

A nosocomial outbreak of Crimean-Congo haemorrhagic fever at Tygerberg Hospital

Part I. Clinical features

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Summary

Crimean-Congo haemorrhagic fever (CCHF) is a rare disease in South Africa. From 1981 to September 1984, 8 sporadic primary cases were reported. An outbreak of CCHF in a large university hospital is described; of 8 patients diagnosed 2 died (the index and a secondary case). Four patients were seriously ill and 2 had a mild illness.

Problems were encountered in diagnosing the disease, which presents initially with influenza-like symptoms, differing only in severity from influenza. However, petechiae and other manifestations of a bleeding tendency distinguished it from influenza in the later phase of the disease. Special investigations, especially those revealing leucopenia and thrombocytopenia, were critically important in early diagnosis. The dilemma of handling this highly contagious disease is that definite virological diagnosis is time-consuming and is conducted in only one high-security laboratory 1600 km distant. A further case was admitted 3 months later from a different locality and confirmed virologically but no secondary cases could be confirmed or traced.

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The lethal results of an outbreak of Crimean-Congo haemorrhagic fever (CCHF) in a hospital setting have been reported from Rashid Hospital, Dubai, United Arab Emirates¹ and Central Government Hospital, Rawalpindi, Pakistan.² In both these outbreaks the diagnosis of CCHF was made retrospectively after the hospital staff became ill. At Rashid Hospital 2 patients died. During the outbreak in Rawalpindi there were 6 secondary cases, 3 fatal. Of 7 tertiary cases none died.

An outbreak of CCHF in Tygerberg Hospital, a 2000-bed teaching hospital near Cape Town, is reported. The danger of exposure to a highly contagious, undiagnosed disease in large

hospitals in South Africa cannot be underestimated. The Department of Internal Medicine at Tygerberg Hospital admits more than 14000 patients a year, including very ill patients with disease patterns which can be confused with the clinical picture of CCHF. The 2 patients who died had no circulating antibodies, and a period of 3-8 days was required for viral culture to be positive. The logistic consequences included isolation and treatment of highly suspect cases without causing undue concern to family members and the public while the final diagnosis was awaited.

The purpose of this report is to present the most important symptoms and signs of CCHF to facilitate early diagnosis and treatment. We include the spectrum of signs and symptoms with which CCHF may present and the relevant differential diagnosis of haemorrhagic fevers. It is emphasized that patients were placed in different categories based on clinical and laboratory findings for prognostic and therapeutic purposes. This is particularly important for early institution of barrier nursing while the diagnosis is being finalized. Patient survival depends on a team effort to which general physicians, haematologists, intensive care specialists, laboratory personnel, highly trained nursing staff and hospital administrators can contribute.

Patients and methods

Patients were categorized in three groups depending on clinical presentation. The 2 patients in group A both died, while the 4 patients in group B were extremely ill. Group C includes 2 patients with an attenuated disease course. Patient A1 represents the index case and A2 a staff member who was secondarily infected. Case histories of patients in groups B and C have been summarized and the special investigations of all patients are shown in Table I.

Case A1

The index case was a 26-year-old railway worker from Darling in the south-western Cape. On admission to hospital there was no history of a tick bite. He had contact with animals and was very fond of riding; his own horse was later found to have antibodies to CCHF. He was a cleaner of railway trucks used to transport cattle. A tick had been found on his neck before he became ill.

The patient had not visited any area outside the south-western Cape for several months before his illness. On 28 August 1984 (day 1 of his illness) he complained of myalgia, a sore throat and fever. On 1 September 1984 (day 5) he consulted his general practitioner at Vredenburg, the nearest fairly large town. The clinical findings then were a temperature of 38,2°C and an inflamed throat. He was treated with an antibiotic and analgesics. On 2 September (day 6) he developed haematemesis and haematuria. On 3 September (day 7) massive haematemesis occurred and he was admitted to Vredenburg Hospital. The patient became hypotensive and 2 units of

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TABLE I. THE MOST IMPORTANT SPECIAL INVESTIGATIONS (ADMISSION VALUES)

	A1	A2	B1	B2	B3	B4	C1	C2
Haemoglobin (g/dl)	10,5	17,0	13,5	15,6	15	11,5	13,1	13,8
White cell count (x 10 ⁹ /l)	7,8	17,0	2,7	4,1	3,0	2,6	2,0	3,8
Platelets (x 10 ⁹ /l)	14	43,0	129,0	264	50,0	15,0	25,0	238
			32,0*	53,0*				
GGT (U/l)	125	249			124		138+	
Total bilirubin (μmol/l)	41*	31			<16			36
Creatinine (mmol/l)	355							
Prothrombin ratio	1,6	1,19	1,03	1,29	N	N	N	
PTT (s)	48,4	40	33,5	4,5	34	39,5	38,5	
				81,1*	115			
FDP (g/ml)		<10	10	<10	40*			
			>40*	>40*				
Fibrinogen (mg/100 ml)	23	108	240	265		190	N	
Fibrinogen monomers	-ve	-/ve	-ve	-ve	-	-	-	
Viral antibody	-ve	-ve	+	+	+	+	+	+
Viral cultures	+	+	+	+	+	+	+	-

*Lowest or highest abnormal values.

GGT = γ-glutamyl transferase; PTT = partial thromboplastin time; FDP = fibrinogen degradation products; N = normal.

group O Rh-negative blood were transfused before his transfer to Tygerberg Hospital.

On admission to Tygerberg Hospital the patient was febrile and confused and unable to give a history. His temperature was 39°C, pulse 140/min and blood pressure 140/80 mmHg. Active bleeding from the upper gastro-intestinal tract was evident. Petechiae were observed over the thorax and arms. He was tachypnoeic, but the respiratory system was normal. Chronic left otitis externa was present. His abdomen was tender with no organomegaly. Viral haemorrhagic fever was then considered, although no previous cases had been described in the Western Cape. Partial barrier nursing was instituted within 24 hours and total barrier nursing within 48 hours of admission. During days 7-10 of his illness he developed respiratory failure and progressive hepatorenal failure.

The clotting profile was continually monitored and corrected to control the bleeding tendency. Severe oedema and pleural effusions developed. It became increasingly difficult to maintain a satisfactory blood pressure, and the patient died 12 days after the onset of his illness. First confirmation of the suspected diagnosis was obtained from positive immunofluorescence for CCHF on liver smears obtained at autopsy. This was supported by a positive culture of CCHF on mice and tissue culture as reported by the National Institute of Virology, Sandringham, Johannesburg.

Case A2

The patient, a 36-year-old surgeon, presented with severe headache, myalgia, a low-grade fever and loss of appetite. These symptoms persisted for a period of 5 days, during which the patient treated himself at home with analgesics. He was referred by his general practitioner because of his persisting illness and low-grade jaundice.

On admission to hospital he denied contact with the index case and had not been bitten by a tick. He had, however, cut his finger during amputation of a septic leg stump 10 days before the onset of his illness. Information later confirmed that he and another doctor had both visited the patient in the surgical intensive care unit where the index case was being nursed before institution of barrier nursing (Fig. 1). On admission he had a temperature of 37,2°C, a pulse rate of

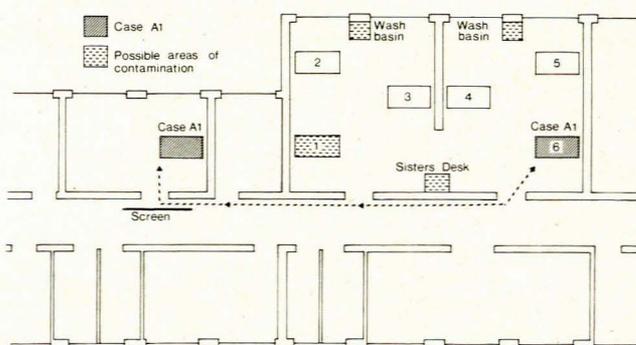


Fig. 1. Diagram of the Surgical Intensive Care Unit.

120/min and a blood pressure of 150/100 mmHg. The extremities were cold and the liver was palpable and tender. Isolated petechiae were evident on the abdomen and thorax. Slight jaundice was present and a nearly healed wound was found on a finger. A preliminary diagnosis of staphylococcal septicaemia related to the injured finger was made. Viral hepatitis was also considered, but because of denial of direct contact a diagnosis of CCHF was not seriously entertained. Blood was, however, sent for virology to exclude CCHF.

Vascular collapse occurred within 16 hours of admission. After resuscitation he was transferred to the respiratory intensive care unit. Blood cultures were done. The patient became stuporous and ventilation was instituted. Severe haemorrhage into the tissues after a radial artery puncture necessitated a fasciotomy and suturing of the radial artery. Gastro-intestinal bleeding and abdominal distension due to retroperitoneal haemorrhage caused great concern. Lung oedema developed and cardiac support with dopamine 60 μg/kg/min was necessary. The patient became oliguric and diuresis could not be obtained with high dosages of furosemide. The patient died 3 days after admission in spite of active multi-organ support. Circulating antibodies to the virus could not be demonstrated. The diagnosis was made on virus culture, the results of which became available 1 day before the patient's death.

Special investigations (Table I)

The day-to-day values of haemoglobin, white blood cell counts and platelet counts may have been influenced by administration of the relevant blood products. Abnormal partial thromboplastin time (PTT) values may have been influenced by heparin administration. The values indicated in Table I are therefore those obtained on admission to hospital, or where indicated with an asterisk the highest or lowest determination obtained during the illness. The days after admission on which confirmation of the diagnosis was received, from either positive serum antibody levels or viral cultures, are indicated for each patient.

Patient A1 was anaemic on admission to hospital with a haemoglobin value of 10,5 g/dl, a normal white cell count, and a platelet count of $14 \times 10^9/l$ (Table I). Hepatorenal failure developed. On admission the patient's clotting profile was normal but low levels of fibrinogen (23 mg/100 ml) were recorded. No fibrinogen monomers were present. Evidence was found of immune complex activation in case A1 with a zero total complement level, a C3 level of 25 mg/ml (normal 50-120 mg/ml) and a C4 level of less than 6 mg/ml (normal 20-40 mg/ml). A value of 56% for circulating immune complexes (normal 0-30%) was present in case A1 and an elevated C-reactive protein value of 45 g/ml (normal 0-10 g/ml) was found. Patient A2 had leucocytosis on admission.

Group B

The 4 patients in this group were all senior nursing sisters who had been involved in the care of the index case in the surgical intensive care ward. Patients B1, B2 and B3 had been exposed to the index case before institution of barrier nursing (Fig. 2). Patient B4 had been responsible for institution of the barrier nursing facilities. She had only worked in the corridor outside the specific room and had no direct contact with the patient. Patient B1 inoculated herself with a needle. Symptoms began simultaneously in all 4 nurses 5 days after institution of barrier nursing, with headache, fever and severe myalgia. Patient B1 complained of a sore throat and vomiting, B2 and

B3 were particularly aware of painful eyes and B4 was particularly aware of abdominal pain and arthralgia.

On admission to hospital the following signs were found. Fever (37,5-40°C) was recorded, accompanied by tachycardia of 108/min (100-120/min). A mild degree of tachypnoea was present in 3 patients (B1, B2 and B3). The blood pressure was normal in all four patients. The influenza-like picture was characterized in the early stages by injected conjunctivae in patients B1, B2 and B3. An early clinical finding in all 4 patients was right upper quadrant tenderness without jaundice or hepatomegaly. Patient B2 had terminal neck stiffness as a presenting sign. On days 4-6 after the onset of symptoms a bleeding tendency appeared in all 4 patients (Fig. 3): it was characterized by vaginal bleeding, petechiae, gingival bleeding, melaena and epistaxis. Haemorrhage in the form of vaginal bleeding was a major problem only in patient B1. Peri-orbital and peripheral oedema developed late in 3 patients (B1, B2 and B3). Individual clinical characteristics were a marked maculopapular rash in patient B1, while patient B2 was the only surviving patient who experienced marked central nervous system depression. She became very drowsy but developed no localizing neurological signs. A late manifestation of her illness on day 12 was suprapubic pain, with haematuria but no dysuria. Nausea and vomiting on day 13 of her illness were successfully managed by slow intragastric tube feeding.

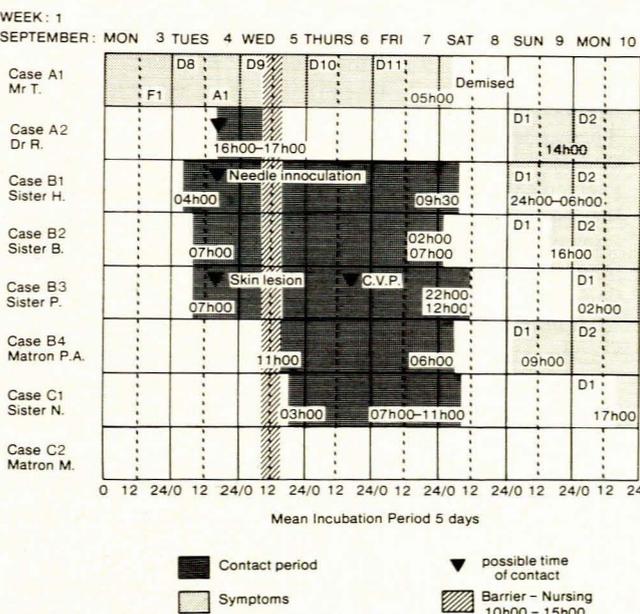


Fig. 2. CCHF patients: incubation period/onset of symptoms.

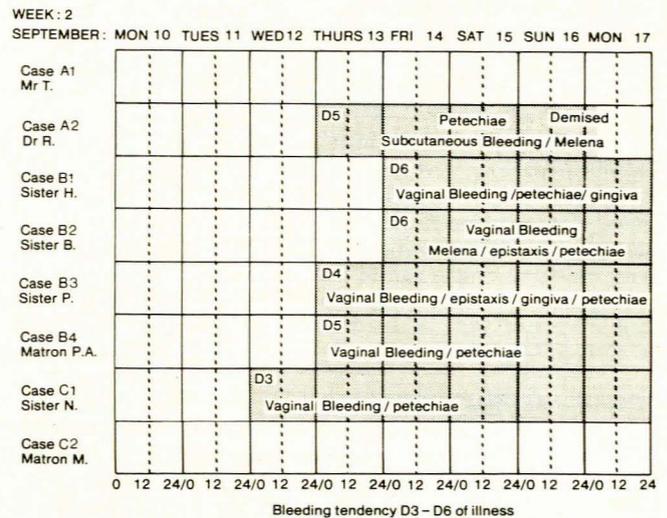


Fig. 3. CCHF patients: onset of bleeding.

Patient B4 developed a 5 cm enlarged tender liver as an outstanding feature of her clinical picture.

Special investigations (Table I)

Haemoglobin values were normal with the exception of patient B4 (11,5 g/dl) (Table I). Leucopenia was found in all 4 patients, the mean white cell count being $3,0 \times 10^9/l$. The initial normal platelet counts dropped precipitously in 2 patients so that thrombocytopenia presented in all 4 subjects. Gross abnormalities of the clotting profile were not found in spite of the haemorrhagic tendency. The only abnormalities were in patient B2 whose PTT was lengthened from 41,5 to 83,1 seconds and whose fibrinogen degradation products (FDP) increased from 10 to more than 40 g/ml. In patient B3 the otherwise normal clotting profile was at one point characterized by a PTT which lengthened from 34 to 115 seconds, and an

FDP value of 40 g/ml. These temporary changes in the clotting profile became evident after onset of haemorrhage.

Viral antibody titres and positive CCHF cultures were found in all 4 patients. Serum urea and creatinine values as well as bilirubin values remained normal throughout. Changes in liver enzyme patterns with an elevation of the γ -glutamyl transferase (GGT) values were late manifestations. This feature will be discussed in detail in part III of this study.

Group C

Two patients presented with an attenuated disease course and an uncharacteristic clinical picture. Patient C1 had been in charge of the barrier nursing of the index case, but had no direct contact and claimed that she had only worked in the corridor outside the patient's room. Patient C2 had been in direct contact with all 7 CCHF patients. She assisted with the removal of a skin biopsy specimen from patient B2, and inoculated herself with a needle. Patient C1 presented with severe headache, abdominal pain, fever, injected conjunctivae and vomiting. Her initial symptoms disappeared but she subsequently presented with symptoms of vaginal bleeding and petechiae. On admission she was afebrile, with a pulse of 100/min and blood pressure 130/90 mmHg. The conjunctivae were normal and there was no abdominal tenderness. She remained asymptomatic.

The symptoms in case C2 were complicated by severe stress and fatigue. She had complained of headaches and malaise before the needle inoculation, but her symptoms then deteriorated. A single dose of interferon, as well as a 4-day course of zalcitabine, a prophylactic antiviral agent, and hyperimmune serum were administered. Within hours after administration of the interferon, side-effects of fever, myalgia and nausea were documented. She developed clinical jaundice and anaemia (haemoglobin 9,2 g/dl). Headache, nausea and dizziness continued after cessation of the prophylactic agents but no bleeding tendency developed. Patients C1 and C2 were discharged, symptom-free, 18 days and 14 days respectively after admission to hospital.

Special investigations (Table I)

Normal haemoglobin values with low white cell counts of 10 and $3,8 \times 10^9/l$ were recorded in these 2 patients. Patient C1 had a low platelet count of $25,0 \times 10^9/l$. The clotting profile remained normal with the exception of a prolonged PT in patient C1 (38,5 seconds). This value may have been influenced by administration of heparin. Elevation of the liver enzyme values (GGT 138 U/l) was recorded in patient C1. The abnormal serum bilirubin value of 36 mmol/l found in patient C2 could have been caused by interferon and/or zalcitabine. Circulating viral antibody titres were positive in both but viral cultures became positive only in patient C1.

Discussion

Crimean haemorrhagic fever used to be a rare disease in the RSA. Crimean haemorrhagic fever was diagnosed for the first time in 1975 in 2 Australian students who became ill after a tour through Zimbabwe. One patient died and a nursing sister became ill.³ An extensive outbreak of Rift Valley fever occurred at the same time with 7 fatal cases.³

The first case of CCHF was reported in 1981.⁴ A 13-year-old boy developed acute influenza-like symptoms after spending a week camping in the western Transvaal. A tick of the *Haemaphysalis* species was found attached to his scalp. He died of

a haemorrhagic illness and CCHF was virologically confirmed.⁴ During November 1983 a farmer near Kimberley in the northern Cape developed CCHF after handling livestock but survived. The third case was that of a businessman who had a cattle farm in the Transvaal, who recovered; he had no history of a tick bite, but recalls dehorning and castrating cattle shortly before his illness. During January 1984 a dairy farmer near Frankfort in the Orange Free State and 4 of his workers became ill; 1 of the workers died. CCHF was positively diagnosed in the whole group. Some of his cattle came from the Darling district; two were ill and had been attended by the farmer and workers. Five of the original Frankfort cattle tested for CCHF had increased antibody titres, while 17 out of 20 of the cattle introduced from the Cape had antibodies of significantly elevated titres indicating recent infection.⁵ The Darling area had previously been considered a low-risk area with a 3,4% prevalence of positive antibody titres to CCHF in cattle on record. Frankfort had been identified as a high-risk area with positive antibody titres in 39,5% of cattle.⁵ Swanepoel and Shepherd⁵ suggested that importation of the new herd from a low-risk area, Darling, to a high-risk area had made them more vulnerable to CCHF.

Of the 8 cases of CCHF diagnosed and admitted to local hospitals in the RSA between 1981 and January 1984 2 patients died. Barrier nursing was instituted late during their illnesses, and no secondary case occurred. All 8 cases reported in the RSA up to September 1984 were in males and 7 had close contact with animals. Agricultural workers are at the highest risk, especially during spring and summer when ticks are most active.⁶

The predominant symptoms shown by 6 of the 8 patients at Tygerberg Hospital are listed in Table II. These data were collected by a daily checklist for symptoms and signs and a flow chart for the special investigations. An inadequate history was obtained in case A1. In case C2 the full clinical picture of CCHF did not develop, and symptoms could have been influenced by interferon administration. The clinical findings of 7 of the 8 patients are set out in Table III.

TABLE II. MOST IMPORTANT SYMPTOMS IN 6 CASES

Headache	}	6 patients (100%)
Backache		
Fever		
Myalgia		
Arthralgia		
Mood changes		
Bleeding tendency	}	5 patients (80%)
Oedema		
Injected conjunctivae		
Dizziness	}	4 patients (60%)
Photophobia		
Diarrhoea	}	3 patients (50%)
Skin rash		
Sore throat	}	1 patient (16%)
Cough		

*Cases A1 and C2 were omitted.

The mean incubation period in our patients was 5 days. The typical clinical picture includes a history of a tick bite or contact with a patient with CCHF. Approximately 5 days later fever, severe headache, myalgia and lower backache develop. On examination our patients were feverish, with tachycardia, tender abdomen and liver, and a bleeding tendency. Petechiae and other manifestations of a bleeding tendency developed 3-6 days after the onset of illness (Fig. 3). The temperature

TABLE III. MOST IMPORTANT SIGNS IN 7 CASES

Fever	}	7 cases (100%)
Tender abdomen		
Tender hepatomegaly		
Petechiae		
Dizziness (postural)	}	5 cases (70%)
Tachycardia		
Oedema		4 cases (55%)
Peri-orbital oedema		3 cases (42%)
Injected conjunctivae	}	2 cases (25%)
Jaundice		
Skin rash		1 case (16%)
Gingival ulcers		1 case

subsided 5-10 days after the onset of the illness. The severity of the symptoms and the bleeding tendency distinguished it from an influenza-like illness. When leucopenia and thrombocytopenia accompany the clinical picture the diagnosis of a viral haemorrhagic fever should be strongly considered. Leucocytosis was evident in only 4 cases and may confuse clinical judgement.

The patients at Tygerberg Hospital were divided retrospectively according to the severity of their clinical picture. Group A patients (cases A1 and A2) presented with cerebral depression, jaundice, vascular collapse, and severe bleeding tendency and died of multiple-organ failure. These features indicate an extremely grave prognosis. Group B patients (cases B1-4) represented the intermediate group with the classic symptoms and signs. Group C patients (cases C1 and C2) presented with an attenuated disease with mild symptoms and signs. The special investigations and treatment also differed according to the severity of the disease. It is therefore evident that CCHF can present with a spectrum of severity ranging from critical illness to a mild influenza-like disease. This spectrum may be due to individual responses, ability to produce endogenous antibody, primary, secondary or tertiary infection and modification due to treatment. Special investigations were limited because of the high risk of contamination of the routine laboratories. Blood bank, haematology and chemical pathology laboratories were established in the isolation ward for daily routine tests.

Full blood counts revealed a severe post-haemorrhagic anaemia in the 2 patients who died. In all 8 cases there was some degree of normocytic normochromic anaemia. The total white cell count was low or normal in 7 of the 8 cases. Marked leucopenia ($< 2,0 \times 10^9/l$) was present in 3 cases. Leucocytosis and a leuco-erythroblastic reaction were present in case A2. Toxic granulation and a shift to the left were also a feature without any evidence of bacterial infection making the differentiation from septicaemia extremely difficult. The presenting blood picture was that of a relative neutrophilia and lymphopenia which later changed to a lymphocytosis. Despite the leucopenia, secondary bacterial infection was documented only in case B2. A mild growth of *Escherichia coli* was cultured from this patient's urine.

Thrombocytopenia was a feature in all patients except in C2, who had a mild illness. Low platelet counts and low fibrinogen levels are features of dengue haemorrhagic fever, with possible increased destruction of platelets.⁷ Platelet function could not be studied as we could not use the normal laboratory facilities, but the normal mean platelet volume in our patients suggests peripheral destruction of platelets.⁸ The clotting profile will be discussed in detail in part III of this study, but was seldom abnormal.

Low serum potassium levels were recorded in 5 of the 8 patients; sodium and chloride levels remained normal. Raised

serum urea and creatinine levels were recorded in the 2 patients who died (cases A1 and A2).

Liver enzyme values were maximally elevated late in the illness (a mean of 12 days after onset). The liver was very tender and enlarged at the onset of the disease with only mild increased liver enzyme values. The highest values were recorded in the convalescent phase, when the liver was no longer palpable. This picture differs from that in other forms of viral hepatitis where high liver enzyme values are present early. The 2 patients who died had high serum bilirubin values. Jaundice and markedly elevated liver enzymes at first diagnosis may indicate a poor prognosis.

The presence of virus antibody and/or a positive culture are essential features for the final diagnosis. Positive antibody titres with a negative culture in the appropriate clinical setting indicate attenuated disease (case C2).

Virological and serological investigations were performed at the National Institute for Virology for objective diagnosis. The distance to Johannesburg and the period of 3-8 days before a diagnosis could be confirmed remained a major problem. Treatment should not be delayed but should be initiated in a highly suspicious case.

After the CCHF outbreak many patients were referred to Tygerberg Hospital in order to have the disease excluded. Ten patients were regarded as highly suspicious cases and in 9 of them virological studies were negative (Table IV). Only 1 patient, an ostrich farmer, had proven CCHF. Exposure while slaughtering infected ostriches was suspected since antibody titres for CCHF were increased in some of the birds. This is the first report of ostriches as a possible source of this disease. It is evident that all domestic animals which can transmit the disease need to be identified in *Hyalomma*-infested areas. The most important differential diagnosis of viral haemorrhagic fever as experienced after the CCHF epidemic was the haemorrhagic form of tick-bite fever (Table IV).

The spectrum of possible causes of a haemorrhagic fever is wide. We use the following criteria to identify the high-risk patient: (i) history of a tick bite or exposure to animals in a farming community; (ii) severe influenza-like symptoms and fever followed within 3-5 days by a bleeding tendency; and (iii) low platelet and/or white cell count associated with criteria (i) and (ii).

Patients with tick-bite fever who respond swiftly to antibiotic treatment have a normal haematological picture and no bleeding tendency and are therefore excluded.

A simple flow-chart to follow in suspicious cases is shown in Table V. Eight possible differential diagnoses, with the relevant special investigations, are given.

Conclusion

A recent outbreak of CCHF in a large university teaching hospital has been described. The differences between previous outbreaks of CCHF in the RSA and the present one were the danger of spread in a large hospital and the occurrence of secondary and tertiary cases. A strict protocol for handling suspected viral haemorrhagic fever cases was formulated. Subsequent to the reported CCHF epidemic, an ostrich farmer suspected of having CCHF was immediately isolated according to this strict protocol and no secondary cases occurred.

The criteria for differentiating the haemorrhagic fevers have been put to the test and proved helpful. For the clinician it is, however, virtually impossible to distinguish the different forms of haemorrhagic fevers absolutely. Special investigations are not diagnostic and the clinician has to depend indirectly on virological studies for a definite diagnosis. More rapid virological screening tests are essential as the final confirmation is

TABLE IV. PATIENTS SEEN AFTER THE CCHF OUTBREAK: OCTOBER 1984 - MARCH 1985

Age, race, sex	District; possible source of infection	Presenting symptoms and signs	Initial white cell/platelet count (x 10 ⁹ /l)	Relevant special investigations	Final diagnosis
42 yrs White F	Worcester; fleas from rats	Headache, arthralgia, purpuric rash, lymphadenopathy, petechiae	3,4/38,0	VHF - Oxk - 1:8-16 Ox2 - Ox19 -	Possible rickettsiosis typhus
47 yrs White M	Oudtshoorn ostrich farmer; ostrich	Headache, rigors, suffused eyes, bleeding tendency	5,9/58,0	VHF + Oxk 1:16 Ox2 - Ox19 -	Congo-Crimean haemorrhagic fever
30 yrs Coloured M	Montague farm labourer [†]	Headaches, fever jaundice, bleeding tendency	29,0/93,0	VHF - Liver biopsy for VHF - <i>Rickettsia conorii</i> antibodies	Septicaemia with hepatorenal failure
64 yrs White F	Riviersonderend	Headache, fever, purpuric rash, confusion	4,0/311,0	VHF - Ox2 1:40 Ox19 / 1:12 - 80	Tick-bite fever
21 yrs Coloured M	Clanwilliam; camping in veld	Headache, purpuric rash	3,9/93,0	VHF - Ox2 1:640 Ox19 1:640	Tick-bite fever
26 yrs Coloured M	Garies; no history	Comatose, petechiae, bleeding tendency, jaundice	6,5/107,0	VHF - Toxicology Screening + Ox2 Ox19 -	Drug overdose, hepatorenal failure
20 yrs White M	Youngsfield; soldier camping in veld	Headache, fever, purpuric rash, petechiae	12,0/250,0	VHF - Paul Bunnell - Initial Ox2 Ox19 -	Tick-bite fever
24 yrs White F	Oudtshoorn hostel	Flu-like symptoms, petechiae, no fever	2,1/19,0	VHF - Hypercellular bone marrow Oxk - Ox2 - Ox19 -	Idiopathic thrombocytopenic purpura
28 yrs White M	Zaire — Congo River delta	Flu-like symptoms, headache, petechiae	3,6/29,0	VHF - Malaria smears + Oxk - Ox2 - Ox19 -	Malaria
28 yrs White M	Eastern Cape Intensive-care technologist for incubators	Flu-like symptoms, rash, suffused eyes	4,4/118	VHF - Rising measles titre Oxk - Ox2 - Ox19 - Paul Bunnell -	Measles

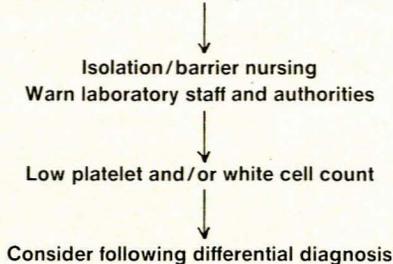
= viral haemorrhagic fevers virological studies; † = died; Ox2, Ox19 = Weil-Felix studies.

TABLE V. DIFFERENTIAL DIAGNOSIS OF HAEMORRHAGIC FEVER

Severe headache, backache, myalgia, arthralgia, mood changes, bleeding tendency, fever

+ Tachycardia, tender abdomen and liver, bleeding tendency, injected conjunctivae

+ Contact with animals in a farming community or tick bite



DIAGNOSIS	RELEVANT SPECIAL INVESTIGATIONS
1. Viral infection	1. Viral haemorrhagic fever Hepatitis A, non-A non-B Measles antibodies (Paul Bunnell)
2. Rickettsial	2. Ovx, Ox2, Ox19
3. Bacterial	3. Blood cultures
4. Spirochaetal	4. Dark field microscopy agglutination test
5. Protozoal	5. Malaria smear
6. Any form of bone marrow infiltration (e.g. leukaemia, lymphoma)	6. Bone marrow
7. Drugs	7. Toxicology, bone marrow
8. Auto-immune diseases	8. Auto-immune screening

possible only after periods of up to 8 days. The importance of early barrier nursing was evident in this outbreak. Most of our secondary cases probably contracted the disease before barrier nursing was instituted. Needle inoculation was a factor in 3 of the 7 patients with secondary infection. None of the contacts of case A2, a secondary contact, contracted CCHF.

This outbreak emphasizes the fact that isolation hospitals away from academic institutions are impractical. Severely ill patients with a bleeding tendency and possible CCHF should be sent to the nearest hospital where the expertise and facilities exist. Essential isolation facilities and a protocol for handling suspicious cases in larger hospitals need to be available and in practice. A team consisting of general physicians, haematologists, intensive care specialists, laboratory personnel, highly trained nurses and hospital administrators represent the minimum staff requirements for effective handling of the group of viral haemorrhagic fevers.

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Nuus en Kommentaar/News and Comment

Babamelk en fluoriedinname

Die voorskrif van aanvullende fluoried vir kinders in gebiede waar die water nie genoeg bevat nie word algemeen aanbeveel, maar daar het al by geleentheid verslae oor emalje-fluorose verskyn waar fluoriedaanvullings benewens die fluoried in die dieet geneem is.

Teen hierdie agtergrond het Van Wyk *et al.* (*J Dent Assoc S Afr* 1985; **40**: 179) 12 babamelkformules wat die algemeenste in Suid-Afrika gebruik word vir hul totale fluoriedinhoud getoets. Hulle het ook monsters van moedersmelk en koemelk getoets en die daaglikse fluoriedinname bereken van babas wat moedersmelk, koemelk of 'n melkformule drink.

Hul bevindings het getoon dat die fluoried in melkformules sonder verdere aanvulling toereikend vir die baba is. Hulle het

dus tot die gevolgtrekking gekom dat babas in 'n nie-gefluorideerde streek wat babamelkformules drink geen fluoriedaanvulling nodig het voordat hulle na koemelk oorskakel nie. Gevolglik ontvang babas wat in 'n streek met gefluorideerde water bly en melkformules drink 'n te groot daaglikse dosis fluoried. Babas wat moedersmelk en koemelk drink moet egter kort na geboorte met fluoriedaanvulling begin om die optimumvoordeel van hierdie noodsaaklike mikrovoedings-element te verkry. Die klinikus moet volkome bewus wees van al die potensieële fluoriedbronne in die kind se dieet voordat hy fluoriedaanvulling voorskryf en daar word ook aanbeveel dat vervaardigers van babamelk die fluoriedinhoud van hul produkte aandui. Die skrywers beveel aan dat babamelk met gedistilleerde water i.p.v. kraanwater voorberei word in gebiede waar die water gefluorideer is of waar dit relatief hoë fluoriedvlakke bevat.