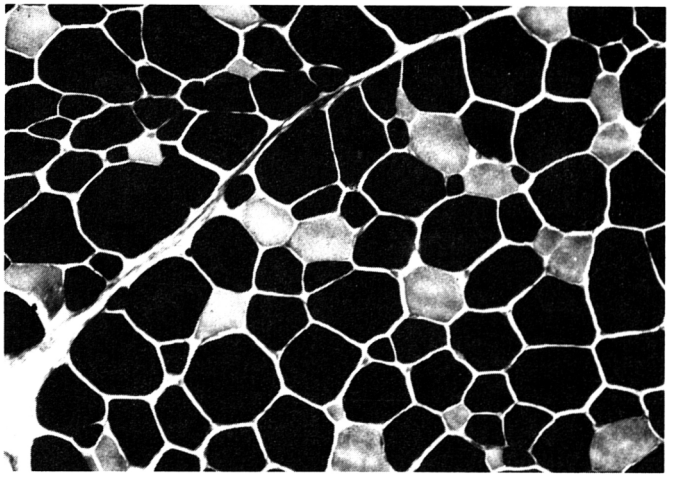

FIGURE 25. Intrafascicular normal distribution of type I (light) and II (dark) myocytes in healthy bovine white muscle. Alkali stable Myosin ATPase.

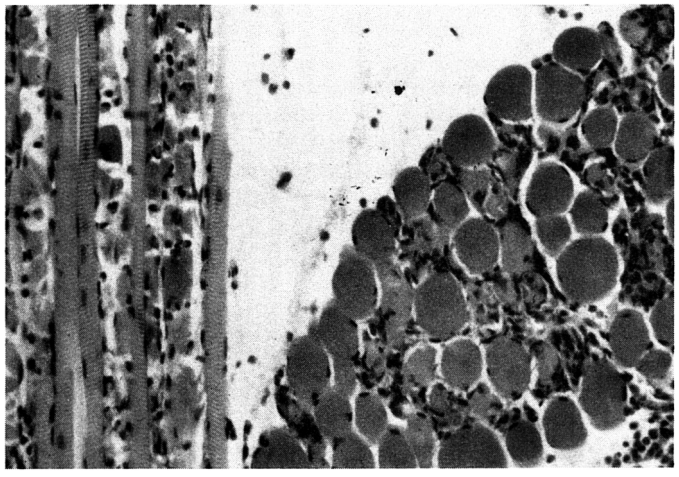

FIGURE 23. Phagocytosis of degenerated skeletal myocytes. HE

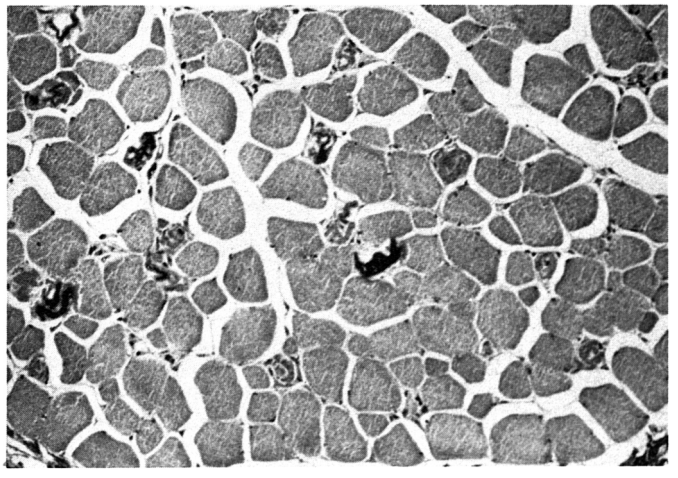

FIGURE 26. Focal myodegeneration. Note distribution of degenerated myocytes is similar to that of type I cells is Figure 25. MSB

TABLE 1. Percentage of muscle cell types [I, II and intermediate (INT)] in M. gluteus medius of healthy, acutely diseased and diseased/recovered yearling cattle from a field incident of WMD.

Animals	Days after after onset of disease	Highest plasma CPK u/l @ 30°C	Diseased	II + INT	I
Normal (Mean of 2)	—	<200	0	79	21
Acute disease	+ 3	72,340	26	74	0***
Acute disease	+ 6	40,190	29	67	4***
Disease/ recovered	+ 9	11,250	0	72	28
Disease/ recovered	+49	32,150	0	85	15

*** P <.001

Type 1 cells were 5½ times more susceptible to disease than type II + INT cells (P<.001)

In cases of sudden death only equivocal pallor of cardiac muscle (Fig 19) may occur, and this presents a problem of pathological diagnosis of myodegeneration even after histological and ultrastructural examination, unless muscle cell death existed in the live animal for at least 30-40 minutes before death. Diagnostic difficulties also result because autolytic changes can mimic those in paracute disease.

Microscopically the acute and sub-acute lesions are similar in cardiac and skeletal muscle. Early myodegeneration is recognised by hyaline, floccular (Fig 20), granular change and sometime cellular calcification (Fig 21 and 22). This is initially briefly accompanied by a mild influx of neutrophil leukocytes and followed by a macrophage response and phagocytosis (Figs 23 and 24). In skeletal muscles type I myocytes in some muscles are preferentially susceptible (Figs 25, 26 and Table 1). Another change which is sometimes observed is contraction band necrosis often accompanied by mitochondrial inclusions

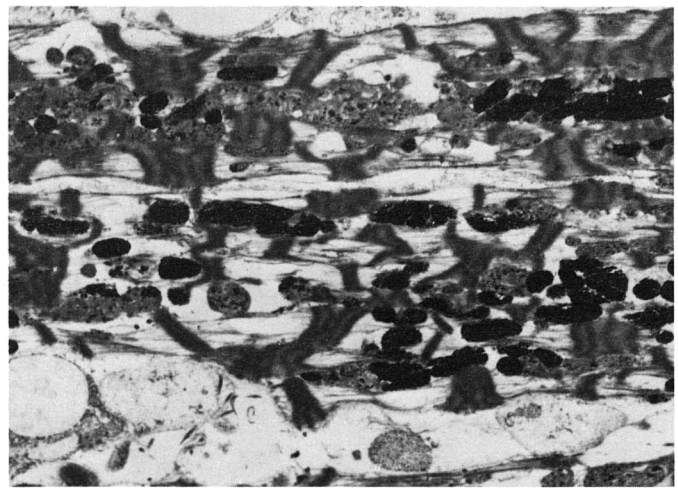

FIGURE 28. Calcified mitochondria and mineralised mitochondrial inclusions in cardiac myocyte, showing peracute necrosis. Electron micrograph x 16,000

(Fig 27). The former change may result when blood reflows into an area which has been transiently ischaemic. The non-specific myodegeneration develops as a result of mitochondrial calcium overload (Fig 28), following an increase in sarcoplasmic Ca++ concentration due to sarcolemmal damage and failure of the calcium pump (Wrogemann and Pena 1976). In non-fatal cases cardiac muscle repairs by fibrosis but skeletal muscle can repair virtually completely, if the damage is not to severe, by proliferation and fusion of satellite cells (Fig 29). Because of the non-specific nature of the cardiac and skeletal reaction an aetiologic diagnosis cannot be made on the histopathological lesions alone.

We have no evidence for or against the operation of genetic factors. If there are any they are related to the effect of genotype on selenium status.

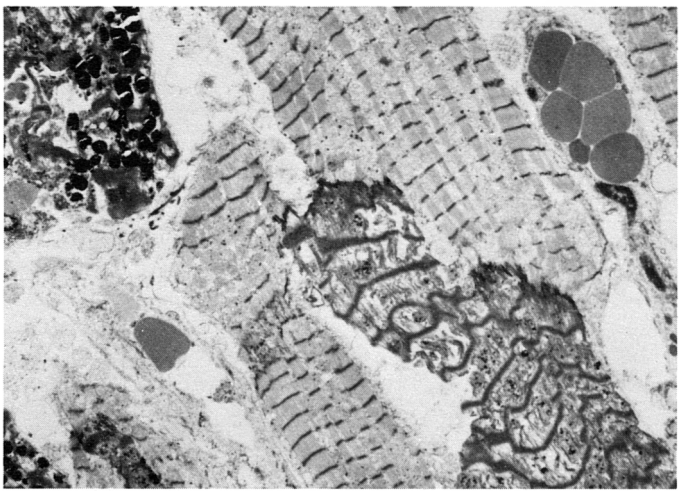

FIGURE 27. Cardiac myodegeneration with contraction band necrosis and mitochondrial inclusions. Necrosis terminates at intercalated discs. Electron micrograph x 2,750

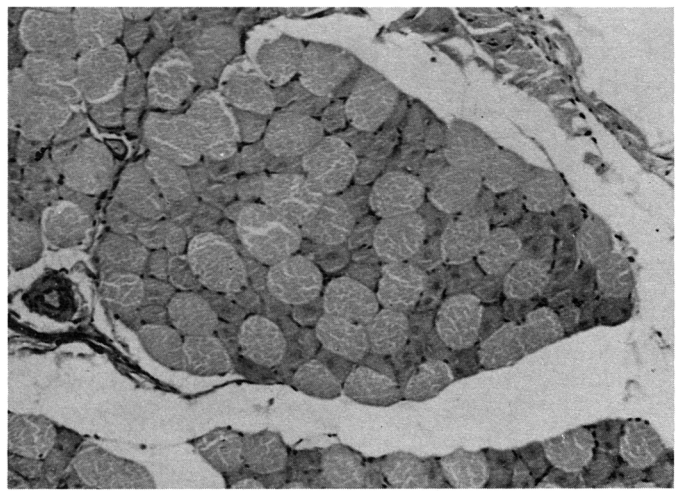

FIGURE 29. Intrafascicular distribution of regenerating (dark) myocytes rich in RNA and with internal nuclei is akin to distribution of type I cells of healthy muscle (Figure 25). Methyl Green Pyronin.

Aetiology of White Muscle Disease

1. Micronutrient deficiency of Vitamin E and/or Selenium.
2. Promoters:—

   Polyunsaturated Fatty Acids (PUFA's). Higher levels in spring grass than in grass at other seasons.

   Sudden increase in exercise. Occurs following spring turn out after winter housing.

   Climatic stress. Cold, wet and windy weather after spring turn out.

   In dairy cows—Parturition.

   In calves—Excitement such as that produced at the time of feeding milk.
3. Genetic factors. If any of these are related to the effect of genotype on selenium status.

Conclusions

WMD is the most common and most economically important ruminant myopathy. In recent years the age range of affected animals has been extended. Reasons suggested for this change are:—

A greater proportion of livestock are now fed on feeds produced on the farm where they are kept. This has exposed hitherto unsuspected selenium-deficient areas in Great Britain. The use of unsupplemented diets and propionic acid-treated or alkali-treated cereals are added hazards.

Weather conditions appear to be major factors affecting annual incidence. WMD is preventable by:—

1. Maintaining adequate dietary intake of vitamin E and selenium, if necessary by feed supplementation.
2. Allowing cattle time to adapt to, or sheep protection from, harsh environmental conditions.

Parenteral administration of vitamin E and selenium is effective for treatment. Some forms with repeated injection are useful also for prevention.

References

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