

Historical Perspectives

Dr Mahgoub Osman Karrar who wrote the first clinical report on Ebola virus disease worldwide

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EDITORIAL NOTE:

Dr Ibrahim Hassan Fahal cordially contributed this article and sent the original document of the late Dr Mahjoub Osman Karrar who wrote the first clinical report on Ebola virus disease worldwide in 1976. On 4 October 1976, an epidemiologist from the Central Ministry of Health, Sudan, Dr Ali Ahmed Idris, accompanied by a clinical team of physicians arrived in Maridi to investigate an unknown haemorrhagic fever epidemic that devastated this town in Equatoria Region of southern Sudan (Currently, South Sudan) with an alarmingly high mortality rate including 41 of the Hospital Staff and the only doctor managing the patients (the late Dr Abdeen Khairy) [1,2]. The team of physicians who accompanied Dr Ali Ahmed Idris consisted of Dr Mahgoub Osman Karrar and Dr Awad Osman Mahdi (both were Medical Registrars at Khartoum Hospital, Khartoum) and Dr Hyder Hamza who had just finished his housemanship [2]. Dr Ali Ahmed Idris stayed in Maridi and Nzara for 5 days (till 9 October 1976), whereas the rest of the group (Drs Magoub, Awad and Hyder) joined the Hospital Staff in Maridi and dealt with the patients till the end of the epidemic [2]. Dr Mahgoub Osman Karrar compiled his clinical observations in a document and presented his findings to the Regional Minister of Health, Dr Justin Yac, and the other health authorities (Figure 1). He called the outbreak “MARIDI VIRUS DISEASE” (Figure 2). The original document was in Roneo (mimeograph) format. A reproduction of it is to be found below with careful maintenance of its style except for APPENDIX I and APPENDIX II which have been redrawn for clarity.

How to cite this:

Fahal IH. Dr Mahgoub Osman Karrar who wrote the first clinical report on Ebola virus disease worldwide. Sudan J Paediatr 2014;14(2):101 - 111.

Dr Mahgoub Osman Karrar was a lifelong advocate of Sudan, a physician, an inspiring colleague, a historian, a vivid reader and a humble person. He graduated from the Faculty of Medicine, University of Khartoum in 1972 [3] and held house appointments in Khartoum before becoming a registrar in medicine. His selection to head the medical team to investigate and manage the hemorrhagic fever epidemic in Maridi, Equatoria Region in the southern region of Sudan (currently, South Sudan) in October 1976 was a testimonial of his early clinical competency, organizational skills and attention to details that he has always kept and became his second nature. The report published in this issue of the journal on “Maridi Virus Disease” is a historical account of the work that he and his colleagues had undertaken in 1976 (Figures 1 and 2).



Figure 1 – Team leader Dr Mahgoub Osman Karrar in Maridi Hospital (first from left) briefing Dr Justin Yac, the Regional Minister of Health and Social Welfare (second from left) on the progress of the disease and measures undertaken. (Figure scanned from a photo in a newspaper).

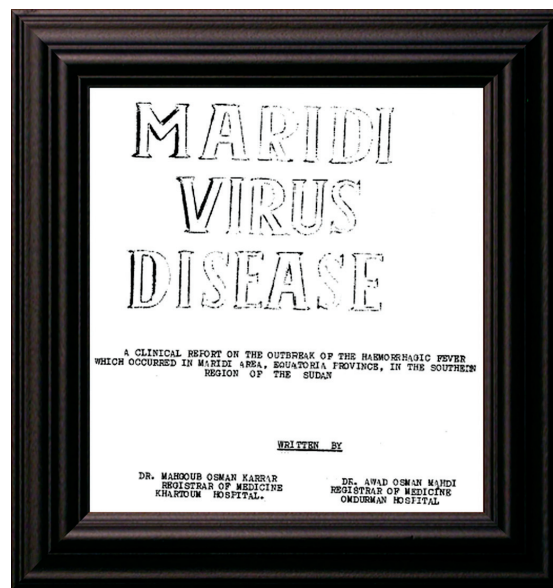


Figure 2 – The title page of the document which has been printed in Roneo (mimeograph) format.

Mahgoub then moved to the United Kingdom (UK) in early 1980s, trained in medicine and obtained membership of the Royal College of Physicians of London.

In the UK, Mahgoub co-founded Sudan Doctors Union, UK & Ireland branch and was pivotal in its success. His organizational skills were evident in the meticulous documentation of its early days, a Union that continues to lead Sudan medicine in the UK to the present time.

Mahgoub worked in various parts of the UK and following a myocardial infarction he retired from medicine. Following his early retirement, Mahgoub concentrated on his lifelong love and advocacy to Sudanese People welfare. He had an archive of many hundreds of documents and books on Sudan.

His lifelong humble personality made him stand out among his peers. He died in Khartoum in September 2008 from metastatic lung carcinoma.

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MARIDI VIRUS DISEASE

A CLINICAL REPORT OF THE OUTBREAK OF THE HAEMORRHAGIC FEVER WHICH OCCURRED IN MARIDI AREA, EQUATORIA PROVINCES, IN THE SOUTHERN REGION OF THE SUDAN.

WRITTEN BY

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INTRODUCTION

On the 3rd of October, 1976 a medical team headed to MARIDI, in Equatoria Province, in the Southern Region of the Sudan, to investigate an outbreak of a haemorrhagic fever which started in Nzara area and then flared up in the epidemic form in Maridi area.

The team was formed of an epidemiologist and the following medical doctors:-

Dr. Mahgoub Osman Karrar
Dr. El Awad Osman Mahdi and
Dr. Hyder Hamza.

Till we reached Juba on the same day there was no written information or data about the outbreak.

In Juba we read the first report written by Dr. Babiker El Tahir (Virologist) who visited the area on the 29th of September with a Laboratory team.

The report contained a comment on some of the clinical manifestations of the disease plus other epidemiological data and recommendations about control and protection.

We arrived at Maridi on the 4th of October 1976. This was the only team of clinicians to reach the area of the epidemic.

In Maridi the medical team joined the two medical officers working in Maridi Civil Hospital, (Dr. Isaiah Mayom and Dr. Abdel Ghani Bakri).

MARIDI HOSPITAL:-

Maridi Hospital is composed of five major wards, and its capacity is about 80 beds. The wards are well spaced from each other, but the hospital as a whole is lacking any type of fence or barrier.

At the start of the outbreak there was also no proper quarantine. The early cases were admitted in three of the general wards and the patients were attended by their relatives. Also barrier nursing and doctoring was not instituted at that time.

It is to be mentioned that during that period most of the hospital staff, including the late Dr. Abdeen

Kheiri and some relatives of patients contracted the disease from the wards, and about 50% of them died (The last two weeks of September).

The death of the doctor in charge of the hospital (Dr. Isaiah Mayom was in duty in Nzara) and 50% of the affected nursing staff caused some disorganization in the hospital work which lead to improper recording and management of cases.

Later on Dr. Isaiah and Dr. Abdul Ghani reached the area and started to organize the work.

CLINICAL MANIFESTATIONS AND OTHER FORM OF PRESENTATION OF THE DISEASE

All the clinical manifestations of the disease which will follow were seen in patients already hospitalized and in the subsequent fresh cases reported to us in the period from 4/10/76 to 21/11/76.

The clinical manifestations include the common presentation of the disease and some Obstetrical, Gynaecological and Psychiatric manifestations.

Premonitory Symptoms:-

In many patients the disease starts with a flu-like illness, followed by malaise and severe myalgia which lasts for about 24 – 48 hours, to be followed by the major manifestations which are:-

(I) Fever:

This occurred in more than 95% of the cases. The fever is of sudden onset, with a temperature ranging mostly between 100°F – 102.5°F. It does not go beyond 102.5°F. It is not accompanied by rigors or sweats.

In some cases who came with marked respiratory tract involvement the temperature

reach up to 103°F - 104°F (Due to secondary Pneumonitis).

The fever was resistant to antipyretic measure instituted including cold fomite. It subsides by itself within 3 – 5 days.

(II) Headache:

About 80% of cases complained of severe headache, mostly in the temporal region and was accompanied by neck pain.

Both occur in the febrile period and last for 3 – 5 days.

(III) Dryness of the Throat:

Almost all patients complained of dryness of the throat accompanied with pain which extends retrosternally. This dryness and soreness of the throat caused them to refrain from ingestion of food or fluid during the early stages of the disease.

(IV) Chest and abdominal pain:

All patients complained of either chest or abdominal pain at a variable stage of the illness. The chest pain, stabbing in nature is mostly in the right side of the chest in the lower intercostal spaces in the mid-axillary line. The abdominal pain is always restricted to the right hypochondrium (Most probably originating from the liver).

(V) Vomiting:

Projectile in nature, and usually following a period of marked nausea and anorexia. It usually occurs after ingestion of food or fluid and may develop into haematemesis in those with bleeding tendency. The vomiting is usually accompanied by diarrhoea.

(VI) Diarrhoea:

This is a severe painless, quickly dehydrating diarrhoea, with up to 10 -20 motions per days. The

stool is watery, with no mucus or blood, but later on changing into melaena in about 50% of causes.

The vomiting usually stops in the first few days, but the diarrhoea continues for a longer period and then gradually subsides when the patient starts to recover.

(VII) **Haemorrhagic and bleeding tendency:**

It was observed by Dr. Abdel Ghani and Dr. Isaiah that at the start of the outbreak, especially during the last two weeks of September, about 75% of patients showed bleeding tendency. Later on we observed that the percentage of patients showing the bleeding manifestations dropped to about 10 – 15% and they were not so serious as to warrant any blood transfusion.

The bleeding manifestations were in the form of :-

- a. Epistaxis
- b. Haematemesis and melaena
- c. Purpura
- d. Vaginal bleeding

(VIII) **C.N.S. Involvement:**

Central nervous system involvement occurred in about 10% - 15% of cases. They showed signs of meningeal irritation. Severe headache, neck pain and marked neck rigidity with positive Kernig's sign was detected. They also developed rigidity of all the limbs, with absent reflexes.

Systematic C.N.S examination was not feasible in these patients due to their conditions, as most of them were in semicomatose.

The general picture was that of meningoencephalitis.

Almost all patients who showed these signs of C.N.S involvement died later on.

(IX) **Kidney Involvement:**

This was detected in about 30% of patients who died.

- Some patients showed proteinuria while some others showed haematuria (Macroscopic).
- One patient, a child of 14 years of age, developed haemoglobinuria (coincidentally we discovered that she was M.T. positive and she had already received Quinine, hence the possibility of black-water fever was put in mind). Later on she developed anuria and died with signs of renal failure.
- Some patients developed oliguria which progressed quickly into anuria with frank symptoms and signs of Uraemia.

(X) **Skin Manifestations:**

This occurred in less than 15% of cases. They took either of two forms:-

a) Skin rash

This occurs in second to fourth (2-4) days of illness. It is maculopapular in nature. It is non itchy. It spreads quickly, taking a distribution starting in the thighs and buttocks and extending to involve the trunk and upper extremities. It spares the face, hands, feet and flexures. The rash disappears within 24 – 48 hours leaving no signs behind.

In one patient some desquamation of the skin occurs in the affected areas.

(b) **Purpuric rash: -**

Seen in these patients with haemorrhagic tendency. It may occur in any part of the body especially the trunk.

In one patient areas of ecchymosis were seen at pressure sites.

(XI) Cardiac Involvement :- (Myocarditis)

Signs of myocarditis occurred in about 5% of cases who died. This could explain the sudden death which occurred in a number of patients after developing sudden attacks of acute heart failure. Some of them were apparently recovered.

(XII) Orchitis :-

One patient who showed the typical picture of the disease developed severe pain in the right testis accomplished by fever, swelling and tenderness. On examination the picture was that of acute orchitis. Later on his general condition improved and the orchitis subsided.

(XIII) Psychiatric Manifestations :-

Many patients showed abnormal behavior either during the acute stage of the disease or in the recovery period. Many patients showed typical picture of toxic Psychosis. This occurred in the early stages and was not accomplished by any symptoms or signs of organ failure.

Three (3) patients showed schizophrenic behavior with :-

- Hallucinations.
- Flight of ideas.
- Paranoid ideas.

(XIV) Obstetrical and Gynecological Presentations :-

These, though put under the clinical manifestations of the disease can be considered also as complications. They occurred in a good percentage of patients as to justify putting them among the manifestations.

(a) Abortion :-

Three patients had abortion. Two of them showed the typical picture of the disease while the third

presented with vaginal bleeding and was the wife of definite case. The three have variable periods of amenorrhea. They all recovered and discharged in a good condition.

(b) Premature Labour :-

Three patients had premature labour. All with amenorrhea of more than twenty eight (28) weeks. Two of them recovered but their babies died. The third one died while her premature baby (seven months) was still surviving, till we left the area.

(c) Vaginal Bleeding :-

Few patients presented with the clinical picture of the disease plus vaginal bleeding which was not related to the normal menstrual period (Metrorrhagia).

PHYSICAL EXAMINATION

Most of the patients brought to the hospital in the acute stages of the disease, showed marked degree of toxemia, dehydration and weakness and usually showed clouding of consciousness.

In addition to the clinical manifestations already mentioned the following POSITIVE signs were also observed.

Temperature :-

Described under the clinical manifestations.

Pulse :-

All patients showed relatives bradycardia compared to the rise of temperature.

Blood Pressure :-

Almost all the patients showed low blood pressure confirming with the degree of dehydration.

Eyes :-

All patients in the acute stage showed injection of the conjunctival with few patients showing subconjunctival haemorrhages.

CLINICAL JAUNDICE DID NOT OCCUR IN ANY PATIENT AT ANY STAGE OF THE DISEASE.

Oral Cavity :-

Mouth ulceration (Aphthous stomatitis), and angular stomatitis were detected in some patients. Congestion of the throat and injection of the soft plate were observed in all the patients complaining of pain in the throat.

Heart :-

Auscultation of the heart did not show any abnormally apart from tachycardia in dyspnoeic patients who were suspected to have myococaditis. No dysrrhythmia was detected.

Respiratory System :-

- The respiratory rate varied with the rise in temperature and with the occurrence of complications e.g. pneumonia, myococaditis and uraemia.
- Tenderness in the lower intercostal spaces commonly in the right side.
- Crepitations and rhonchi in the lower zones of the lungs were detected in most patients during the course of the illness. Pleural rub was detected in few patients.

Abdomen :-

In 60% of patients tenderness in the right hypochondrium was detected. The liver and spleen did not show any enlargement during the course of the disease (Few cases showed hepatomegaly or splenomegaly). This was not given any consideration

as far as the disease is concerned - in this tropical area were other pathologies prevail).

C.N.S :-

Systematic examination of the C.N.S was not feasible in those patients with C.N.S involvement due to their condition as they were either comatose or in semi-coma.

Examination of the pupils showed that they are equal and reactive.

The positive signs found were those of meningeal irritation e.g. neck rigidity and positive Kernig's sign.

There was also spasticity of all the limbs but the reflexes were absent.

COURSE OF THE DISEASE.

The state of consciousness of patients varies with the stage of the illness. Most patients brought in the early stages of the disease showed clouding of consciousness. The patient either regains his consciousness or goes into coma which carries bad prognosis.

In a third group of patients it was observed that they go into a state similar to that of typhoid (coma vigil) from which the patient may improve gradually or deteriorate.

The patient is usually in a variable state of dehydration which is due to :-

- Vomiting
- Diarrhoea
- Inability to take fluids orally.

Improvement comes on gradually when vomiting stops and fever subsides. The diarrhoea continues for a long time (10 – 14 days).

Patients quickly loose weight and those recovered were left with a remarkable degree of emaciation. In those who recovered a state of generalized weakness continues for few weeks before they can resume their normal activities.

No residual signs were detected in those who recovered.

The clinical picture of those who died was complicated by signs and symptoms of failure of one of the following systems :-

1. C.N.S.
2. Heart
3. Renal
4. Respiratory.

LABORATORY INVESTIGATIONS.

Due to lack of facilities only the following investigations and results could be obtained in Maridi Hospital.

(A) Urine analysis :-

This showed proteinuria and haematuria.

These findings were not constant in all patients.

NO BILE PIGMENTS WERE DETECTED.

(B) Stool analysis

Some patients showed R.B.Cs and mucus. Coincidental parasitic and worm infestation was detected in some patients

(C) Haematological :-

- i. It is to be mentioned that more than 90% of patients showed positive blood films for malaria (M.T.). Hence antimalarial therapy was given as a routine to every patient.
- ii. Blood film for spirochaetes was negative.
- iii. Leucocytosis
Leukocytosis was observed to occur from the fifth day (5th) of the disease onwards. The range usually lying between 15,000 – 30,000/ c.m. But some patients had a count of more than 40,000. (In one patient who had C.N.S. involvement a count of 48,000 was detected).

No patient showed leucopenia.

iv. Thrombocytopenia

A low platelet count was detected especially in

those patients with bleeding tendency.

N.B.

(a) Hes's test:

Was done to few patients and was negative.

(b) Liver and kidney function tests were not done due to lack of facilities.

DIAGNOSIS

No definitive diagnosis was put but from the clinical picture of disease. Mode of transmission and death plus the above mentioned laboratory investigations done, certain diseases could be excluded:

- Yellow fever.
- Enteric fever.
- Malaria and Blackwater fever.
- Relapsing fever.

A provisional diagnosis was put as a **COMMUNICABLE DISEASE CAUSED BY A PANTROPIC HAEMORRHAGIC VIRUS TRANSMITTED BY CLOSE CONTACT AND HAVING NO VECTOR.**

On this assumption we instituted our lines of management of cases.

MANAGEMENT.

(A) PROTECTIVE MEASURES :-

- i. Restrict isolation of patients in proper quarantines.
- ii. Barrier nursing and doctoring was instituted (use of disposable gowns, masks, gloves and caps)
- iii. Application of strict antiseptic measure of patients excreta and use of disposable instruments.
- iv. Burial of dead bodies immediately by authorities i.e . not delivered to relatives, so that minimal handling is done.

(B) Anti-malaria therapy.

This was given as a routine to every patient

(Chloroquine Phosphate).

(C) Antibiotics:-

Broad spectrum antibiotics were used, mainly in the form of tetracycline either orally or parenterally.

(D) Symptomatic and supportive :-

- v. Antipyretics
 - Mainly in the form of cold fomites.
 - Salicylates being avoided due to the haemorrhagic tendency.
 - Anti-emetics.
- vi. Antidiarrhoeal.
- vii. Sedatives.
- viii. Vitamins and tonics.

(E) Monitoring of fluid input and output to detect those with renal involvement.

N.B.

- i. (i) Steroids were tried in only one shocked patient. She died later on.
- ii. (ii) Blood transfusion was not done to any patient as there was no severe bleeding or loss of blood as to warrant for it.
- iii. (iii) Plasma from convalescent patients was collected and sent abroad for preparation of immune sera.

COMPLICATIONS.

i. Dehydration and electrolyte disturbance :

Marked dehydration was observed in almost all patients.

It is to be mentioned that due to lack of facilities electrolyte disturbances were diagnosed on clinical basis alone e.g.

- Tetany was diagnosed in one patient who developed carpo-pedal spasm and positive chovstek's sign.
- Many patients complained of muscular cramps and abdominal distention.

ii. Pneumonia:

Pneumonia from secondary infection was

observed in 40% of cases.

iii. Acute cardiac failure :-

This occurred in those who developed myocarditis.

iv. Renal failure :-

About 20% of those who died showed symptoms and signs of uremia. This could be due to :-

- Direct kidney involvement.
- Pre-renal element.

v. (v) Toxic Psychosis :-

Many patients developed some degree of abnormal behavior. Few patients showed schizophrenic behavior.

vi. Obstetrical and Gynecological :-

- (a) Abortion.
- (b) Premature labour.
- (c) Vaginal bleeding

CAUSES OF DEATH.

From the clinical manifestations of the disease and possible direct causes of deaths, the virus is most probably a pantropic one affecting almost every organ in the body, with severe affection of some organs more than the others.

It was observed that in those who died the course of the disease was complicated by one of the following:-

- i. Dehydration.
- ii. Renal failure.
- iii. Pneumonia.
- iv. Acute cardiac failure.
- v. C.N.S. involvement (encephalitis).

N.B.

There were no solid clinical manifestations as to indicate Liver cell failure.

OBSERVATION.

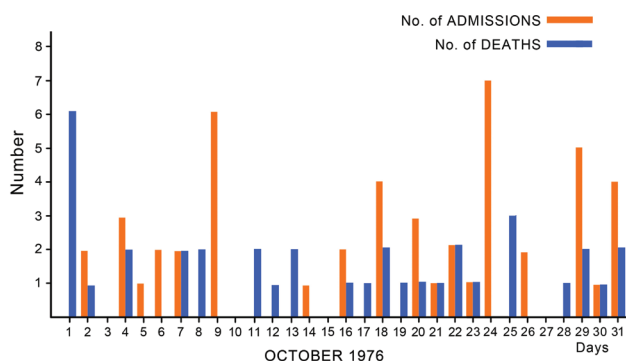
The following comments were decided from observation of patients found already in Maridi Hospital on our arrival on the 4th October, 1976 and from subsequent fresh cases which were admitted to hospital in the period 4.10.1976 – 21st November 1976.

(I)

(A) Admissions :-

- No. of inpatients on our arrival was 32
- No. of admissions in the period from 4.10.76 – 21.11.76 70
- Total No. of cases studied 102
(Appendix I & II)

APPENDIX I

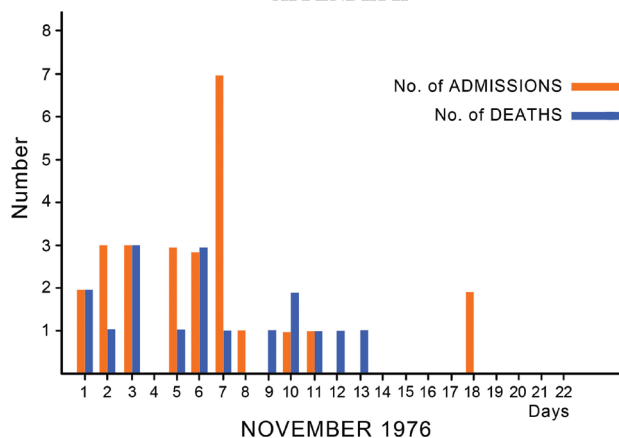


APPENDIX I – Admissions and deaths in Maridi Hospital (October 1976).

Deaths :-

- No. of deaths on our arrival was 31
- No. of deaths in the period from 4.10.76 – 21.11.76 was 45
- Total No. of deaths till 21st November 1976 76
(Appendix I & II)

APPENDIX II



APPENDIX II – Admissions and deaths in Maridi Hospital (November 1976).

(B) Hospital staff:-

- Total No. affected 79
- Total No. of deaths 41

N.B.

Total No. of hospital staff before the epidemic was 115

(ii) INCUBATION PERIOD :-

This was decided from analysis of data and different recording sheets found in the hospital and from the mode of infection of new cases especially those of the hospital staff.

The incubation period most probably varies between 6 – 14 days.

(III) MODE OF TRANSMISSION :-

The disease seems to be transmitted by close contact with overt cases.

Infectivity being high during the early acute stages of the disease NO PROBABILITY OF VECTOR TRANSMISSION

(IV) SEX DISTRIBUTION :-

It was observed that males were affected more than females.

(V) AGE DISTRIBUTION :-

- i. No incidence of disease among children less than 10 years of age.

- ii. Incidence also low in people above 50 years of age.
- iii. Most age group affected lie between 10 – 40 years.

(VI) MORTALITY RATE :-

(A) In the early days of the outbreak especially the last two weeks of September 1976 the incidence of the disease and the mortality rate were very high especially among the hospital staff. This was due to:-

- i. As the disease was not realized and its infectivity was not known precautions and protective measures were not taken at that time.
- ii. The disorganization which occurred in the hospital due to the death of the doctor and 50% of the nursing staff.
- iii. The early cases were admitted to the general wards with other patients and were attended by their relatives.

(B) People started to take their patients and ran away into the bush –away from the hospital- to take native medicine of witches (KUJOR). This caused spread of the disease and death of these patients added to the rise of the mortality rate. (In fact two of the KUJOR contracted the disease. One of them died and the other recovered).

Acknowledgement.

We would like to thank Dr. Isaiah Mayom and Dr. Abdel Ghani Bakri and Dr. Hydar Hamza for their co-operation and help in the collection of some information and data for this information report. Also Dr. Abdel Rahman Banda (Bacteriologist – Military Corps) and Captain Novello Nylok (Lab. Assistant) for the help they gave to us by doing some Laboratory investigations. Thanks also to Mr. Justin English who typed this report.