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BOVINE CEREBRAL THEILERIOSIS – A REPORT ON TWO CASES OCCURRING IN THE UNION.

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INTRODUCTION.

Turning sickness of cattle, a very fatal disease, has long been known to occur in the East Coast fever enzootic areas of Uganda, Kenya and Tanganyika. It is characterised by circling or turning movements made by affected animals. Mettam (1934) drew attention to the discovery of schizonts indistinguishable from those of the genus *Theileria* Bettencourt, (Franca and Borges, 1907), in cattle suffering from this disease in Uganda. Mettam and Carmichael (1936) described the clinical symptoms and pathology of this infection in 24 animals in East Africa. All these animals had been raised in the East Coast fever enzootic areas, and of these 63 per cent were known to have suffered from *Theileria parva* (Theiler, 1904) infection a few months before developing symptoms of turning sickness. The disease affects cattle of both sexes and all breeds, being most common in young stock between six months and two years of age.

The course of turning sickness may be acute, sub-acute or chronic. In the acute form animals develop violent nervous symptoms, turning or spinning in one direction until dizzy, when they collapse. When consciousness returns the animal rises to its feet, and may nibble at the grass. In the sub-acute cases the turning movements are not so rapid, and the depression not so pronounced. The animal may stand with its head pushed against a tree. In the chronic form animals exhibit muscular inco-ordination and blindness. Affected cattle show no hyperthermia. The course of the disease varies from two days to six months. Daubney (1938) observed the disease to persist for periods of up to 24 months. All cases of turning sickness terminate fatally.

At autopsy characteristic lesions are found in the brain. In acute cases the blood vessels of the brain are congested; there are blood extravasations in the meninges, and the choroid plexus of the ventricles are swollen and dark red in colour. In chronic cases necrosis, atrophy, fibrosis and cavity-formation are found, the lesions being most frequently observed in the white matter of the cerebral hemispheres. A local or diffuse pale yellow discoloration is a constant feature of chronic cases, and small cavities containing a citron-coloured fluid are found in all parts of the hemispheres. The spleen, lymphatic glands, liver and lungs exhibit no noteworthy features However, a multiple localised ulcerative abomasitis and kidney lesions resembling those of East Coast fever were encountered in a limited number of animals.

Histologically the predominant lesion in the brain is a blocking of the smaller arteries and arterioles by dense masses of lymphocytes. In acute cases Koch bodies are present in large numbers in films made from the cerebral

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haemorrhages. It is uncommon to find erythrocytic *Theileria* parasites in any numbers in the blood but in some animals schizonts are found in the peripheral blood. In some cases Koch bodies are present in lymphatic gland and spleen smears. In chronic cases, in which the haemorrhages had been absorbed, schizonts were not demonstrable. Daubney (1938) on the other hand, states that Koch bodies can be found in the brains of affected animals for periods of up to 24 months after the appearance of symptoms.

Attempts to transmit turning sickness by inoculation of brain tissue or blood by various routes to animals either immune or susceptible to East Coast fever failed. Similarly attempts to transmit the disease by injection of tick emulsions were unsuccessful (Mettam and Carmichael, 1936). Daubney (1938) reports that ticks (*Rhipicephalus appendiculatus*) feeding on affected animals could, after moulting, transmit East Coast fever to susceptible animals.

Curasson (1941) refers to a cerebral form of bovine theileriosis in French West Africa causing turning sickness. Affected animals push against a wall and show great excitement lasting until they fall exhausted and die. He states that both *Theileria parva* (Theiler, 1904) and *Theileria mutans* (Theiler, 1906) occur in West Africa. Since it has become apparent from information submitted recently to the Interafrican Bureau for Epizootic Diseases, Kenya, that East Coast fever does not occur in West Africa, it is permissible to deduce that this form of cerebral theileriosis is in all probability due to *Theileria mutans* infection.

A third form of protozoal encephalitis has been described by Carpano (1932) in a cow in Abyssinia and by Carmichael (1938) also in a cow in Uganda. These investigators state that both animals exhibited symptoms typical of turning sickness. Cerebral haemorrhage involving the head of the caudate nucleus and extending into the corpus striatum was observed at autopsy. Sections of the cerebral cortex showed congestion of the capillaries with a varying degree of perivascular infiltration, whilst sections through the lesions showed rupture of the capillaries and masses of trypanosomes in various stages of development. Leishmanial and crithidial forms and mature trypanosomes mixed with monocytes, erythrocytes and a few polymorphs were seen.

From the above description it becomes apparent that the aetiology and the pathogenesis of turning sickness is still obscure. Carmichael (1939) suggests that the *Theileria* sp. and *Trypanosoma* sp. found in the cerebral lesions may be secondary invaders.

This paper serves to record the occurrence in the Union of South Africa of a disease of cattle associated with nervous symptoms and paralysis, characterised by marked pathological changes in the brain, smears and sections of which reveal the presence of schizonts of a *Theileria* sp. This disease bears a marked similarity to turning sickness as described by Mettam and Carmichael (1934).

Description of Cases Encountered in the Union.

Case I.

The animal in question was an ox, approximately 3 years old. It was a Hereford cross and had been purchased as a weaned calf from Northam in the district of Rustenburg. After purchase it had grazed only on the farm Haakdoringboom, Pretoria district, belonging to Mr. J. Maynard.

The animal was first reported ill by the owner on the 5th May, 1955. It was found lying down and unable to rise. The herd boy had previously noticed a tendency for the animal to sway in the hindquarters when driven fast. The farm was visited two days later when the owner reported that there was no improvement. The ox was found lying down flat on its right side and had been unable to rise for three days. There were signs that it had struggled in attempting to rise. The head was thrown back and occasional galloping movements would be executed by the front legs. There was frothing at the mouth. The temperature was subnormal.

As it was obvious that the animal would not recover, slaughter was advised and a post-mortem examination conducted.

Post-Mortem Findings.

The examination revealed a carcass in fair condition. The internal organs revealed nothing unusual. The vertebral canal in the loin region was cut open but no abnormal lesions could be found. The brain was exposed for the purpose of preparing brain smears to eliminate *Rickettsia ruminantium* (Cowdry, 1925) infection and it was here that the most striking lesions were noticed. The brain was removed and taken *in toto* to the laboratory for histological examination.

The peculiar yellow discoloration of the brain together with extensive haemorrhages immediately attracted attention. Most of the blood present on the brain had undoubtedly accumulated there after the throat had been cut, but as histological examination subsequently proved, extensive haemorrhages had occurred prior to death. The meninges showed hyperaemia, thickening and haemorrhagic infiltration especially on the dorsal aspects of the cerebral hemispheres and cerebellum. On the cut surface the haemorrhages were noticed to extend into the sulci to such a degree that the cerebral convolutions were in parts pushed well apart from each other. The cerebellum in particular showed focal areas of intense yellow pigmentation.

Smear Examination.

It is interesting to note that difficulty was experienced in preparing smears from the brain which had a much tougher consistency than normal. While examining smears of the hippocampus for *Rickettsia ruminantium* a Koch body was found, and it was only then that turning sickness was suspected. The histopathological examination subsequently proved this suspicion to be correct. Other smears made from the hippocampus and also from various parts of the brain were thoroughly examined but no further schizonts could be found. Smears were not made from the haemorrhagic areas.

Blood smears revealed the presence of *Theileria mutans* (Theiler, 1906) in very small numbers. Unfortunately smears were not made from the spleen and lymphatic glands and the presence or absence of Koch bodies in these organs could not be determined.

Histopathology.

Striking changes occurred histologically in the meninges which showed a lymphocytic leptomeningitis with extensive perivascular haemorrhages and thrombosis of the blood vessels. The brain substance proper showed a non-purulent perivascular encephalitis with focal areas of demyelinisation and glial proliferation. Extensive pigmentation (haemosiderosis) occurred in the cerebellum.

The Meninges.—The blood vessels of the arachnoid space and the pia mater were distended with red blood corpuscles and extensive perivascular haemorrhages were present (fig. 1). Some of the blood vessels contained mainly lymphoid cells (fig. 2) many of which showed clear mitoses. Koch bodies were present in many of these lymphoid cells (fig. 3). Thrombosis was present in a few blood vessels and fibrin which had accumulated on the damaged intimal lining was in the process of being organised. The thrombosed vessels also contained necrobiotic cell debris. There was marked perivascular exudation of fibrin and infiltration of lymphoid cells, occasional plasma cells and neutrophils.

The Brain.—The cerebrum showed hyperaemia. Many of the blood vessels contained lymphoid cells which showed the presence of Koch bodies in their cytoplasm. In certain areas there was perivascular infiltration of small lymphocytes ("cuffing"). The ganglion and glia cells did not show any particular abnormal changes.

The mid-brain showed a few focal areas of demyelinisation and proliferation of glial elements. Some of the blood vessels showed distinct "cuffing" by lymphocytes mainly of the small type (fig. 4). Koch bodies could not be demonstrated in the cells outside the blood vessels.

Marked changes occurred in the cerebellum. The cells of the molecular layer were in certain areas heavily laden with yellowish brown pigment granules which gave a positive Berliner Blou reaction (fig. 5). Focal areas of demyelinisation also occurred in this layer. The Purkinje cells showed varying degrees of degeneration. The nuclei were shrunken and the nuclear membranes irregular. Some of the nuclei showed karyolysis and pyknosis. The cytoplasm tended to lose its granular appearance and become homogeneous. In certain areas the Purkinje cells had completely disappeared. There was diminution of the cellular content as well as total disappearance of the cells of the granular layer in some places. Some of the cells in the apparently normal areas also contained haemosiderin.

Case II.

A second case of this disease was encountered in the Rustenburg district on the farm Nooitgedacht, belonging to Mr. Z. Young. The subject was a two year old grade Afrikaner bull. On the morning of the 9th December, 1955, the animal showed a staggering gait. In the afternoon it was found lying down unconscious, the eye-lids stiffly closed and salivating profusely. Sweating was noticed to occur on the right side of the body only. The next day the animal stood up for a short while but went down again. The owner injected 1 gm. of Terramycin and 10 c.c. Aristamid intravenously—a procedure to which marked resistance was offered. On the 11th December 48 c.c. Aristamid was injected intravenously but the condition of the animal deteriorated rapidly. There was still profuse salivation. The animal could not drink, but swallowed water provided it was dosed. On the 12th December the state veterinarian of Rustenburg was called out. He found the animal *in extremis* with sunken eyes and making kicking movements. A post-mortem was performed after the animal had been killed by cutting the throat.

The internal organs did not show any abnormal changes. The surface of the brain, however, was reddish in colour and the right cerebral hemisphere showed haemorrhagic infiltration and softening on the cut surface. Specimens of the brain were submitted in 10 per cent formalin for histological examination.

Microscopically the lesions closely resembled those described in the first case. The meningeal changes were almost identical. The most marked changes occurred in the cerebrum, medulla oblongata and caudate nucleus. The capillary blood vessels were prominent and most of them were blocked by large lymphocytes containing Koch bodies. Many of the lymphocytes showed clear mitoses which suggested a marked intravascular lymphoid hyperplasia. A large number of the capillaries showed thrombosis with damage to the intimal lining in some of them. Around such vessels there was extensive haemorrhage as well as exudation of fibrin and lymphoid cells. Scattered haemorrhages were also present in the brain substance. Degenerative and necrobiotic changes occurred in the ganglion cells and the white matter showed demyelinisation.

Since the medulla oblongata was extensively affected, the authors had reason to believe that similar changes might perhaps also have occurred in the spinal cord. The cerebellar changes, pigmentation and perivascular cuffing by small lymphocytes noticed in the first case, were absent in this case.

Histopathology of a Case of Turning Sickness from Uganda.

Brain specimens of a case of turning sickness from Uganda were kindly supplied to this institute by Dr. Carmichael of May Baker Ltd., England. The histopathological examination revealed the following changes:—

Cerebrum.—The capillaries of the pia mater and the brain substance were well filled with red blood corpuscles and lymphocytes. Slight perivascular infiltration of lymphocytes, as well as slight perivascular haemorrhage were evident. Most of the lymphocytes contained Koch bodies.

Midbrain.—Hyperaemia and occasional slight perivascular haemorrhage were evident.

Cerebellum.—The blood vessels were filled with red blood corpuscles and lymphocytes, many of which contained Koch bodies. There was a slight perivascular infiltration of lymphocytes in the meninges and in the brain substance. The Purkinje cells showed degenerative changes.

Discussion.

The cases described here bear a marked similarity to the cases of turning sickness as described by Mettam and Carmichael (1934). There are a few differences in the histopathology of the Transvaal cases and that of the specimens at our disposal of a case from Uganda. There are far fewer haemorrhages in the meninges of the Uganda case and there is also no evidence of demyelinisation, pigmentation or thrombosis of the blood vessels. The lymphoid cells accumulated around the blood vessels, most probably exuded through the vessel walls during the process of haemorrhage per diapedesis. Koch bodies are evident in these cells whereas in the Transvaal cases Koch bodies could not be demonstrated in the small lymphocytes of the "cuffs". Mettam and Carmichael (1934) only rarely found Koch bodies in the cells of the "cuffs" in those cases which showed a genuine "cuffing". The large haemorrhagic areas in the brain of a few of the Uganda cases were actually in the brain substance itself, resulting in serious damage to the surrounding brain tissue. The most extensive haemorrhages noticed in the Transvaal cases were mainly confined to the meninges.

It is, however, not considered that these differences are significant as the histological changes can vary depending on the severity of the disease and the time of slaughter or death after the onset of symptoms.

Whereas the cases described by Mettam and Carmichael were all associated with East Coast fever, the possibility of the Transvaal cases being associated with *Theileria parva* (Theiler, 1904) infection is very remote indeed. East Coast fever was last diagnosed in the Pretoria and Rustenburg districts early in 1920. *Theileria mutans* infection is, however, very prevalent in these areas and as it is at the moment the only known *Theileria* species to occur there, it is considered that the cases of bovine cerebral theileriosis described in this paper is associated with *Theileria mutans* infection. This also appears to be the case in West Africa where East Coast fever does not occur, but where cerebral theileriosis is well known.

As cases of turning sickness may be associated with either *Theileria* species or *Trypanosoma theileri* one cannot lose sight of the fact that these protozoa may be merely secondary invaders in a brain already infected by an agent such as a virus, the nature of which is at present obscure. [Carmichael (1939)].

Summary and Conclusions.

1. Two cases of bovine cerebral theileriosis in the Union of South Africa due to *Theileria mutans* are described.

2. Clinically the animals exhibited a staggering and swaying gait, prostration, struggling and galloping movements, frothing at the mouth, and a subnormal temperature.

3. Macroscopically the brain showed focal yellow discoloration, hyperaemia and thickening of the meninges, and haemorrhagic infiltration of the dorsal region of the cerebrum and cerebellum.

4. Microscopically a lymphocytic leptomeningitis, perivascular encephalitis, focal demyelinisation, glial proliferation, thrombosis of the blood vessels, and Koch bodies in the lymphoid cells were present.

5. This disease bears marked similarity to turning sickness due to *Theileria parva* described in East Africa and presumably due to *Theileria mutans* described in West Africa.

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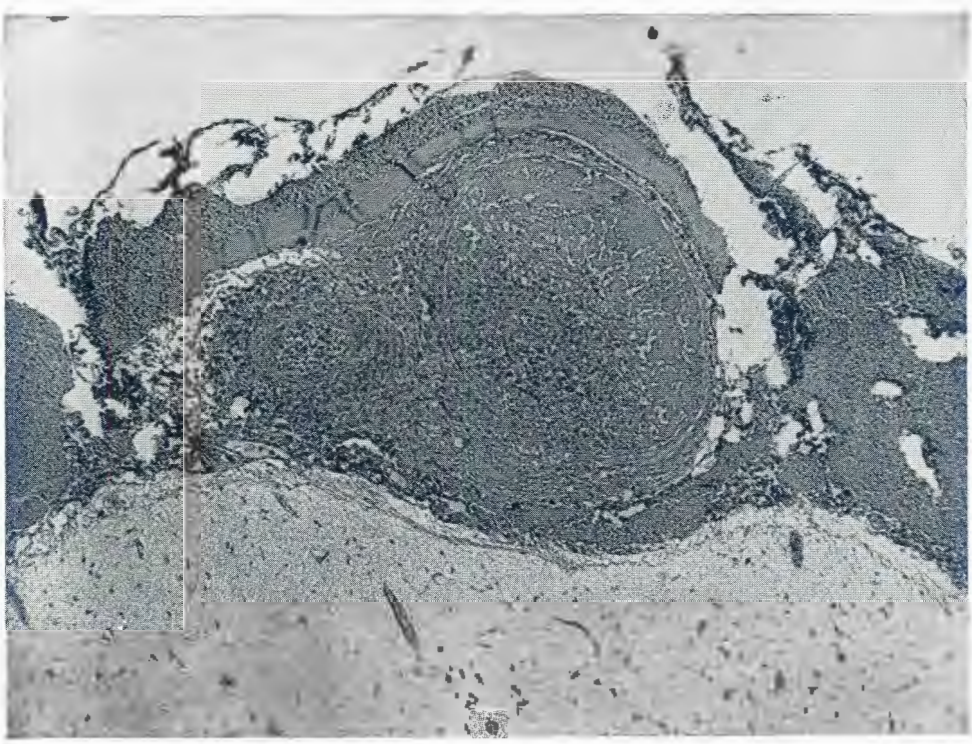

FIG. 1.—Specimen 49353. Cerebrum. Meningeal haemorrage. Thrombosis of the blood vesse on the right. HE × 60.

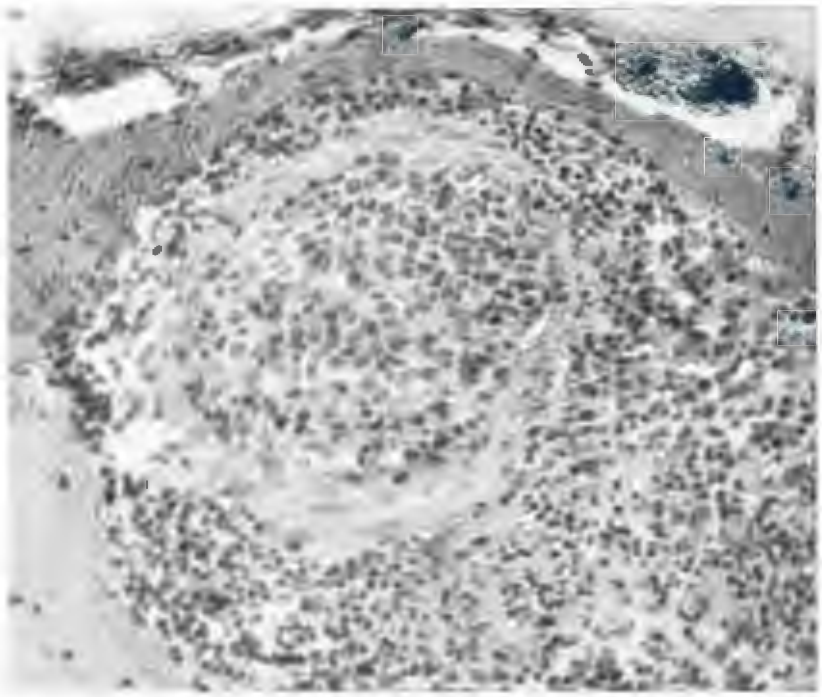

FIG. 2.—Specimen 49353. Meninges. Intravascular hyperplasia of lymphoid cells. Haemorrhage and fibrinous exudation around blood vessel with infiltration of lymphoid cells. HE × 200.

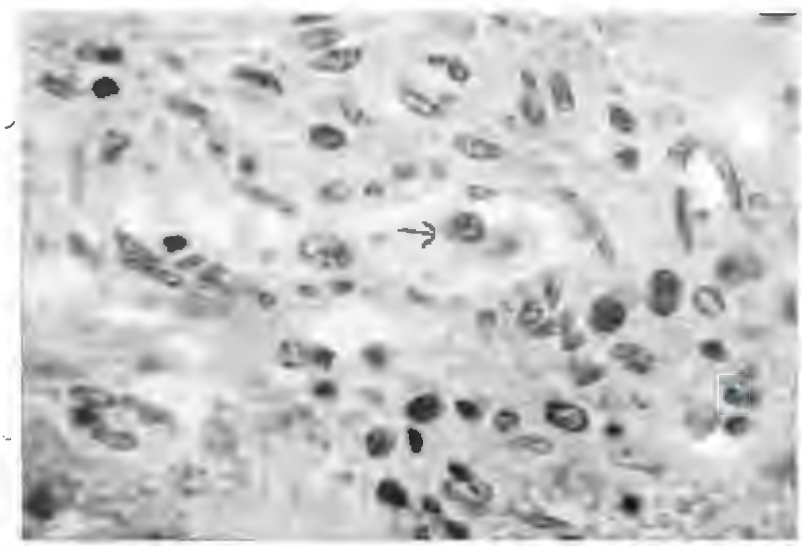

FIG. 3.—Specimen 49353. Brain. Lymphocyte showing a Koch body (indicated by arrow) in a blood vessel. HE × 1150.

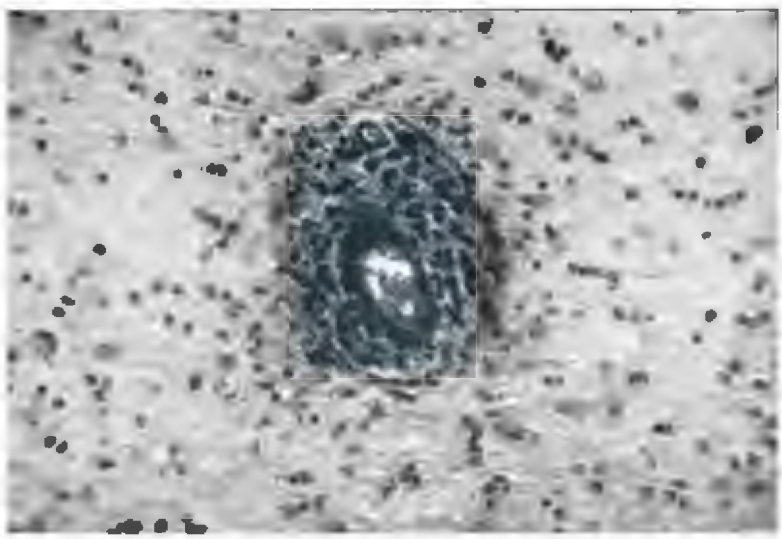

FIG. 4.—Specimen 49353. Midbrain. Blood vessel showing perivascular infiltration of lymphocytes. Giemsa. × 487.

FIG. 5.—Specimen 49353. Cerebellum. Haemosiderosis of the cells of the molecular layer. Note demyelinisation and absence of Purkinje cells and granular layer. BB. × 487.