MYOCARDIAL PATHOLOGY OF DOMESTIC RUMINANTS IN SOUTHERN AFRICA

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Myocardial pathology of ruminants in southern Africa, including lesions associated with toxic plants, other toxic agents, infectious and nutritional deficiency, is discussed with regard to recognition and to aetiological diagnosis. Findings are included which have not been published elsewhere. The importance and difficulties in recognition of myocardial lesions at an early stage are emphasized. Further research into the pathology of cardiac failure caused by toxic plants is clearly needed.

Key words: Myocardial pathology, ruminants, cardiotoxic plants and substances.

INTRODUCTION

Cardiac failure in domestic ruminants can result from a variety of toxic, infectious and nutritional causes in southern Africa. Numerous indigenous plant species are known to be cardiotoxic47,52, and stock losses caused by some of these species are of considerable economic importance21,32. Since cardiac failure in farm livestock is often acute, affected animals are usually found dead. The opportunity for clinical examination, therefore, is limited, and necropsy is frequently the starting-point of diagnostic investigation.

Herein we discuss the myocardial pathology of ruminants in southern Africa, and perpend its diagnostic potential and limitations. Findings from necropsy material examined in recent years by the Section of Pathology, Veterinary Research Institute (VRI), Onderstepoort are included which have not been published elsewhere.

RECOGNITION AND INTERPRETATION OF CARDIAC LESIONS

Macroscopical Examination

To assess cardiac failure at necropsy it is imperative to examine the other organs as well as the heart itself. Passive congestion, oedema of the lungs and/or thoracic, pericardial or peritoneal effusion, if present, may be more important evidence of cardiac failure than are changes in the heart itself. These extracardiac changes are manifestations of cardiac dysfunction whereas most myocardial lesions, themselves, provide no direct evidence of cardiac dysfunction.

Some myocardial lesions are readily discernible grossly, particularly when they are sharply demarcated or extensive. Cardiac lesions in many cases of white muscle disease23 and gousiekte44, for example, can be detected by gross examination. Since many lesions, however, are not detectable grossly, failure to find them should not preclude macroscopic examination.

Delays are often inevitable before necropsies can be done on farm stock, so that post-mortem autolysis is common and may complicate the recognition of lesions. Diffuse myocardial pallor, often more conspicuous in the endocardial zone, may occur as a result of post-mortem autolysis, but the tissue should be examined microscopically if a lesion is suspected. We have also observed irregular, pale areas in the ventricular walls. The only microscopical change that could be detected in these areas was a marked paucity of erythrocytes in the capillaries, and we believe that the pallor may be a manifestation of irregular blood redistribution caused by local differences in the degree of rigor mortis. The size of the cardiac chambers and the thickness of the ventricular wall can vary with the stage and degree of rigor mortis, and such variations may be confused with moderate ventricular hypertrophy, atrophy or dilatation. Accurate assessment of ventricular hypertrophy or atrophy requires weighing of the ventricles, but few figures for ventricular weights of normal ruminants are available. Ventricular weights of Merino sheep in South Africa have been measured and analyzed in relation to body mass, sex and age37, but the results show considerable variation, and it is unlikely that the weighing of hearts will prove useful in field investigations.

Microscopical Examination

Certain features occur regularly in the myocardium of cattle, sheep and goats with no history to suspect cardiac dysfunction. Awareness of such features is essential to histopathological assessment. Sarcocysts are common, and there is rarely any tissue reaction associated with them. Small foci of lymphocytic infiltration have been found in the myocardium interstitium of many hearts from normal sheep37. Vacuolation of cardiac myocytes and reduced packing density of myofibrils in the subendocardial myocardium have been seen commonly in bovine hearts in Britain16. We have seen similar vacuolation occasionally in hearts of normal cattle and sheep (Fig. 1).

Artifacts with routine haematoxylin and eosin (HE) staining can also cause confusion. The intensity of eosinophilia of cardiac myocytes in sections differs in line with knife scores, and myocyte fascicles cut transversely stain more weakly than those cut longitudinally. Post-mortem autolytic changes include pale staining of myocardocytes and the appearance of gaps between them. Even staining throughout the tissue, large amounts of formalin artifact pigment and the presence of numerous

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bacteria are features of myocardial autolysis which serve to distinguish it from necrosis\textsuperscript{10}.

In many cases of sudden death myocardial lesions are not obvious. It becomes important to determine the earliest light microscopical manifestations of myocardial injury in these cases, and to distinguish them from artifacts and autolytic changes. It is here that we encounter difficulties. Increased eosinophilia of cardiac myocytes occurs as an early event in myocardial ischaemia\textsuperscript{24}. It has been reported that variations of myocyte eosinophilia are strongly indicative of myocardial necrosis in cattle, and that such changes do not usually occur in significant numbers of cells in normal myocardium even with substantial delays in fixation\textsuperscript{10}. We have seen variations in eosinophilia not only in hearts from cases of acute cardiac failure but also in normal hearts, and we are reluctant to accept them as firm evidence of injury. Empirical staining methods have been developed to differentiate injured myocytes at any early stage. These include modifications\textsuperscript{16,25,40} of an acid fuchsin method\textsuperscript{43} by which injured myocytes can be identified by their intense fuchinophilia before any changes are detectable in HE sections. A haematoxylin – basic fuchsin-picric acid (HBFP) method has also been developed\textsuperscript{44}, which has been found effective in detecting ischaemic injury as early as 30 min after vascular ligation. This method has been reported as useful in examining bovine hearts but results are sometimes unaccountably inferior\textsuperscript{10}. On occasion we have applied an acid fuchsin technique\textsuperscript{44} to myocardium from sheep that had died of acute cardiac failure but our results have been variable. It is clear that the success of these empirical methods depends upon strict attention to staining concentrations and times and on careful comparison with positive and negative control sections.

Irregular contraction of sarcomeres is identifiable by HE staining but appears more clearly in sections stained by Mallory's phosphotungstic acid haematoxylin\textsuperscript{22} or Heidenhain's iron haematoxylin\textsuperscript{45}. We recommend the use of either of these methods where acute cardiac failure is suspected.

Electron Microscopy

Electron microscopy has proved of value in identifying and clarifying early features of myocardial injury in cattle\textsuperscript{10}, despite the fact that its routine use for field material is usually limited to formalin-fixed tissues. Interpretation, however, must be made with caution. Mitochondrial matrical electron-dense bodies, for example, increase in number with time after death in bovine myocardium\textsuperscript{10}. Studies of delayed fixation of canine myocardium have revealed that several ultrastructural changes occur during autolysis which resemble those occurring in ischaemic injury\textsuperscript{42,43}.

**CARDIOTOXIC PLANTS**

**Plants Containing Cardiac Glycosides**

Cardiac glycoside poisoning of cattle and sheep is of considerable economic importance in South Africa compared to other countries. This is probably due to the large variety and wide distribution of plants here which contain cardiac glycosides and the fact that most stock is kept under range conditions\textsuperscript{32}. The most important of these plants are species of *Homeria* and *Moraea*, which
are commonly known as 'tulp', species of *Urginea, Ornithoglossum* and *Pseudogalania*, known as 'slangkop' and species of *Cotyledon, Kalanchoe* and *Tylecodon*. Less important plants include *Melianthus comosus, Bowea volubils, Nerium oleander, Thevetia peruviana, Digitalis spp, Asclepias fruticosa, Acokanthera spp, Adenium spp and Strophanthus spp*.

Severe cardiac arrhythmias, leading to ventricular fibrillation have been described in poisoning of ruminants by some of the cardiac glycoside-containing plants, but associated myocardial pathology has not been studied in detail. An assay method for cardiac glycosides has been adapted for use on ruminant tissues and rumen contents (R A Schultz and T W Naudé 1975, VRI, Onderstepoort, unpublished work), but the method is time-consuming and is not in routine use. In numerous necropsies of cattle and sheep with a history of suspected tulp or slangkop poisoning we have sometimes found extracardiac evidence of congestive cardiac failure, but gross and microscopic findings have been limited to epicardial and endocardial haemorrhages. In occasional cases, however, and particularly where the history suggested that the animal had lived for several days after ingestion of the toxic plant, we have found scattered foci of myocardial necrosis, sometimes with mononuclear inflammatory cell infiltrates and evidence of early fibroplasia. These findings suggest that morphological evidence of myocardial injury in cardiac glycoside poisoning in ruminants may be more consistent than has been recognized, and that efforts should be made to identify it at an earlier stage.

Poisoning by *Cotyledon* and *Kalanchoe* spp is normally manifest as a chronic disease known as "krimpsiekte" [19], which is characterized by clinical signs referable to nervous system dysfunction rather than to cardiac failure. It has been shown experimentally that cardiac glycosides extracted from *Cotyledon, Kalanchoe lanceolata* and *Tylecodon glandiflorus* caused krimpsiekte when small doses were given repeatedly to sheep. When large doses were given, however, acute disease with evidence of cardiac failure resulted [33]. In some of these cases multifocal myocardial degeneration and necrosis, often with lymphocytic, lymphoblastic and macrophage infiltrations, were observed. Microscopical examination of myocardium should not be neglected if poisoning by these plants is suspected.

### 'Gousiekte'

'Gousiekte' is the name given to a disease of ruminants which is characterized by sudden death from cardiac failure which is caused by ingestion of certain plants of the family Rubiaceae. Plants shown to cause gousiekte are *Pavetta schumanniana*, *Pavetta harborii* and *Fadogia monticola*. 'Gousiekte' is a plant toxicosis of economic importance in South Africa [31]. There is a latent period of 4-8 weeks between ingestion of the plant and the time that deaths occur. Many, but not all, cases show macroscopical evidence of congestive cardiac failure, including generalized congestion, ascites, hydropericardium, hydrothorax and pulmonary oedema. Such cases resemble heartwater macroscopically, and brain smears should be examined. Features which may help to distinguish heartwater are the presence of abomasal oedema, nephrosis and wetness of the cut surface of the brain. An early report [48] described marked ventricular dilatation as a consistent feature, but subsequent observations [44] including our own indicate that ventricular dilatation occurs in only a small proportion of cases. In many cases the ventricular walls are thinner than normal and have a tough consistency. Irregular areas of pallor, especially in the endocardium, may be observed, in some cases, however, macroscopical changes in the heart are not recognizable. Microscopical examination reveals foci or areas of loss of myofibres with replacement by fibrous tissue. Atrophy of myofibres may be evident, and lymphocytic infiltrates of varying intensity are often present [21, 44, 44]. These lesions are generally more pronounced in the endocardial zone. They are found most consistently in the cardiac apex, which has been recommended as the area of choice for routine examination. Connective tissue stains can be useful to appreciate the extent of fibroplasia. The identity of the toxic principle in gousiekte is not known and the pathogenesis is not clear. Selective loss of myosin filaments from cardiac myocytes has been reported as an early change in a preliminary ultrastructural study [33], but there is clearly a need for more research into the pathogenesis.

### Dichapetalum cymosum

*Dichapetalum cymosum* ('gifblaar') is an important cause of stock losses in certain areas. The toxic principle of the plant is monofluoracetate acid [32], which is converted within the body to fluorocitrate [39]. There is no chemical test for the routine diagnosis of gifblaar poisoning. Citrate levels in heart muscle and diaphragm have been found to be elevated in experimental monofluoracetate poisoning in sheep, but the stability of citrate in the tissues requires further investigation [41]. In most field cases of 'gifblaar' poisoning death occurs within a few hours after ingestion of the plant. In ruminants peritoneal, thoracic and pericardial effusion have been documented [46]. In most cases, however, no pathological features of diagnostic value have been found, and diagnosis must be based on circumstantial evidence and the finding of *D. cymosum* leaves in the rumen contents. This lack of pathological findings is to be expected, since no consistent pathological changes were observed in an experimental study of acute fluoracetate toxicosis in sheep [32]. Here, again, application of methods to detect early myocardial injury might be useful.

Myocardial lesions have been seen occasionally in ruminants that have died after grazing on veld containing *D. cymosum* [41], and some of these animals were known to have ingested *D. cymosum* several days before they died. These lesions consist of multiple small foci of myocardial necrosis or loss of myofibres (Fig. 2), often with lymphocytic infiltrates and early fibroplasia. Similar lesions have been produced experimentally in sheep by the administration of low doses of monofluoracetate over a prolonged period [41]. These lesions also resemble those caused by *Acacia georgiana*, an Australian plant that contains lower levels of monofluoracetate than does gifblaar [53]. This evidence suggests that the myocardial lesions seen in ruminants after grazing on veld containing *D. cymosum* are a manifestation of chronic *D. cymosum* poisoning. It is important to distinguish these lesions from those of gousiekte, since *D. cymosum* and plants causing gousiekte can occur in the same veld. In contrast to gousiekte, the lesions in monofluoracetate poisoning tend to be multifocal and
FIG. 2: Focus of loss of myocytes with fibroplasia in bovine myocardium; D. cymosum poisoning. HE X 600

FIG. 3: Necrosis and mineralization of myocytes, fibroplasia and mixed inflammatory cell infiltrates including multinucleated giant cell (arrow) in bovine myocardium; hybrid vetch poisoning. HE X 600
distributed throughout the myocardium. Fibroplasia is less marked.

Other Plants
Distinctive lesions occur in *Vicia villosa* (hairy vetch) poisoning, and these lesions involve the myocardium in some cases. Similar myocardial lesions have been described in an outbreak of suspected poisoning by a hybrid vetch in South Africa. The lesions were often detectable macroscopically as irregular, yellowish grey foci or streaks, and microscopically they consisted of fibrous tissue containing necrotic and mineralized myofibres and infiltrates of mononuclear cells, eosinophils, plasma cells and multinucleated giant cells (Fig. 3).

*Galania africana*, a plant that grows in certain areas of the Karoo, has been implicated as the cause of 'waterpens', a condition characterized by severe ascites, in sheep and goats. The plant was believed to be hepatotoxic because marked liver lesions were found in cases of 'waterpens'. In a retrospective study of field cases of 'waterpens', however, we have found microscopical changes in the liver (Fig. 4) compatible with chronic congestive right ventricular failure, and multifocal myocardial lesions, including vascular degeneration, hyaline degeneration and necrosis, mononuclear cell infiltration and fibrosis (Fig. 5).

An outbreak of a disease in sheep in South Africa has been described in which there was widespread arterial calcification. Evidence of congestive cardiac failure, including thoracic, pericardial and peritoneal effusion and pulmonary oedema, was found in many of these sheep. The hearts of many of them were dilated, and focal calcification of cardiac myofibres and myocardial infarction were observed in several. It was assumed that these cardiac changes were secondary to the arterial pathology. The cause of the outbreak was not identified, but the possibility of a plant toxicosis was not dismissed.

Another plant that may be cardiotoxic is *Thesium namaquense*. The pathology of this plant remains to be investigated.

**OTHER TOXICOSES**

Outbreaks of sudden deaths in sheep in South Africa attributed to monensin toxicosis have been reported. Affected sheep showed macroscopical evidence of congestive cardiac failure. Myocardial lesions varied from small foci to extensive areas of necrosis with mild, mixed inflammatory cell infiltrates and early fibroplasia. The distribution of the more severe myocardial lesions was predominantly in the epicardial zone, and it was suggested that this may be a useful diagnostic feature. This suggestion, however, may be misleading. The number of cases examined was small, and in a study of experimental monensin toxicosis in sheep predominance of the lesions within the epicardial zone was not reported.

Sudden deaths in sheep also occurred after accidental overdosage with salinomycin, an ionophore antibiotic similar to monensin. Myocardial lesions in these cases resembled those in monensin toxicosis (S.S. Bastianello 1983, Faculty of Veterinary Science, University of Pretoria, personal communication).

**INFECTIOUS AGENTS**

**Bacteria**
Myocardial abscesses and multifocal or diffuse fibrinous purulent myocarditis occur sporadically in ruminants in South Africa. Bacteria which have been isolated include *Pasteurella* spp and *Corynbacterium pyogenes*. Lesions of tuberculosis may also involve the myocardium. Recently several bovine cases of blackleg ('sponsiekte'), caused by *Clostridium chauvoei*, have been encountered in which fibrinopurulent epicarditis and gangrenous myocarditis were present, in addition to the skeletal muscles typical of the disease.

**Viruses**
Necrotizing myocarditis can occur in young ruminants in foot and mouth disease. In malignant catarrhal fever ('snotsiekte') of cattle the perivascular lesion frequently involves the myocardium. Myocardial degeneration and necrosis of the papillary muscle of the left ventricle have been described as a consistent lesion in bluetongue disease of sheep, and our own observations agree with this.

**Protozoa**
Myocardial interstitial lymphocytic proliferation occurs in East Coast fever, caused by *Theileria parva parva*. Myocarditis has been reported as a fairly constant lesion in Corridor disease of cattle, caused by *Theileria parva lawrencei*, and we have seen marked myocardial perivascular lymphoblastic proliferation consistently in this disease. Sarcocysts have been mentioned above.

**Metazoa**
Occasional myocardial granulomas have been associated with cysticerci in ruminants. Myocardial infarction caused by larvae of *Gedoelstia* spp. has been described in sheep in South West Africa. Cardiac lesions associated with the nematode, *Cordophillus sagittus*, have been described in kudu, and recently this parasite has been found in cattle (J. Boomker and Anna Verster 1983, VRI Onderstepoort, unpublished observations).

**NUTRITIONAL CAUSES**

**White Muscle Disease**
Cardiac lesions of white muscle disease in lambs have been reported in South Africa, and we have seen such lesions in young cattle, sheep and goats. The lesions do not differ from those described elsewhere.

Outbreaks of sudden death in young dairy calves in Britain have been investigated in which patchy myocardial pallor was seen macroscopically. HBFP staining revealed areas in which myocardial fibres stained intensely with fuchsin, suggesting peracute myocardial injury. Lesions typical of white muscle disease were absent, but there was biochemical evidence of selenium deficiency in in-contact calves. Further deaths ceased after selenium supplementation. These findings indicate that acute cardiac failure associated with selenium deficiency may occur without the typical lesions. No such cases have yet been reported in southern Africa, but the importance of detecting early myocardial lesions is again emphasized.

**Copper Deficiency**
A condition associated with copper deficiency in cattle
FIG. 4: Centrilobal fibrosis with bridging between adjacent lobules and duplication of the central vein in ovine liver; Galenia africana poisoning. HE X 200

FIG. 5: Focus of vacuolation and loss of myocytes with fibroplasia in ovine myocardium; Galenia africana poisoning. HE X 200
known as "falling disease" is recognized in Australia. Affected animals die suddenly, and there is marked myocardial fibrosis. Although certain soils in southern Africa are copper-deficient, this condition has not yet been reported here.

CENTRAL NERVOUS SYSTEM INJURY

The occurrence of multifocal myocardial necrosis following injury to the central nervous system has been documented in domestic animals, including a few cases in cattle, sheep and goats. The diagnosis in these cases included listeriosis, polioencephalomalacia, meningoencephalitis and cerebral trauma. Systematic examination of the heart should not be neglected in cases of cerebral disease.

NEOPLASIA

We have seen lymphosarcomas with myocardial localization occasionally in cattle, but other neoplasms in the hearts of ruminants in southern Africa appear to be rare. A rhadomyosarcoma in the heart of a sheep has been documented.

CONCLUSIONS

Morphological examination of ruminant myocardium is useful in the etiological diagnosis of certain conditions such as white muscle disease, gousiekte and hairy vetch poisoning, but its value in the diagnosis of many conditions will remain limited unless the early manifestations of injury can be characterized and recognized.

The pathology caused by many cardiotoxic plants in southern Africa, some of which cause stock losses of economic importance, has received little attention and needs further study.

When myocardial lesions are recognized, their nature often does not betray their specific cause. Myocardial reactions in response to injury by a variety of agents tend to follow a similar pattern of degeneration, necrosis, inflammatory cell infiltration and resolution, some aspects of which have been discussed previously. Differences observed in lesions, therefore, often reflect only their stage of chronicity, rather than the nature of the injurious agent. Myocardial lymphocytic infiltration occurs in plant toxocides and other toxocides. It is clear such infiltrates do not necessarily indicate an infectious cause.

ACKNOWLEDGEMENTS

We wish to thank the staff of the Section of Pathology for preparing the histological sections, the Section of Photography for developing the histological sections, the Section of Photography for developing the histological sections, the Section of Pathology for preparing the manuscript.

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BOOK REVIEW

POULTRY DISEASES

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The second edition of Poultry Diseases has been altered to incorporate the important recent advances in poultry diseases with the inclusion of certain diseases not mentioned in the first edition, viz. infectious coryza (Haemophilus paragallinarum), adenovirus, reviruses and neoplastic conditions. A new chapter on the avian immune system is a welcome addition. Unfortunately erosion diseases with a multifactorial aetiology related to ventilation and management deficiencies are not sufficiently emphasized while the chapter on how to conduct a field investigation is of considerable merit. The omission of certain chapters in the first edition does not in any way detract from the book’s value. Students and practitioners will find this volume very informative as the book provides a good overview of poultry diseases, their aetiology, symptoms and methods of control and should serve as a useful companion book to other books on this subject.

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