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THE PATHOLOGY OF HEARTWATER. III. A REVIEW

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ABSTRACT

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The pathological changes in cattle, sheep, goats, mice and various game species infected with *Cowdria ruminantium* are summarized. Macroscopical lesions in most animals include effusion of body cavities, oedema of the lungs and lymph nodes and splenomegaly. Apart from the presence of heartwater organisms in most organs the histopathological lesions are not striking. The ultrastructural lesions in the lungs of sheep and goats infected with the Ball 3 strain of heartwater, and mice infected with the Welgevonden strain, are discussed. Damage to capillary endothelial cells of the alveoli is limited and the mild cytopathic changes in parasitized cells indicate that the damage caused by the organisms is most probably not responsible for the increased vascular permeability associated with the disease. Pathological changes in domestic ruminants and game animals are briefly compared.

INTRODUCTION

In 1877 Webb emphasized the importance of heartwater and identified the disease as a major cause of stock losses in the Eastern Province of the Cape of Good Hope. Subsequently numerous reports on the pathology of heartwater were published including 2 comprehensive studies involving large numbers of cattle, sheep and goats (Steck, 1928; Alexander, 1931).

Cowdry (1926) concluded that the organisms cause little damage to parasitized cells. Ultrastructural studies of the lung lesions in sheep, goats and mice infected with heartwater revealed that damage to the capillary endothelial cells of the alveoli was mild and possibly not responsible for the increased vascular permeability associated with the disease (Prozesky & Du Plessis, 1985b; Prozesky & Du Plessis, 1985c).

Most attempts to infect various laboratory animals with *Cowdria ruminantium* have been unsuccessful (Uilenberg, 1983). Du Plessis & Kümm (1971) isolated the Kümm strain from a goat which was pathogenic to mice, sheep and goats and subsequently 3 additional strains, pathogenic to cattle, sheep, goats and mice were isolated (MacKenzie & Van Rooyen, 1981; Du Plessis, 1985; P. K. J. MacKenzie, personal communication, 1986). This prompted researchers to compare the pathological changes in ruminants and mice in view of the possible role of laboratory animals as models to study the pathogenesis of heartwater (Prozesky & Du Plessis, 1985b).

Heartwater may cause an inapparent, transient reaction in some game animals but may be responsible for clinical disease and mortalities in others (Young & Basson, 1973). Reports on the pathological changes in game animals that died of heartwater are limited. The available information indicates that the lesions concur to a large extent with the changes described in domestic ruminants.

A large number of necropsies are performed annually on fatal cases of heartwater in domestic ruminants at the Veterinary Research Institute (VRI), Onderstepoort. The purpose of this report is to summarise the results of necropsies carried out by the author and other pathologists in the Section of Pathology, VRI, during the period 1976–1986. The pathological lesions in domestic ruminants, mice and game animals infected with *C. ruminantium* are also reviewed and compared.

Domestic ruminants

Pathology

Macroscopical pathology: Lesions in cattle, sheep and goats are fairly similar, although quite variable in extent and some changes are more common in certain species than in others (Steck, 1928, Uilenberg, 1981). In most animals a tentative diagnosis of heartwater can be made on macroscopical lesions alone, but an unequivocal diagnosis requires the demonstration of *C. ruminantium* in either brain smears or histopathological sections (Prozesky, 1987).

Effusion of body cavities is a very common change in most fatal cases of the disease (Fig. 1). The transparent or slightly turbid light yellow fluid often coagulates on exposure to air. In the survey conducted by Steck, hydrothorax amounted to several litres in bovines, about a half a litre in sheep, and rarely exceeded 20 mℓ in goats (Steck, 1928).

As indicated by the name 'heartwater', a hydropericardium is a striking change in most animals that die of the disease (Fig. 2) and is usually more pronounced in sheep and goats than in cattle (Henning, 1956).

Oedema of the lungs is a regular finding in heartwater-infected animals and appears to be more severe in most animals that die of the peracute form of the disease (Van de Pypekamp & Prozesky, 1987). The interlobular septae of the lungs, mediastinum and associated lymph nodes are oedematous and serous frothy fluid oozes from the cut surface of the lung. The trachea and bronchi are often congested and contain a serofibrinous exudate.

Splenomegaly is present in the majority of animals. In sheep and goats the spleen is often not strikingly enlarged. The cut surface is dark red in colour and has a

FIG. 1 Hydrothorax in a sheep

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FIG. 2 Hydropericardium in a sheep

pulpy consistency. Other workers also found splenomegaly to be infrequently present in sheep and goats suffering from the disease (Uilenberg, 1971; Andreasen, 1974; Ilemobade, 1976). In animals that die of the peracute form of heartwater it is often impossible to make a diagnosis on the macroscopical lesions alone; splenomegaly, epi- and endocardial haemorrhages are sometimes the only significant changes (Alexander, 1931).

Steck (1928) found in less than 25 % of the animals examined by him that the kidneys were swollen and slightly pale in sheep and goats and often congested in cattle. The perirenal tissue was oedematous in a low percentage of cattle, sheep and goats on which necropsies were performed at the VRI (Fig. 3).

Prozesky & Du Plessis (1985a) described the kidney lesions in Angora goats experimentally infected with *C. ruminantium*. In fatal cases that were specifically treated for heartwater it was found that after the first day of the febrile reaction the kidneys were markedly swollen and pale, and there was oedema of the perirenal tissue.

Congestion and/or oedema of the mucosa of the abomasum (Fig. 4 & 5) are regularly seen in cattle and are less common in sheep and goats. Enterorrhagia (affecting the small and large intestine) is present in a small percentage of domestic ruminants.

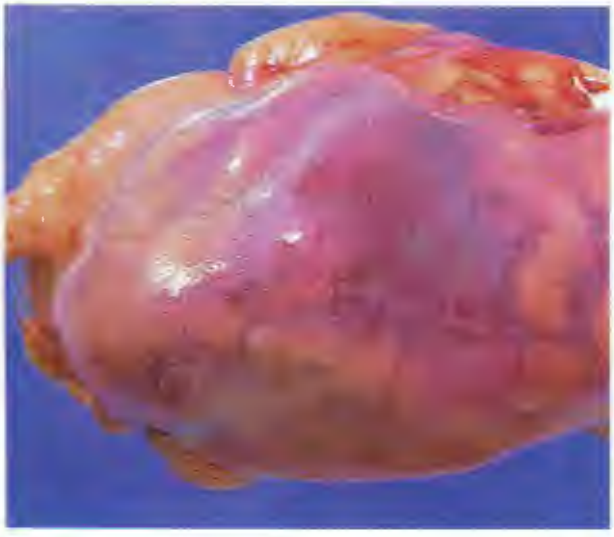
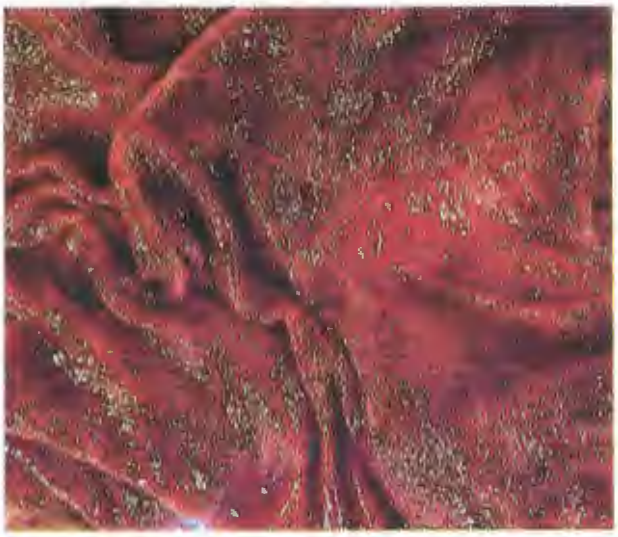


FIG. 3 Perirenal oedema in a bovine



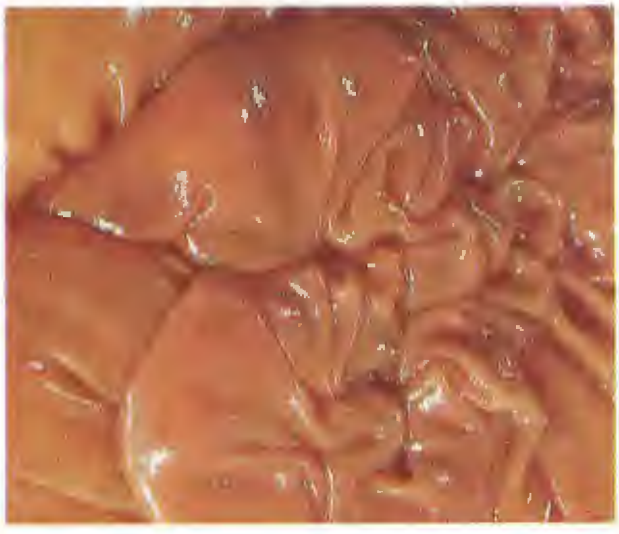


FIG. 4 & 5 In cattle congestion or oedema of the abomasum is often a striking lesion

The lymph nodes are moderately swollen in most animals. The cut surface is moist and petechiae are often present especially in the retropharyngeal, submaxillary, cervical, bronchial and mediastinal lymph nodes (Alexander, 1931). Petechiae are frequently visible on mucus membranes of tissues including those of the urinary bladder, vagina and the conjunctiva (Fig. 6).

Nervous symptoms are frequently seen in animals affected by the peracute and acute forms of heartwater, and are attributed to oedema of the brain (Van de Pypekamp & Prozesky, 1987). Macroscopically it is often difficult and sometimes impossible to detect swelling of the brain. The gyri of the cerebrum may be strikingly swollen and severe oedema of the brain may even result in a partial prolapse of the cerebellum through the foramen magnum.

Most animals that die of heartwater show congestion of the meninges, the accumulation of excessive fluid in the subarachnoid space and thickening of the choroid plexus, which has a dull greyish appearance. In some animals petechiae, ecchymoses and sometimes suggulations are evident in the midbrain, brain stem and cerebellum (Pienaar, Basson & Van der Merwe, 1966).

Hepatic lesions in animals with heartwater are not striking. Apart from a mild hepatomegaly the gall bladder is slightly distended in most animals.

Microscopical pathology: Comprehensive studies on the histopathological changes of heartwater were made (Steck, 1928; Alexander, 1931; Pienaar *et al.*, 1966). Both Steck (1928) and Alexander (1931) concluded that the changes in most organs are not striking and this agrees with the experience of the pathologists at the VRI.

Lungs: An alveolar and interstitial oedema occurs in most animals but is not always discernible histopathologically because the fluid in the alveolar spaces is washed out during the routine processing of the tissue.

Kidneys: Nephrosis is a common change in domestic ruminants that die of heartwater; it was reported to be present in more than 50 % of the animals examined by Steck (1928). Multifocal lymphocytic interstitial nephritis associated with heartwater in cattle, sheep and goats (Steck, 1928) could not be confirmed in subsequent studies (Uilenberg, 1983). Both Cowdry (1926) and Steck (1928) frequently observed heartwater organisms in endothelial cells of glomerular capillaries.

In heartwater-infected angora goats, specifically treated after the first day of the febrile reaction, the proximal and distal convoluted tubules and collecting ducts were dilated. Epithelial cells of non-dilated tubules were swollen and many of the tubules contained hyaline, granular and cellular casts. The Bowman's spaces were dilated and contained variable amounts of eosinophilic fluid. Irreversible kidney damage was most probably the cause of death of these cases (Prozesky & Du Plessis, 1985a).

Brain: Lesions in the brain of cattle, sheep and goats naturally and experimentaly infected with *C. ruminantium* were described by Pienaar *et al.* (1966). Swollen astrocytes which were often necrotic were present in most bovines and in a few sheep and goats in this study. Other lesions included swollen axons, multifocal microcavitations and haemorrhages affecting mainly the midbrain, brain stem, cerebral white matter and cerebral peduncles (Fig. 7). A perivascular accumulation of cells (mainly macrophages and a few neutrophils) and occasionally a vasculitis were observed in all the bovines and *c.* 50 % of the sheep. A diffuse meningitis (mainly macrophages) was present in a few bovines only. In the majority of animals a fibrinous chorioditis occurred and occasionally multifocal glial nodules, mainly confined to the neurophil around small blood vessels, were apparent in the sheep and cattle.

In a small percentage of non-fatal cases of heartwater, complications such as permanent blindness, torticollis and permanent recumbency is manifested (Van de Pypekamp & Prozesky, 1987). Brain lesions in recumbent animals often comprise different degrees of *status spongiosus* and in severe cases the white matter of the entire brain may be affected.

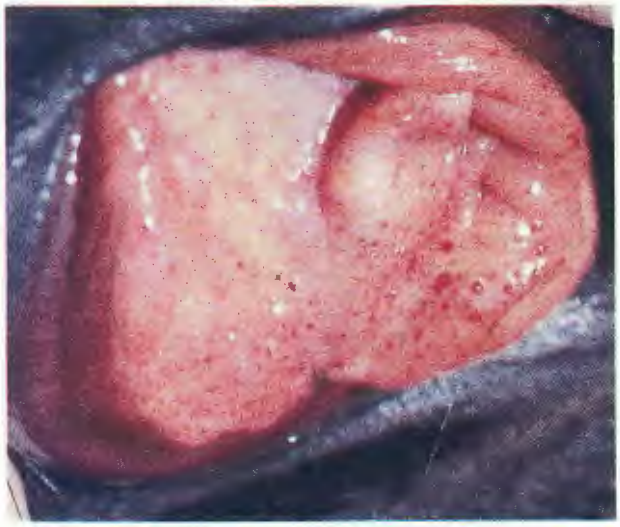


FIG. 6 Petechiae are visible on the conjunctiva of a bovine

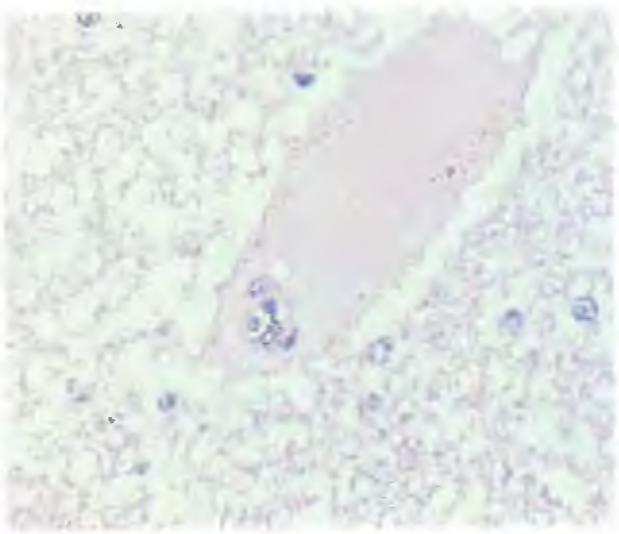


FIG. 7 Brain oedema in a sheep. HE × 1 200

Other organs: In most animals that die of heartwater the hepatic changes are inconspicuous; the lymph nodes are congested and oedematous; and congestion is the only splenic change.

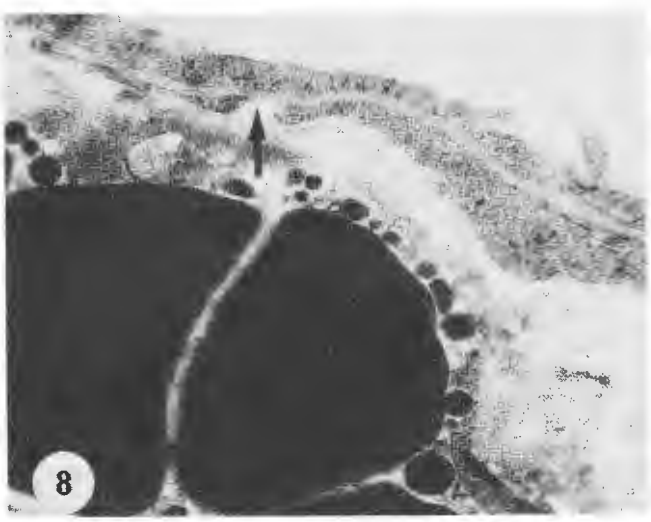
Transmission electron microscopy: Pulmonary changes in sheep and goats infected with the Ball 3 strain of heartwater were described by Prozesky & Du Plessis (1985b). Cytopathic changes in single swollen non-parasitized alveolar endothelial cells included swelling of the mitochondria, dilation of the endoplasmic reticulum and the presence of a few membrane-bound vacuoles which were either empty or contained a fine floccular or amorphous material of medium electron density. Necrotic alveolar endothelial cells were rarely encountered and the interendothelial spaces were infrequently dilated (Fig. 8). A few alveolar epithelial cells (type 1 pneumocytes) were swollen and the cytopathic changes were similar to those reported in the alveolar endothelial cells (Fig. 9).

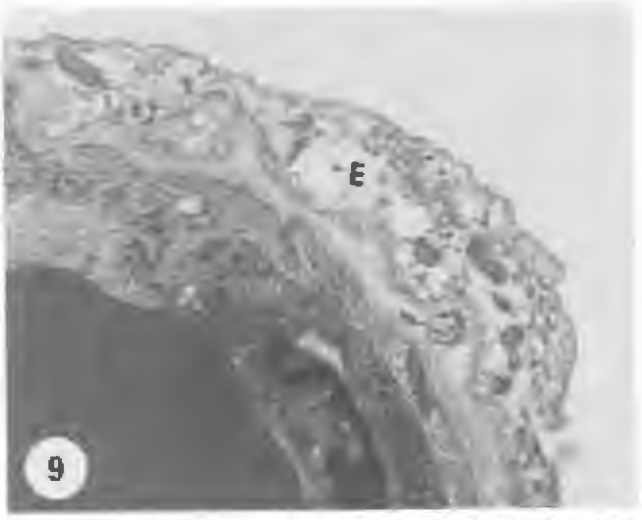
Considering the relatively mild morphological changes in the endothelial cells of the aveoli, it is difficult to account for the severe lung oedema seen grossly. It would seem that there is no correlation between the extent of the lung lesions and the concentration of organisms in endothelial cells (Prozesky & Du Plessis, 1985c). The mild cytopathic changes in parasitized endothelial cells of alveoli indicate that damage to the endothelial cells by the organisms is most probably not responsible for the increased vascular permeability.

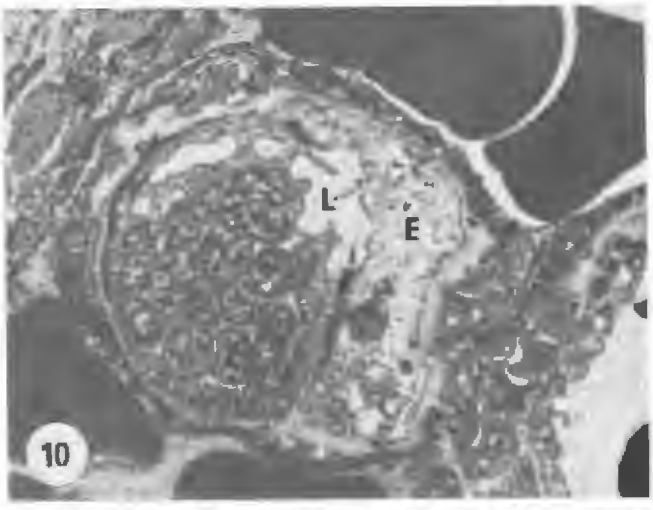
Laboratory animals

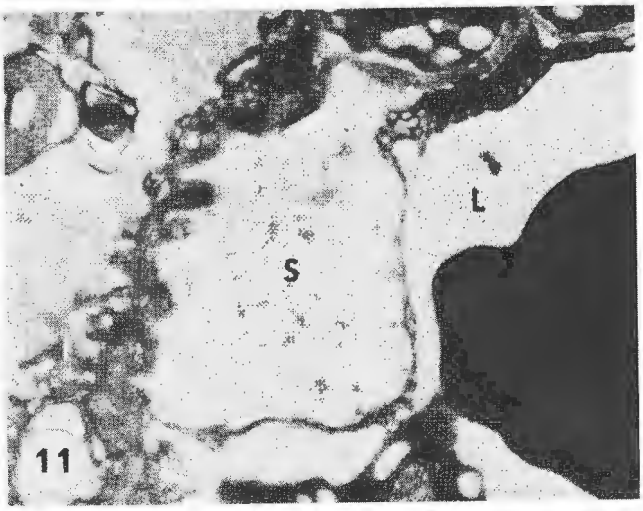
Du Plessis (1985) isolated the Welgevonden strain of heartwater, which is pathogenic for mice, cattle, sheep and goats, from *Amblyomma hebraeum*. Prozesky & Du Plessis (1985b) found that the macroscopical and microscopical changes in domestic ruminants and mice infected with the Welgevonden strain of *C. ruminantium* were very similar. Lesions in mice infected with the Welgevonden strain included the following:

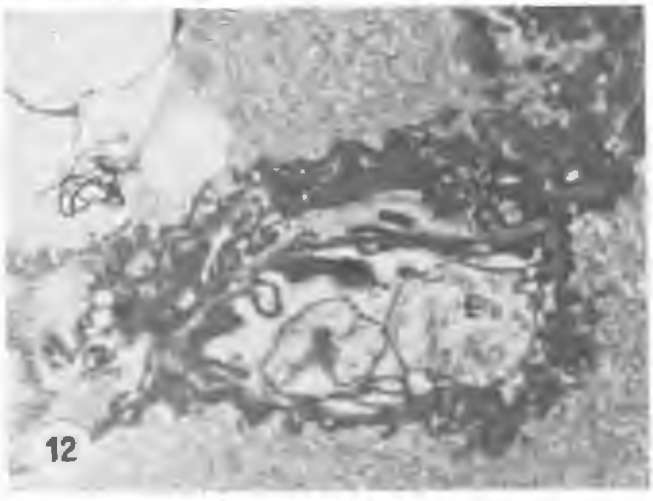
Macroscopical pathology: Effusion of body cavities, hydropericardium, oedema of the lungs and splenomegaly were constant changes in most animals.











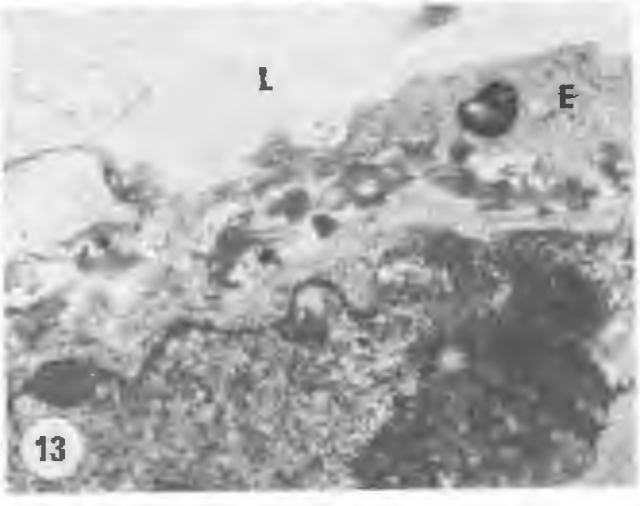


FIG. 8 The interendothelial space (gap) is dilated (arrow): × 10 000
FIG. 9 Swollen alveolar epithelial cells (E): × 9 300
FIG. 10 A parasitized alveolar endothelial cell with swelling of the bordering endothelial cell (E). L = capillary lumen: × 10 000
FIG. 11 The endothelial cells are detached from the basement membrane. S = subendothelial space. L = capillary lumen: × 9 300
FIG. 12 Swollen segments of a capillary endothelial cell (E) containing flocculent material: × 4 000
FIG. 13 Oedema of the wall of a small blood vessel. L = vascular lumen, E = endothelial cell: × 9 300

Microscopical pathology: An alveolar and interstitial oedema was present in the majority of mice. The alveolar spaces contained protein-rich fluid and variable amounts of macrophages and fibrin. Other changes were a mild to moderate diffuse mononuclear interstitial pneumonia and a leucostasis (mainly monocytes). A regular finding in all the animals was the presence of varying numbers of *C. ruminantium* colonies in endothelial cells of the alveolar capillaries (Prozesky & Du Plessis. 1985b).

The parasitized endothelial cells occasionally occluded the capillary lumens. In the majority of these cells no change or, occasionally, mild cytopathic changes were present. More commonly, non-parasitized cells were swollen and frequently contained intracytoplasmic membrane-bound vacuoles. Segments of these cells were often detached from the basement membrane (Fig. 10–12). Necrosis of parasitized and non-parasitized cells was rarely seen and many normal endothelial cells were dispersed between affected cells. In the larger blood vessels the endothelial changes corresponded with the lesions in the alveolar capillary endothelial cells and the vascular walls were oedemaous (Fig. 13). It is difficult to explain the severe lung oedema because of the relatively mild changes in the alveolar walls (Prozesky & Du Plessis, 1985b).

Du Plessis (1975a) infected mice intraperitoneally with liver suspensions obtained from mice infected with the Kümm strain of heartwater. Gross lesions, which varied in extent from mild to pronounced, included a hydrothorax, hydropericardium, oedema of the lungs, splenomegaly, hepatomegaly, oedema of the lymph nodes and atrophy of the thymus (Du Plessis, 1975b).

The most striking microscopical lesions in the mice were a prominent alveolar and interstitial oedema, a mild to moderate diffuse mononuclear interstitial pneumonia and necrosis of lymphocytes in the cortex of the thymus (Du Plessis, 1986, personal communication). Organisms were identified in various cells including Kupffer cells, alveolar epithelial and endothelial cells, reticulo-endothelial cells in the spleen and lymph nodes and endothelial cells of capillaries in various organs.

Game animals

Several species of game animals are susceptible to heartwater and the disease can therefore maintain itself in nature in the complete absence of domestic ruminants (Young & Basson, 1973; Uilenberg, 1983). Naturally contracted fatal cases of heartwater have been reported in a springbuck *(Antidorcas marsupialis),* and eland *(Taurotragus oryx)* and in various exotic ungulates, including the Indian nilghai *(Boselaphus tragocamelus),* fallow deer *(Dama dama),* barbary sheep *(Ammotragus lervia),* Himalyan tahr *(Hemitragus jemlahicus)* and in a moufflon *(Ovis musimon)* (Young & Basson, 1973; Hofmeyr, 1956). Animals experimentally infected by the intravenous inoculation of blood include the blesbok *(Damaliscus dorcas),* black wildebeest *(Connochaetes gnou),* Indian waterbuffalo *(Bubalus bubalus)* and springbuck (Neitz, 1933; Neitz, 1935; Neitz, 1937; Neitz, 1944; Du Plessis & Prozesky, unpublished data, 1984).

Reports on the pathological changes in game that died of heartwater are limited. Young & Basson (1973) described the macro- and microscopical changes in an Eland that contracted the disease naturally and died. The animals showed generalized congestion, hydrothorax, hydropericardium, oedema of the lungs, ascites and splenomegaly. A diagnosis of heartwater was confirmed by the demonstration of numerous heartwater colonies in Giemsa-stained preparations made from the hippocampus and other parts of the brain. The histopathological examination revealed oedema of the brain and a vasculitis similar to the changes described in domestic ruminants (Pienaar *et al.,* 1966).

Du Plessis & Prozesky (unpublished data, 1984) infected 3 black wildebeest (two 6 months old calves and an adult cow), a springbuck, an Indian waterbuffalo and a moufflon with the Ball 3 strain of heartwater. Except for the adult black wildebeeste all the animals reacted with a febrile response and died of the disease.

The lesions in the black wildebeest calves were characterized by a marked generalized congestion, oedema of the lungs, hydrothorax, mild hydropericarium and endocardial haemorrhages. The kidneys were swollen and congested with petechiae in the cortex and edema of the pelvis. Apart from congestion the abomasum mucosa was oedematous with multiple petechiae. Other lesions were a moderate oedema of the lymph nodes, mild hepatomegaly and a moderate splenomegaly. The histopathological lesions were very similar to the changes described in domestic ruminants.

Macroscopical lesions in the springbuck, moufflon and Indian waterbuffalo included oedema of the lungs, hydrothorax, splenomegaly and oedema of the lymph nodes.

In all of the above-mentioned animals a diagnosis of heartwater was confirmed by the demonstration of numerous heartwater organisms in Giemsa-stained preparations made from the hippocampus.

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