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LESIONS IN SHEEP SKELETAL AND OESOPHAGEAL MUSCLE IN VERMEERSIEKTE (*GEIGERIA ORNATIVA* O. HOFFM. POISONING)

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ABSTRACT

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Vermeersiekte in sheep, which is characterized clinically by vomition of ruminal contents, often accompanied by stiffness or paralysis, is caused by various plant species of the genus *Geigeria*. A histopathological study of the skeletal and oesophageal muscles of three experimental and three natural ovine cases revealed lesions in every case. In paraffin sections examined by light microscopy, vacuolation of focal groups of muscle fibres was seen. The sarcoplasm in the vicinity of the vacuoles was hyalinized and single or multiple centrally displaced sarcolemmal nuclei occurred in the vacuoles. A variation in the size of muscle fibres in these foci was seen in the more chronic experimental cases. Small "atrophic" hyalinized fibres with centralization and proliferation of sarcolemmal nuclei were encountered.

Electron micrographs revealed that the vacuoles in the sarcoplasm resulted from focal degeneration of myofibrils in otherwise intact muscle fibres. The thick myofilaments disappeared first, causing dissolution of the A-band in affected myofibrils. Shredding of the remaining thin filaments eventually lead to the complete destruction of myofibrils and the appearance in the fibre of irregular areas of fine granular material, containing remnants of myofilaments, Z-band material and swollen vacuolated mitochondria. Due to excessive loss of myofibrils the diameter of some muscle fibres was reduced.

INTRODUCTION

Regurgitation of ruminal contents through the mouth and nose, from which the Afrikaans name vermeersiekte (literally vomiting sickness) has been derived, is one of the most striking clinical signs of this disease, caused by the ingestion of various species of plants belonging to the genus *Geigeria* of the family Compositae (Steyn, 1949). It is regarded as one of the six most important plant poisoning syndromes in South Africa. The main clinical signs, as described by Du Toit (1928), are general debility and stiffness, followed later by paresis or paralysis and in many cases "vomition". Animals affected with the so-called atypical form of vermeersiekte, referred to as the "lame", "laminitic" or "paralytic" form of the disease, initially show a stiff gait and are inclined to lie down. These early signs of locomotor disturbances may not be noticed unless the sheep are driven and watched carefully. They grow progressively weaker and after a few days are unable to stand unaided. When lifted they stand with their backs arched and their feet close together; muscular tremors are seen, they may take a few steps and then they collapse. Eventually paralysis sets in.

Sheep affected with the "paralytic" form of vermeersiekte often do not show vomition. However, Du Toit (1928) found in experimental work with *Geigeria ornativa* (syn. *G. passerinoides* Harv., *G. africana* Harv.) that sheep may develop only one of these forms or they may exhibit signs of both concurrently. In cases in which one form appears first the other may follow if feeding with the plant is continued long enough.

A plant poisoning syndrome which very closely resembles vermeersiekte occurs in the United States of America (Kingsbury, 1964). It is also caused by species of two genera in the family Compositae, viz. *Helenium* spp. (sneezeweed) and *Hymenoxys* spp. (bitter- or rubberweed).

There are no references in the literature on vermeersiekte to lesions in the locomotor system that would cause either stiffness or paralysis, nor has any lesion been described in the oesophagus which could cause the regurgitation syndrome. To date it has been surmised that vomition was due to stimulation of, or a lesion in, the central nervous system. However, field observations by R. W. Muir (State Veterinarian, Kimberley - personal communication, 1967) have revealed that dilatation of the oesophagus frequently occurs in these cases in which regurgitation is encountered and may be so pronounced that it can easily be detected by clinical examination *in vivo*. This paper describes lesions in the skeletal muscles and in the striated muscle of the oesophagus in experimental and natural cases of vermeersiekte in sheep.

MATERIAL AND METHODS

Experimental cases

One adult Merino (Sheep 1) and two 18-month-old Dorpers (Sheep 2 and 3) were used. Prior to the experiment they were surgically fitted with permanent ruminal fistulae, through which the plant material was introduced. Dried *G. ornativa* collected during 1954 in Griqualand West and stored for 15 years was used and the sheep were dosed with the dry finely ground plant material at a rate of 5g/kg of body mass per day, excluding week-ends. The total number of doses that each animal received is given in Table 1. The animals were stabled and fed on a ration consisting of *c.* 500g of grain concentrate and dried and/or green lucerne hay *ad libitum*. Daily clinical examinations were carried out including ballottement of the oesophagus to ascertain dilatation of this organ, and rectal temperatures were recorded.

Natural cases

Two adult Dorper ewes (Sheep 4 and 5) were obtained from the Koopmansfontein experimental farm in the Griqualand West district. When they were

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TABLE 1 Administration of *G. ornativa* to experimental sheep at a dosage of 5 g/kg/day

Sheep No.	Total No. of doses received	Days stiffness noticed	Days vomition occurred	Day of Death
1	34	33	—	37
2	115	43	—	122
3	106	42–48; 57–67; 92–96; 114, 120	113, 120	120

consigned to the laboratory an outbreak of vermeersiekte due to *G. ornativa* was in progress on this farm and both animals were showing signs of the disease.

In addition a grossly dilated oesophagus (Fig. 1), fixed *in toto* with the lungs, larynx and tongue in 10% formalin, was obtained for study. This material originated from a natural case of vermeersiekte (Sheep 6) from the Griqualand West district.

Material for electron microscopy

Muscle biopsies were taken immediately before autopsy from the vastus lateralis muscle of one experimental sheep (Sheep 3) and one natural case (Sheep 5) according to the technique described by Price, Howes, Sheldon, Hutson, Fitzgerald, Blumberg & Pearson (1965).

The muscle specimens were fixed in 4% glutaraldehyde in Millonig's buffer (Millonig, 1961) at pH 7,2 to 7,4, postfixed in buffered 2% osmium tetroxide, dehydrated and embedded in Araldite (Luft, 1961). From the Araldite blocks sections 1 to 2 μ thick were cut, stained with toluidine blue pyronin (Ito & Winchester, 1963) and examined under a light microscope. Suitable blocks were selected for ultra-thin sectioning. The thin sections for electron microscopy were stained with uranyl acetate (Watson, 1958) and lead citrate (Reynolds, 1963).

Material for light microscopy

Specimens from various muscles of the hind and front limbs, back, neck and from the oesophagus of each animal were excised, placed on cardboard strips, left to dry for 1 to 5 min, labelled and placed in 10% buffered formalin.

Paraffin embedding was used and sections were stained with haematoxylin-eosin (HE).

Clinical pathological determinations

Routine chemical pathological examinations according to standard methods were periodically done on blood from all the experimental cases. These included determinations for sedimentation rate, haemoglobin percentage and serum glutamic oxalacetic and pyruvic transaminases, total bilirubin, blood urea nitrogen, blood glucose, total plasma protein, calcium, sodium, potassium and bicarbonate. Determination of serum creatine phosphokinase (CPK) was done in the case of Sheep 1 (Anon., 1965).

RESULTS

Clinical findings

(a) *Experimental cases*

The clinical findings of this experiment are summarized in Table 1.

Sheep 1 showed slight stiffness on Day 22. Thereafter no locomotor disturbance was observed until Day 33, when marked stiffness was seen. The following day it was unable to stand and remained recumbent until it died on Day 37.

Transient stiffness was observed in Sheep 2 on Day 43. This disappeared and the animal appeared normal until Day 121, when it lay down most of the time. On Day 122 it was unable to rise, exhibited muscle tremors and later died.

Marked stiffness occurred in Sheep 3 on Day 42. It could not rise on the following day and stayed down for 4 days, after which it managed to regain its feet and stand with difficulty. It gradually improved and appeared normal on Day 50. Slight stiffness recurred from Days 57 to 67 and again from Days 92 to 96. Frequent vomition of ruminal contents was noticed on Day 113. This was followed on Day 114 by a stiff gait and slight dragging of the feet. Vomition, muscle tremors and stiffness were recorded on Day 120 when it was killed for autopsy.

Anorexia appeared during the last 4 days in Sheep 1 and during the last 2 days in Sheep 2. In Sheep 3 anorexia seemed to be associated with the bouts of stiffness. This animal also developed a temperature reaction and signs of pneumonia from Day 23 to Day 26. It was treated with penicillin and streptomycin intramuscularly after which these signs disappeared. No temperature reactions occurred in Sheep 1 and 2. Dilatation of the oesophagus could not be detected clinically in any of the animals.

(b) *Natural cases*

Both animals were killed for autopsy the day after their arrival at the laboratory. Sheep 4 was unable to stand and remained in sternal recumbency, whereas Sheep 5 showed no locomotor abnormality. Evidence of recent vomition, seen as soiling of the skin around the mouth and nostrils by ruminal contents, was present in both sheep.

Gross pathological findings

The three experimental sheep were in very poor condition at death. Red hepatization of the apical and cardiac lobes of the right lung was found in Sheep 2 and Sheep 3 had an acute purulent pneumonia with a similar distribution of the lesions. In both Sheep 2 and 3 the oesophagus appeared to be flabby and very slightly dilated. No gross lesions were seen in Sheep 4 and 5, the two natural cases, and these animals were in very good condition when slaughtered. Stasis of the rumen was evident in the experimental sheep, but was absent in the natural cases.

Although the skeletal muscles were closely inspected in all the sheep, no grossly detectable changes were found.

Histopathological findings

(a) *Paraffin sections*

Skeletal muscles. Muscle lesions occurred in all the cases. Small focal groups of fibres or, more rarely,

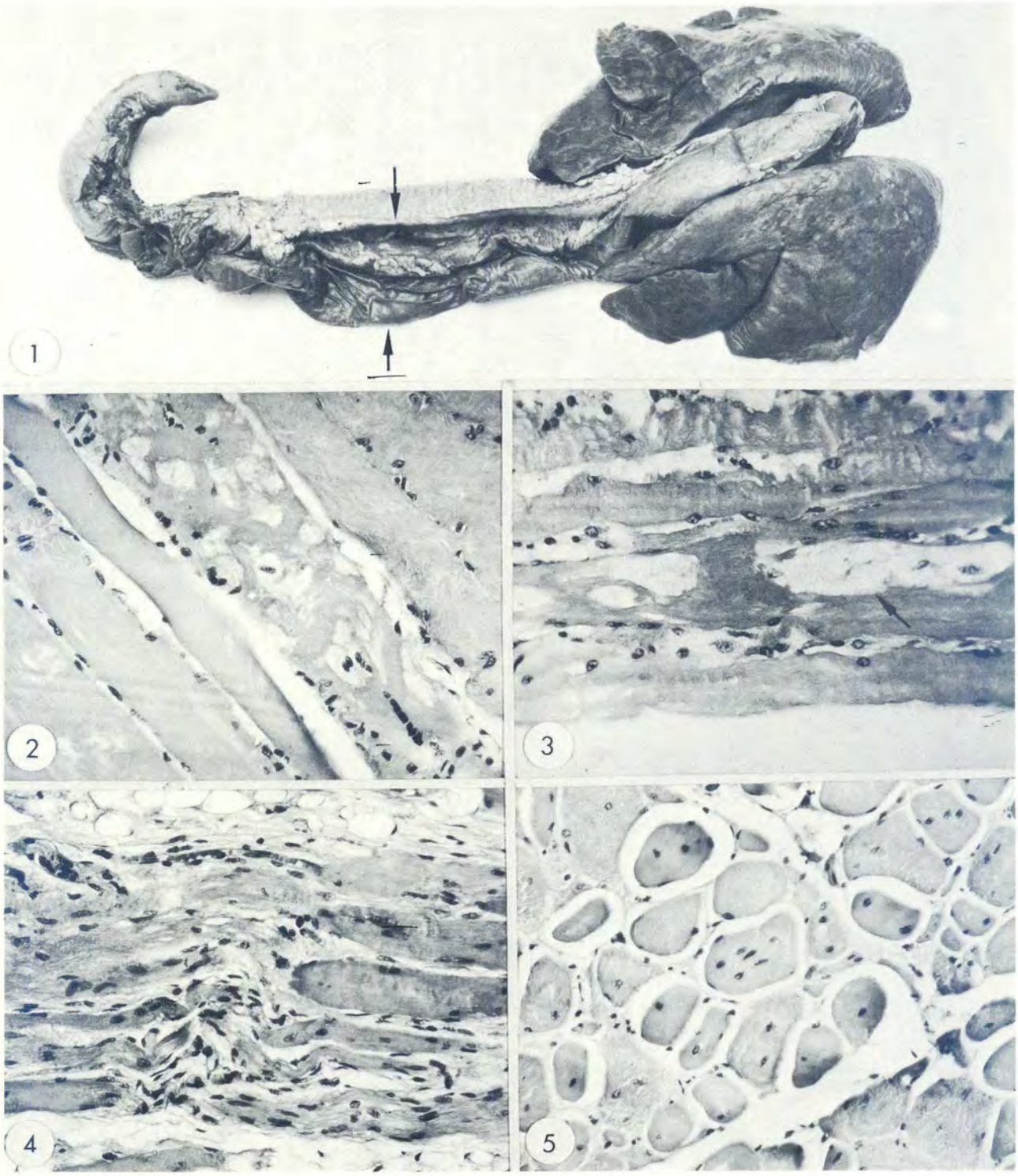


FIG. 1 Fixed gross specimen from a natural case of vermeersiekte (Sheep 6) showing marked dilatation of the oesophagus (arrows).

FIG. 2 A skeletal muscle fibre showing numerous vacuoles throughout its sarcoplasm. Some of the vacuoles contain single or multiple nuclei. HE × 200

FIG. 3 Large vacuoles, within a skeletal muscle fibre, containing nuclei and fine strand-like material (arrow). The sarcoplasm in the vicinity of the vacuoles has a hyaline appearance. HE × 200

FIG. 4 Note variation in the size of skeletal muscle fibres. The small "atrophic" hyalinized fibres show proliferation and centralization of sarcolemmal nuclei. Slight increase of connective tissue is present in the endomysium between these small fibres. HE × 200

FIG. 5 Cross-section of muscle showing a group of hyalinized fibres with central nuclei. HE × 200

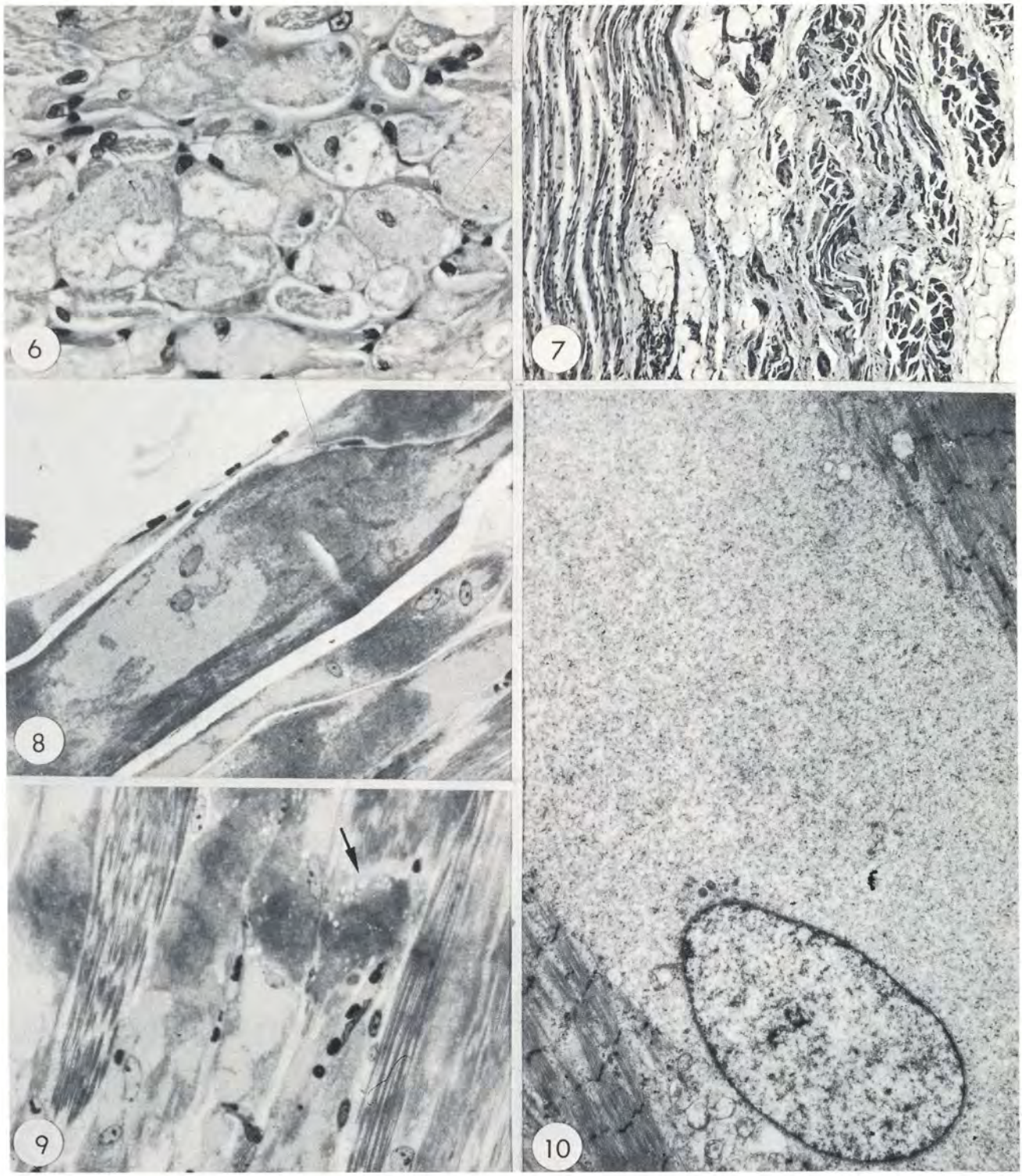


FIG. 6 Cross-section of oesophageal muscle. Group of muscle fibres with vacuolation of sarcoplasm and central nuclei in some. HE × 500

FIG. 7 Oesophagus from the case illustrated in Fig. 1. Pronounced diffuse "atrophy" of muscle fibres in both the inner and outer muscular coat is obvious. HE × 75

FIG. 8 Skeletal muscle. Araldite section. Irregular "empty" areas, corresponding to the vacuoles seen in paraffin sections, in sarcoplasm of fibres with central nuclei. No cross or longitudinal striations are present in the hyalinized sarcoplasm surrounding these areas. Toluidine blue pyronin. × 1 200

FIG. 9 Skeletal muscle. Araldite section. Similar areas to those in Fig. 8 are present in the fibres. Small groups of vacuoles (arrow) representing swollen mitochondria are present on the interface of the "empty" and hyalinized areas of the sarcoplasm. Also note fibres in which the myofibrils appear thinned out and fragmented. Toluidine blue pyronin. × 1 200

FIG. 10 Skeletal muscle. Low magnification electron micrograph of an "empty" area with a central nucleus. The area devoid of myofibrils contain a fine granular substance. × 6 800

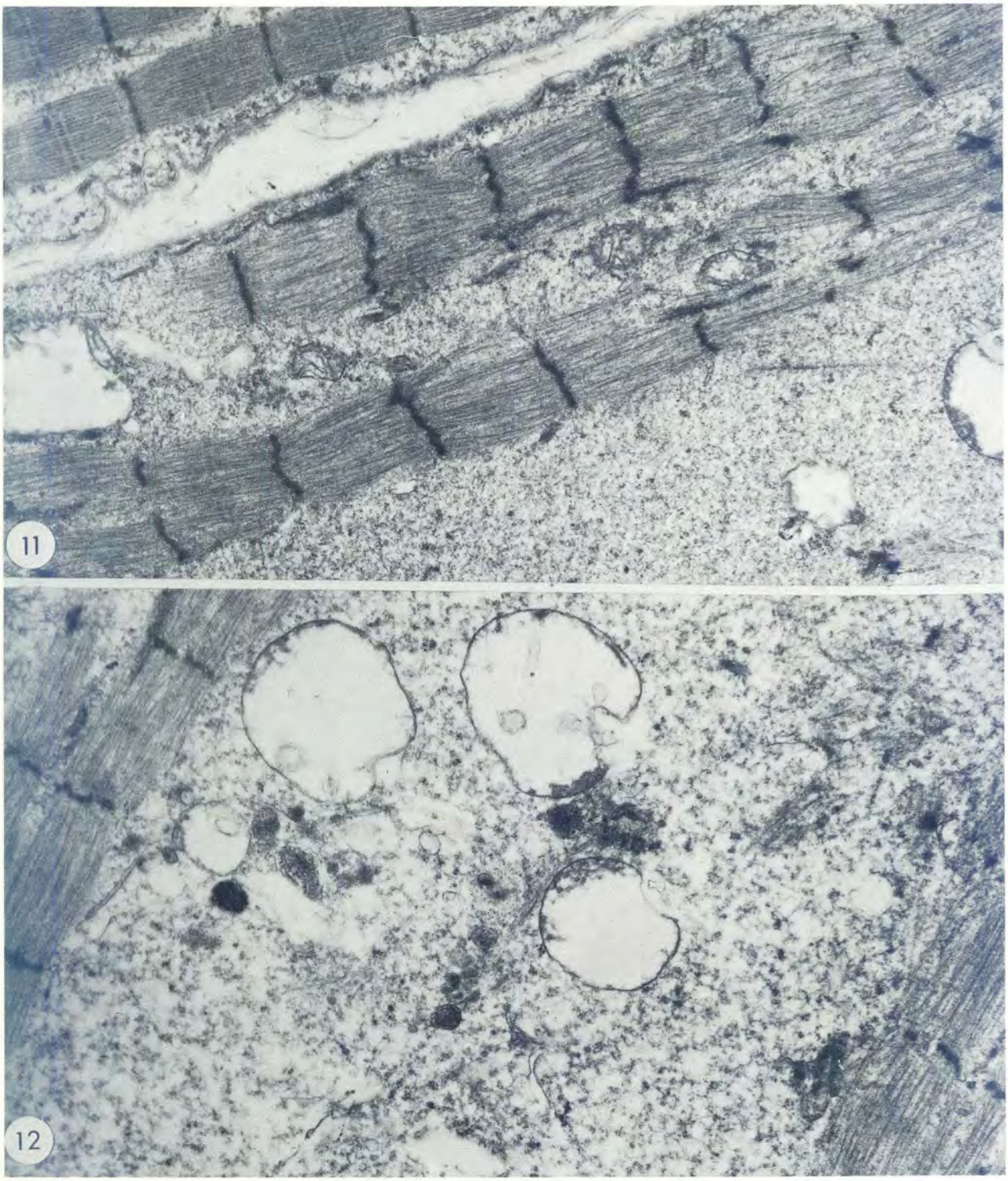
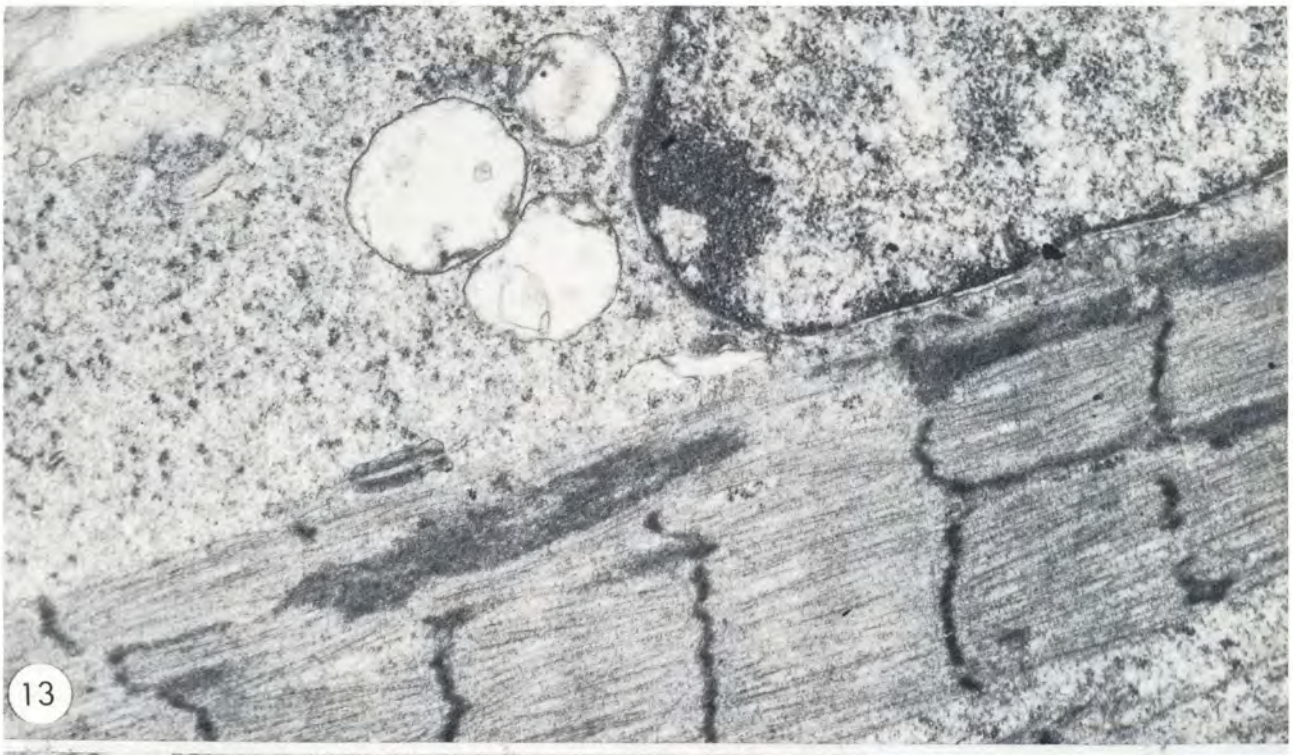


FIG. 11 Skeletal muscle. Subsarcolemmal myofibrils with thinned out appearance due to loss of thick myofilaments. The A-band is no longer visible or only a faint suggestion of it can be seen in some sarcomeres. The Z-bands are thickened, in some places fragmented and tortuous. Compare with normal myofibrils top lefthand corner. Fine densely packed granular material has replaced the myofibrils. Shredding of thin myofilaments from the periphery of the altered myofibrils into the granular mass can be seen. × 12 000

FIG. 12 Skeletal muscle. An "empty" area without myofibrils containing swollen vacuolated mitochondria, remnants of myofilaments and Z-band material and of other organelles. The granular material is not as homogeneous and as densely packed as it is in Fig. 11. × 12 000



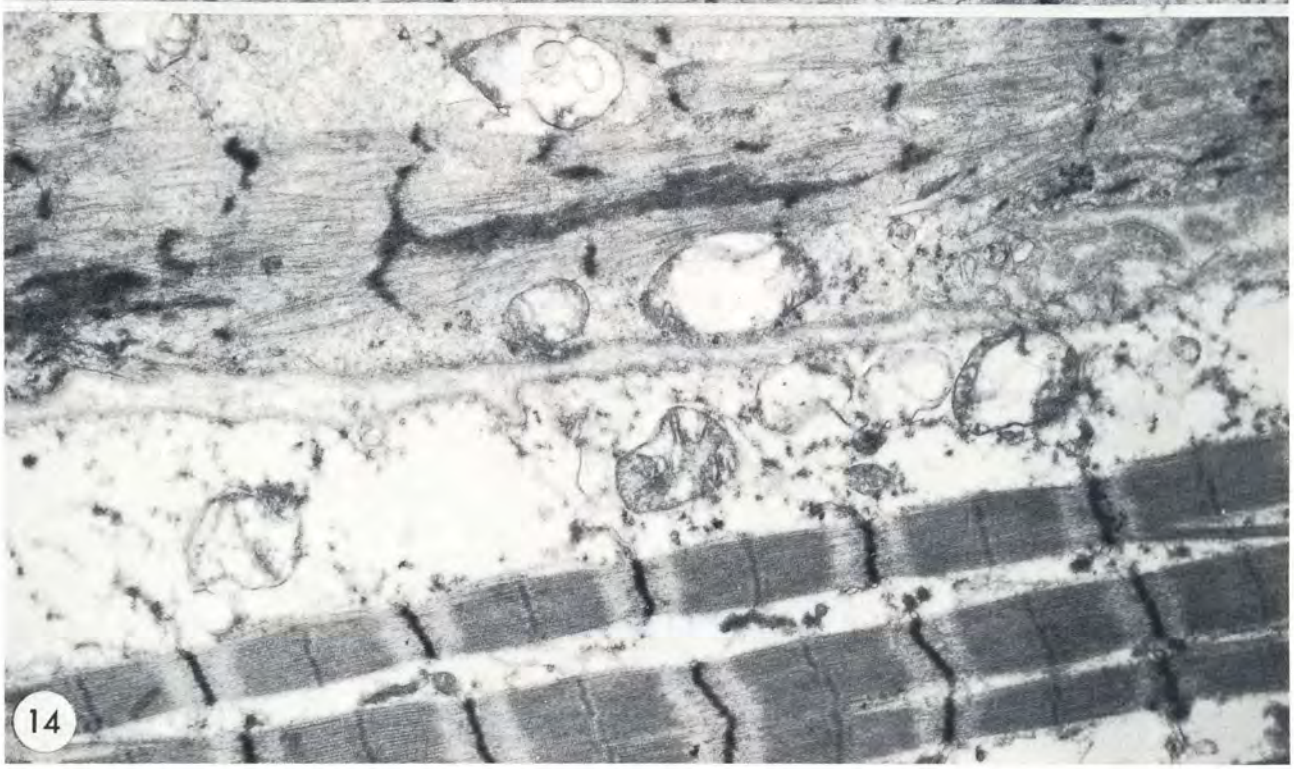


FIG. 13 Skeletal muscle. Irregular masses of dense material, probably derived from the Z-bands, overlying the myofilaments of thinned out myofibrils. Note extension of this material from Z-band to Z-band. × 18 000

FIG. 14 Skeletal muscle. Portions of two adjoining fibres can be seen in this picture. Similar Z-band changes, as shown in Fig. 13, are present in the top fibre. There is also an excessive loss of myofilaments from the affected myofibrils. The sarcoplasm of the bottom fibre has a very clear washed out appearance, the sarcolemma shows some folding and the myofibrils are more widely spaced. × 9 200

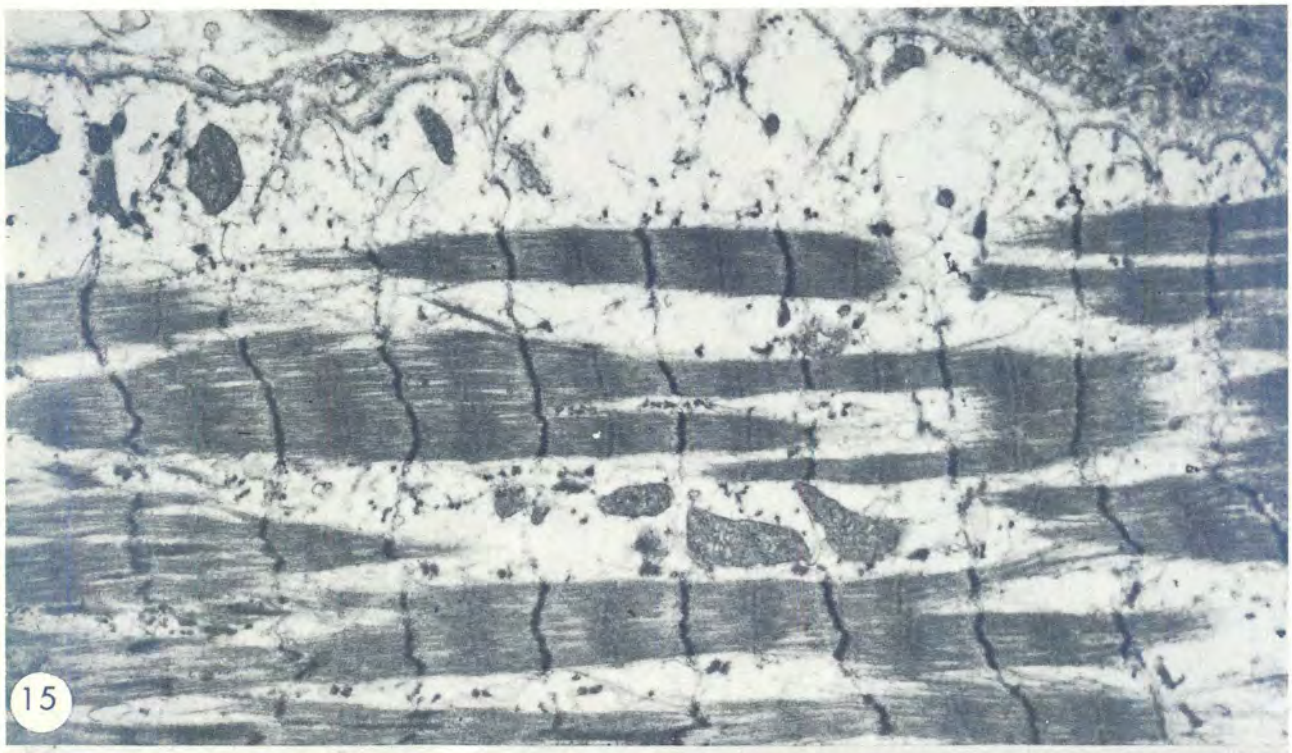


FIG. 15 Skeletal muscle. A fibre showing marked folding of the sarcolemma, clear sarcoplasm, variation in diameter of myofibrils and wide interfibrillary spaces. Complete or partial loss of sarcomeres can be seen in most of the myofibrils giving the fibre a moth-eaten appearance. × 9 200

FIG. 16 Skeletal muscle. Small "atrophic" fibre without any recognisable fibrillar structure. The sarcoplasm contains randomly scattered clumps of Z-band material with attached myofilaments and a centrally situated nucleus. An increase of collagen fibrils, close to the sarcolemma and further away in the endomysium, can be seen. × 9 200

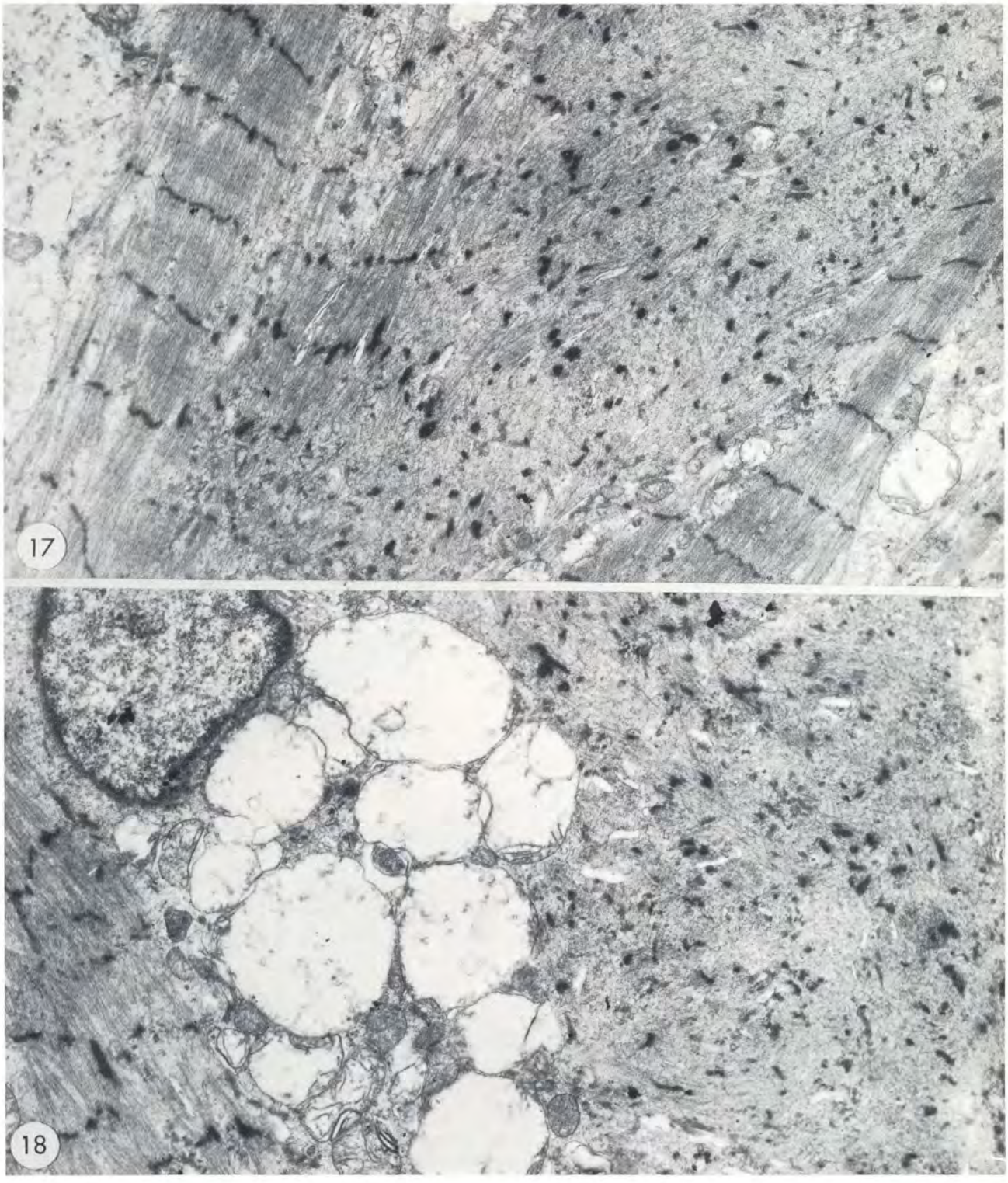


FIG. 17 Skeletal muscle. An area within a muscle fibre consisting of a mass of disorientated myofilaments and clumps of Z-band material, representing the hyalinized areas seen with the light microscope. It is flanked by altered myofibrils from which shredding of myofilaments is taking place. × 8 000

FIG. 18 Skeletal muscle. A group of enlarged and vacuolated mitochondria, with almost total loss of cristae, on the edge of an area similar to that illustrated in Fig. 17. × 10 000

single fibres were affected throughout most of the sections of muscles that were examined. These focal areas were randomly distributed and varied in size and frequency, not only from muscle to muscle, but also in different areas of the same muscle.

In Sheep 1 and 4 vacuolation of groups of fibres was conspicuous (Fig. 2). These vacuoles varied in size but were mostly large and irregularly shaped. Sometimes they took the form of clefts. Fine eosinophilic strands and granules were present within the vacuoles (Fig. 3) and they often contained either single or clusters of centrally placed nuclei (Fig. 2 and 3). The sarcoplasm in the immediate vicinity of the vacuoles frequently had a hyaline appearance with loss of both longitudinal and cross striations (Fig. 3), while some of the peripherally situated sarcolemmal nuclei in this area were pyknotic. Most of these muscle fibres seemed to be only partially damaged. Although fibres that contained localized vacuoles appeared to be swollen along their entire length and were more eosinophilic than normal fibres, the sarcoplasm remote from the vacuoles still exhibited cross and longitudinal striations. Apart from slight proliferation, the sarcolemmal nuclei away from the vacuolated parts seemed unaffected.

Similar changes were seen in Sheep 2, 3 and 5, although the vacuolation of fibres was not as marked. In addition, foci were encountered in which a slight increase of endomysial connective tissue had taken place around the individual fibres. In these foci, which were associated with the areas showing vacuolar changes, the muscle fibres varied in size, some being markedly reduced in diameter (Fig. 4). Centrally situated nuclei, and proliferation of the subsarcolemmal nuclei were common features in these smaller fibres, in which the sarcoplasm had a hyaline appearance. Central nuclei were also found in fibres that appeared normal and in groups of fibres that showed an increase in eosinophilia, although the cross and longitudinal striations were still present (Fig. 5).

Oesophagus. In every sheep the striated muscle of both the inner and outer layers of the oesophageal muscle coat contained lesions. Microscopically these lesions looked like those in the skeletal muscles. In Sheep 1, focal groups of fibres that were more intensely eosinophilic and had vacuolated sarcoplasm and centrally located nuclei were frequent. In some sections almost the whole inner circular layer was affected.

Groups of atrophic fibres with central nuclei were found in Sheep 2. A slight increase of endomysial connective tissue around the smaller fibres similar to that observed in skeletal muscles, was noticeable. Vacuolation of fibres was particularly prominent in Sheep 3 (Fig. 6) and only a few atrophic fibres occurred at the periphery of the outer longitudinal muscle layer. Compared with the experimental cases the two natural cases (Sheep 4 and 5) showed less extensive lesions in the oesophagus. Sections from the oesophagus of Sheep 6, also a natural case, revealed marked atrophy of muscle fibres in both the inner and outer muscle layers (Fig. 7).

(b) *Araldite sections of skeletal muscle*

The vacuoles seen in the muscle fibres in the paraffin sections appeared as irregular clear spaces devoid of myofibrils. Centrally situated nuclei were often seen in these spaces, which contained a finely granular material (Fig. 8) and were surrounded by homogeneous masses of necrotic sarcoplasm with no cross or longitudinal striations (Fig. 8 and 9). These masses corresponded to the hyalinised areas of sarcoplasm seen in the paraffin sections. At the interface between these necrotic clumps of sarcoplasm and the clear spaces smaller, empty-looking vacuoles were frequently present (Fig. 9). An apparent thinning out of the myofibrils was seen in some muscle fibres (Fig. 9). Such fibres were usually close to those showing clear spaces and altered sarcoplasm. The myofibrils were further apart than is normally the case and were separated by intervening clear spaces.

(c) *Electron microscopy*

The clear vacuoles seen with the light microscope consisted of large areas in the sarcoplasm that contained no myofibrils but were filled with a fine granular substance (Fig. 10). In some (Fig. 11) the granular material was densely packed and homogeneous in appearance. In others (Fig. 12) it was more loosely arranged and included clumps of disorientated myofilaments, remnants of Z-bands, sarcoplasmic reticulum and swollen vacuolated mitochondria. These areas occurred centrally in affected fibres as well as immediately under the sarcolemma. They frequently extended over the whole width of the fibre and were merely fringed by one or two myofibrils.

Various changes were noticeable in the myofibrils at the edges of these areas. The Z-bands were thickened, had a wavy or zigzag rather than a straight course and were sometimes fragmented. Myofilaments were irregularly arranged and could be seen shredding off the myofibrils into the "empty" granular areas. Consequently most of the fibrils were less dense or looked thinned out (Fig. 11 and 12). The typical band pattern of the myofibrils was lost because the thick myosin filaments of the A-bands and H-zones from the sarcomeres had disappeared (Fig. 11 and 14). Irregular clumps of dense material frequently overlaid the disarranged myofilaments. It was presumably derived from the Z-bands and was sometimes seen extending from one Z-band to the other (Fig. 13 and 14).

In addition to the granular areas described above, other areas in the muscle fibres were encountered which consisted of masses of tangled myofilaments containing scattered clumps of dark Z-band material with attached myofilaments (Fig. 17 and 18). No fibrillar structure was visible in these clumps. The hyalinized portions of the sarcoplasm seen in the paraffin sections corresponded with these localized areas of myofibril disintegration. The adjacent intact myofibrils showed similar degenerative changes to those surrounding the granular "empty" areas and were also shredding off myofilaments. The mitochondria within and near to these areas were markedly enlarged and vacuolated and showed loss of cristae (Fig. 18). Mitochondria associated with the "empty" granular areas were similarly affected. Groups of enlarged and vacuolated mitochondria in and on the edges of the "empty" granular areas, and the areas consisting of masses of disintegrating myofibrils referred to previously, corresponded to the small vacuoles seen in the Araldite sections with the light microscope.

Changes which seemed to represent intracellular oedema were present in some muscle fibres close to those with marked disintegration of myofibrils. In these fibres the myofilaments were separated by wide interfibrillary spaces (Fig. 14 and 15). The subsar-

colemmal space was also markedly widened and irregular bulging of the sarcolemma was often seen. The sarcoplasm looked very clear and empty. Although most of the myofibrils in these fibres still appeared to be intact several changes in them were noticed. They varied greatly in diameter, some being very thin, apparently due to a loss of myofilaments from their periphery. In many of the myofibrils complete or partial destruction of either single or several adjacent sarcomeres could be seen (Fig. 15). The disappearance of successive sarcomeres and the reduction in the diameter of the myofibrils made these structures look thinned-out and fragmented. Changes similar to those described above were also seen in the Z-bands of these myofibrils.

Muscle fibres that were markedly reduced in diameter were found in Sheep 3, an experimental case (Fig. 16). The sarcolemmal nuclei were centrally placed and frequently no fibrillar structures were present, though in some cases fragments of myofibrils were seen underneath the sarcolemma. The sarcoplasm contained masses of disintegrated myofilaments, clumps of Z-band material and remnants of other organelles, resembling the areas which corresponded to the hyalinized areas under the light microscope and which were associated with the vacuoles (*vide supra*). An increase of collagen fibrils was noticed in the endomysium near these small fibres.

No structural changes were noticed in the sarcolemma of affected fibres. Peripheral nerves and motor endplates encountered in thin sections from Sheep 3 likewise showed no pathological abnormalities.

Chemical pathology

The results obtained by Grosskopf (1964) were confirmed. Except for changes in the CPK serum values, which were only determined in Sheep 1, no marked chemical pathological changes that could be related to clinical signs or lesions seen at autopsy were detected in the experimental animals at any stage. The rise in CPK serum levels in Sheep 1 coincided with the observation of a possible transient stiffness on Day 22. Although the CPK rose sharply to approximately three times the initial serum levels (from 8 sigma units/ml serum to 30 sigma units/ml serum), no further stiffness could be detected clinically until Day 33.

Discussion

The pathological changes in the striated musculature in vermeersiekte recorded here suggest that the toxic principle of *Geigeria ornativa* exerts a cytopathological effect on the muscle fibres. This finding is supported by the sharp rise in the serum CPK levels in the one experimental case in which this enzyme was determined. According to Brown & Wagner (1968), increased plasma CPK activity in sheep will most likely result from myopathy. Essentially normal values are found in a wide variety of diseases of the central nervous system, while muscle atrophy of neurogenic origin scarcely raises the CPK plasma levels.

The most impressive changes take place in the contractile fibrils and show as foci of myofibrillar degeneration within intact muscle cells. The thick myosin filaments are apparently more vulnerable since they disappear first, resulting in the dissolution of the A-band and H-zone. The thin actin filaments and Z-band are more resistant and persist as the main elements of those myofibrils adjoining the focal areas of complete myofibrillar destruction. Shredding of their thick peripheral filaments causes further disintegration of these myofibrils, giving rise initially to tangled masses of myofilaments and Z-band material and eventually to areas consisting only of fine granular debris. This process is accompanied by centralization and multiplication of sarcolemmal nuclei. Marked reduction of myofibrils, and in some cases their complete destruction, leads to the appearance of "atrophic" muscle fibres showing a loss of transverse and longitudinal striations, increased eosinophilia and proliferation and centralization of nuclei, seen with the light microscope, especially in Sheep 3.

Small "atrophic" fibres were not a feature of the lesions in the natural cases. Predominantly vacuolar changes in affected muscle fibres and the well nourished carcasses indicate that these cases probably represent the more acute phase of the disease. The sheep were also slaughtered shortly after the appearance of clinical signs. In contrast, the experimental cases received plant material, which was probably of relatively low toxicity due to prolonged storage, over an extended period (Table 1). From the presence of small "atrophic" fibres, in conjunction with more acute changes, and the abovementioned factors it can be assumed that the lesions in the experimental cases reflect a more advanced or chronic stage of the disease.

No satisfactory explanation for the occurrence of the typical signs of vomition and locomotor disturbances in vermeersiekte has been put forward previously. Steyn (1949) ascribes the vomiting to the direct effect of the toxin on the ruminal wall and the stimulation of the vomiting centre in the medulla oblongata. Grosskopf (1964) is of the opinion that the vomiting act is in fact an ordinary rumination reflex which is not properly controlled, due to some nervous disturbance in the sensitivity of the pharyngeal region.

Apart from the purulent pneumonia which usually follows aspiration of regurgitated material, numerous histological examinations of different organs failed to reveal any pathological changes that could be attributed to vermeersiekte (Grosskopf, 1964). However, the occurrence of the lesions in both the oesophagus and skeletal muscles in the cases described above suggests that they are linked with the clinical manifestations of vomition and locomotor disturbances. In longstanding natural cases a larger percentage of fibres may be expected eventually to become small and "atrophic". The almost total "atrophy" of muscle fibres of both the inner and outer muscle coats of the oesophagus in one natural case (Fig. 7) supports this theory. Diminution of the muscle fibres in the oesophagus will interfere with the normal functioning of this organ and will certainly contribute to the development of oesophageal dilatation, a phenomenon that is commonly seen in natural outbreaks of the disease in sheep (*vide supra*).

The mechanism which results in the development of the muscle lesions in vermeersiekte is not clear at this stage. Myopathies may be of either neuropathic or myopathic origin. Grosskopf (1964) inferred that the symptoms in vermeersiekte may have a neurological background. According to Grosskopf (1964), Smit (1958) demonstrated degeneration, perivascular oedema and focal areas of necrobiosis in the thalamus of affected sheep. In the present study no lesions were

seen in the peripheral nerves of the musculature examined by light microscope. With the electron microscope peripheral nerves and motor endplates in the vicinity of affected muscle fibres in Sheep 3 also appeared morphologically normal. However, examination of the central nervous system was not specifically included in the present study and the reported changes in it must await further investigation.

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