OBSERVATIONS ON THE PATHOGENESIS OF MALIGNANT CATARRHAL FEVER OF DEER

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INTRODUCTION

Malignant catarrhal fever of red deer is most commonly an acute disease characterised by fever, inappetence, diarrhoea, dysentery and death. Haemorrhage is a prominent post-mortem finding in several organs e.g., lung, thymus, lymph nodes and urinary bladder. Intraocular haemorrhage and massive abdominal and retroperitoneal haemorrhage have been observed. The most striking lesions occur in the intestine where petechial and ecchymotic haemorrhages rapidly progress to massive haemorrhage in the terminal stages.

Acute intestinal blood loss resulting in hypovolaemia and shock is a major reason why affected deer die. The pathogenesis of the haemorrhagic syndrome in acute MCF has not been explained. This study was undertaken to define the blood clotting parameters in deer with clinical MCF.

MATERIALS AND METHODS

Four red deer (EFGH) were experimentally infected with the MCF virus as previously described.[7] Three uninoculated deer (BCD) were maintained as controls. All deer were examined daily for clinical signs of MCF and rectal temperatures recorded at each examination. After the onset of pyrexia (>39.5 ^{o}C), deer were examined twice daily until death or euthanasia. All

deer were necropsied as soon as possible after death and appropriate samples were collected in 10% buffered neutral formalin for histopathological examination to confirm the presence of MCF.

Blood samples were collected from all deer 3 days prior to inoculation and thereafter every second day until the first inoculated deer became pyrexic. All test and control deer were then sampled daily. Details of collection and preparation of blood samples and methods used for determination and coagulation parameters are recorded elsewhere.[13] The following parameters were measured: activated partial thromboplastin time (APTT), one stage prothrombin time (OSPT), antithrombin III (ATIII) levels, fibrin degradation products (FDP), activated clotting time (ACT) and platelet count.

RESULTS

All inoculated deer developed MCF between 17 and 19 days post inoculation (DPI). The clinical course lasted from 4 to 6 days. The time of development of pertinent clinical signs is listed in Table 1. Fever was the first abnormality detected, followed 1 to 3 days later by diarrhoea. Dysentery became apparent between 3 and 4 days after the onset of fever. Pathological findings were consistent with MCF of deer.[7] In one deer (H), the abdomen contained several litres of fresh unclotted blood at necropsy.

Histopathological findings included widespread vasculitis of small blood vessels with partial occlusion of the lumen by fibrin thrombi and swollen endothelial cells. Subendothelial fibrin deposits were also present. Sparse to moderate numbers of mononuclear cells were present around blood vessels, within vessel walls or marginating within the lumen.

Changes in platelet counts, APTT, OSPT and the plasma levels of fibrinogen and ATIII activity are recorded in Figs 1 to 5. Table 2 records FDP levels. No abnormal parameters were recorded in control deer. ACT remained within normal limits in all deer, although clot quality was considered to become progressively worse in inoculated deer.

Table 1: The interval from experimental infection to onset of specific clinical signs of MCF

ONSET	DEER E	F	G	H
Fever	17*	17	18	19
Diarrhoea	18	18	21	21
Dark venous blood	18	18	21	-
Dysentery with blood clots	21	-	-	-
Dysentery without blood clots	21	21	21	21
Death/Euthanasia	21	23	21	23

*Number refers to the number of days post-inoculation on which the specified clinical sign was observed.

MCF IN DEER : FDP (*Fibrinogen eq µg/ml*)* IN TEST DEER

	Day	3	7	12	17	18	19	20	21	22	23
DEER	E	1.6	0.8	0.8	6.4●	6.4	6.4	0.8	1.6		
	F	0	0.8	0.8	3.2●	0	0	6.4	6.4	12.8	1.6
	G	0	0	0.8	1.6●	12.8	1.6	6.4	6.4		
	H	0	0	0.8	1.6	1.6	1.6●	0	1.6	12.8	12.8

● = Onset of fever

* *All controls consistently <3.2*

Table 2: Levels of Fibrin Degradation Products (FDP) in 4 deer experimentally infected with MCF are shown

DISCUSSION

All inoculated deer developed abnormalities in the laboratory parameters of blood coagulation, after the onset of pyrexia. These parameters included extended APTT and OSPT, decreased ATIII levels, decreased platelet counts and increased fibrinogen levels. Increased fibrinogen levels were attributable to an acute inflammatory response.

Elevated APTT and OSPT indicate that both the intrinsic and extrinsic coagulation pathways were activated, leading to a depletion of clotting factors. Decreased ATIII levels were attributed to generation of thrombin from prothrombin. Elevated levels of FDP indicated initiation of the fibrinolytic system.

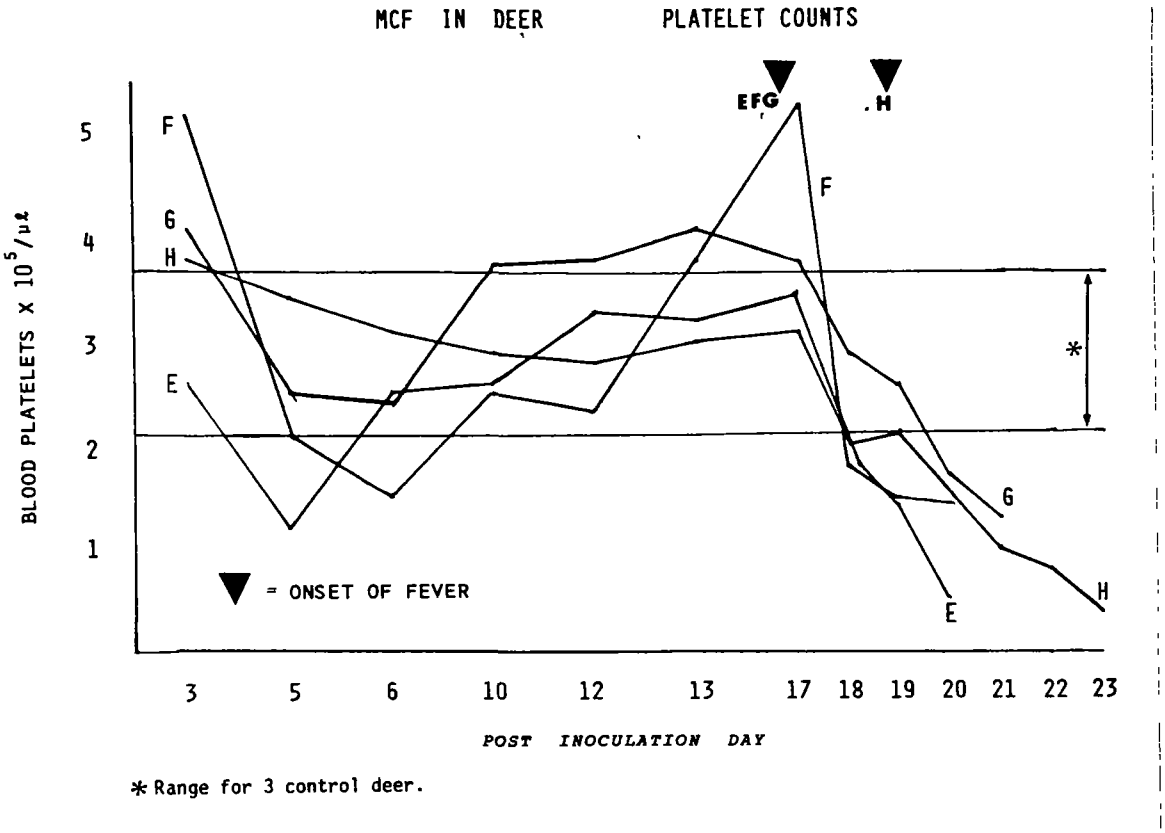

Figure 1. Peripheral blood platelet counts in 4 deer (EFGH) experimentally infected with MCF are shown.

Concurrent consumption of platelets, clotting factors, activation of the fibrinolytic mechanism and the presence of haemorrhage and widespread thrombosis establish a diagnosis of disseminated intravascular coagulation (DIC).[2] A number of viral diseases cause DIC in animals including hog cholera, infectious canine hepatitis, fowl plague and equine viral arteritis.[1]

Vasculitis is common to all these diseases. In deer, vasculitis and thrombosis with associated haemorrhage has been reported with mucosal disease,[10] epizootic haemorrhagic disease (EHD)[3] and MCF.[7]

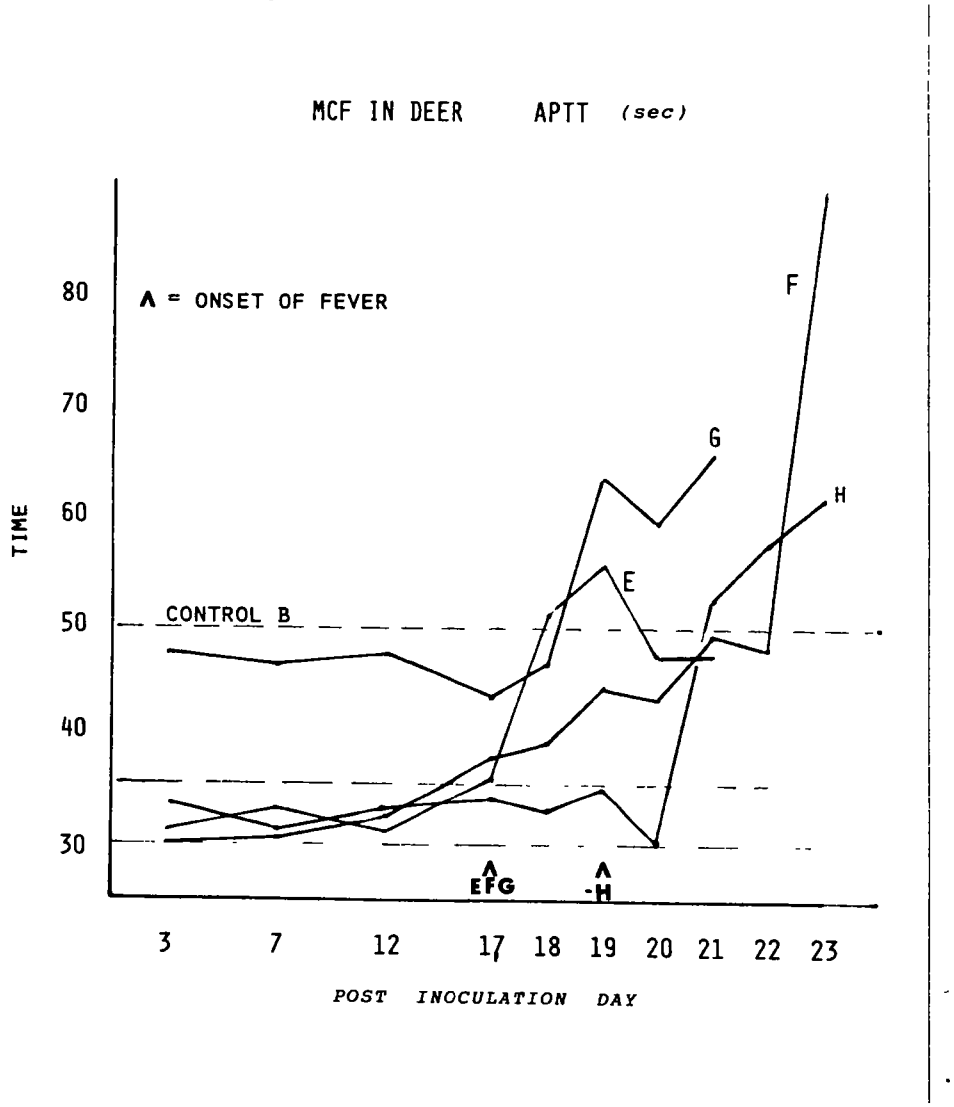

Figure 2. Activated Partial Thromboplastin Times (APTT) in 4 deer experimentally infected with MCF are shown.

Haemorrhagic enteropathy was found in 75% of all cases of deer examined at necropsy at the Invermay Animal Health Laboratory,[6] including cases of MCF, yersiniosis and stress associated with capture, handling and transport. Thrombocytopaenia and abnormalities of blood coagulation have been reported in EHD and have been ascribed to DIC.[3]

DIC may be a common pathogenetic mechanism for several diseases affecting deer. Cervidae spp. may be more prone to develop DIC than other ruminant species. This predisposition to DIC may explain why MCF in deer is frequently an acute disease of high mortality and characterised by haemorrhage, whereas

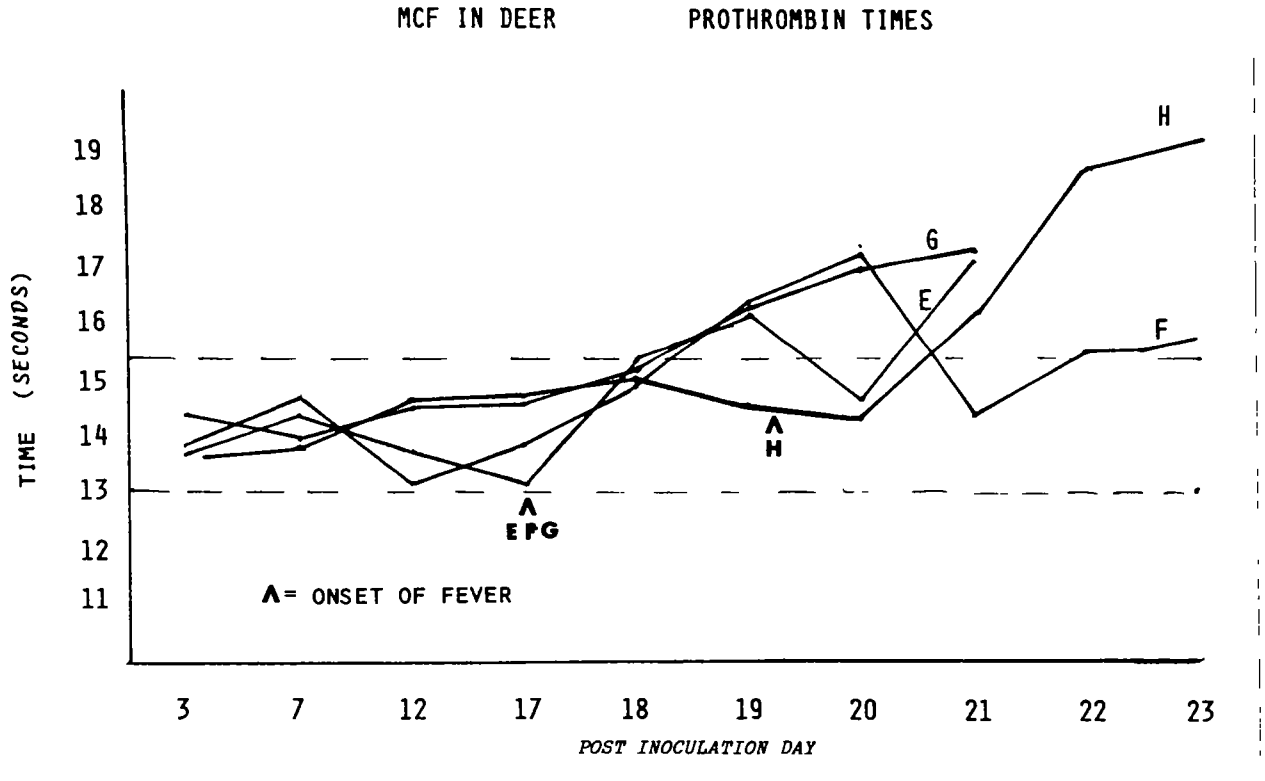

Figure 3. One Stage Prothrombin Times (OSPT) in 4 deer experimentally infected with MCF are shown.

MCF in cattle is usually a chronic disease. Several workers have hypothesised that MCF is an immune mediated disease.[4,5,8,9,11,12] Our findings do not oppose this view but they indicate that DIC does develop in acute MCF of deer and is an important pathogenetic mechanism in the development of systemic haemorrhage, haemorrhagic enteritis and severe dysentery in MCF. It is likely that DIC contributes significantly to the acute nature and high mortality of MCF.

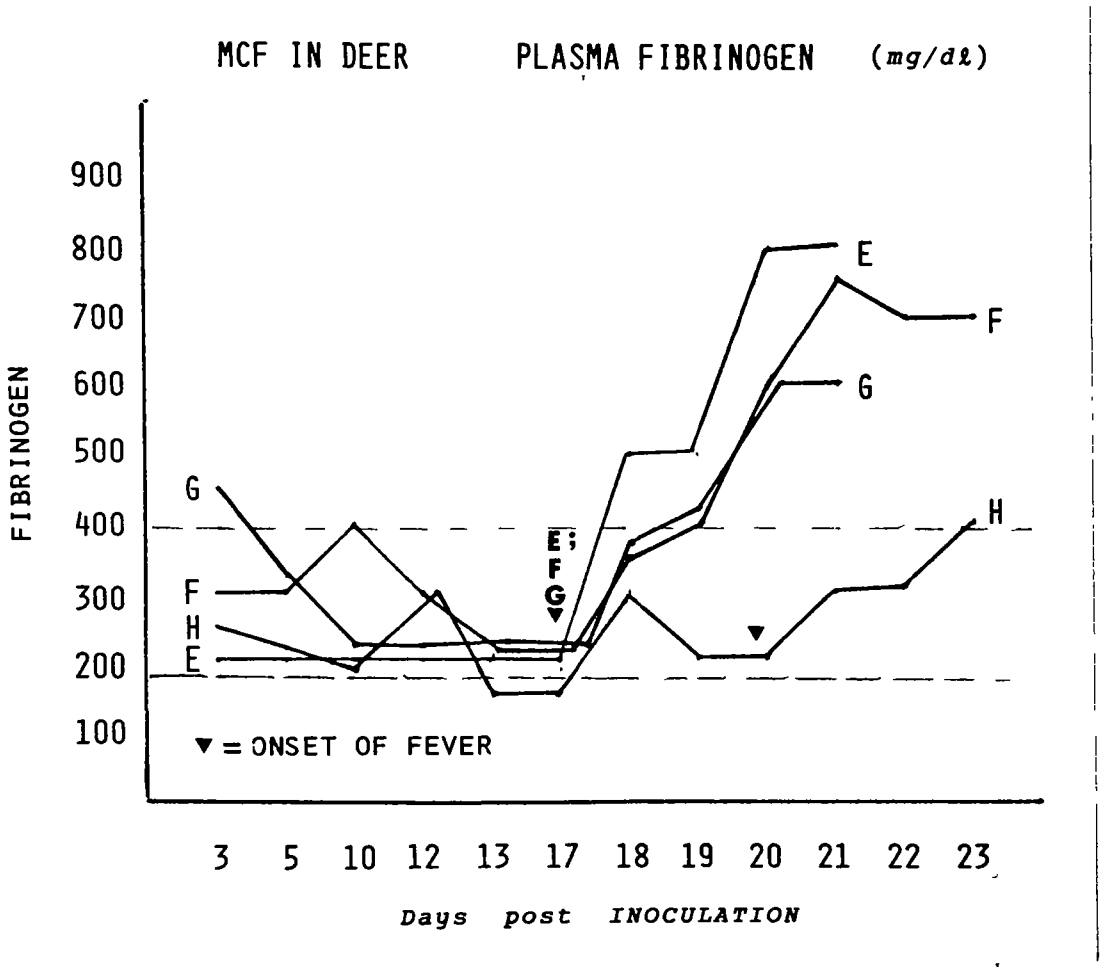

Figure 4. Plasma Fibrinogen Levels (PFL) in 4 deer experimentally infected with MCF are shown.

SUMMARY

Changes in blood coagulation parameters were followed in 4 red deer (Cervus elaphus) experimentally infected with malignant catarrhal fever (MCF) of deer. Blood platelet counts, activated partial thromboplastin time (APTT), one-stage pro-thrombin time (OSPT), activated clotting time (ACT), plasma anti-thrombin III (ATIII) activity, fibrinogen degradation production (FDP) and fibrinogen levels were measured. Inoculated deer became pyrexic after 17 or 19 days. Thereafter they developed watery diarrhoea which rapidly became haemorrhagic. The course of the clinical disease ranged from 4 to 6 days before the animals were euthanased or died. All inoculated deer developed abnormalities in laboratory parameters of blood coagulation. These

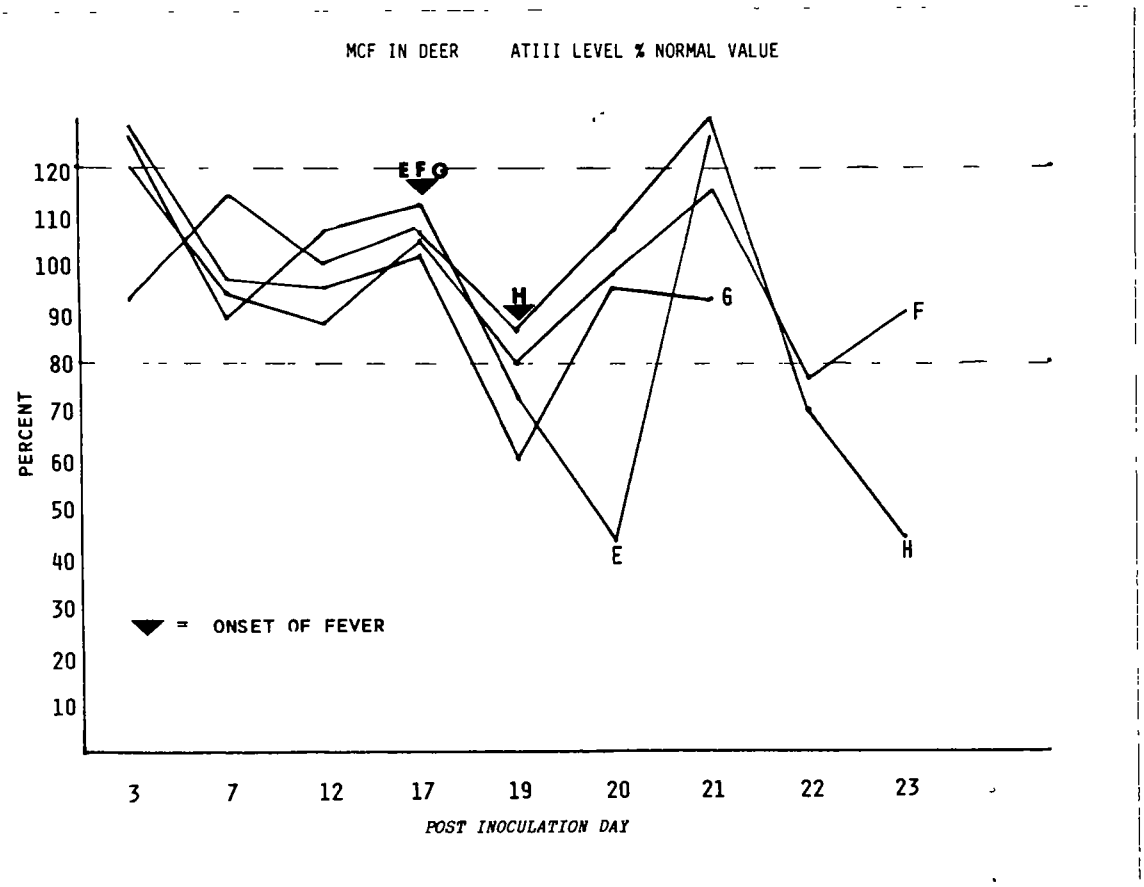

Figure 5. Anti-Thrombin III (ATIII) levels in 4 deer experimentally infected with MCF are shown.

varied within and between animals, but the coagulation profiles of all 4 animals remained abnormal until death. Post-mortem findings were typical of MCF and included extensive systemic petechiation, severe haemorrhage in the alimentary canal and vasculitis with disseminated thrombosis. Abnormal coagulation parameters included extension of APTT and OSPT, increased FDP, decreased ATIII and platelet counts and increased fibrinogen levels. The increases in fibrinogen were compatible with the acute phase response. The other coagulation abnormalities, haemorrhage and thrombosis were indicative of disseminated intravascular coagulation (DIC) with consumption coagulopathy. ACT remained normal in all deer although final clot quality was considered to be poor.

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