

# ANNALS OF THE ACTM

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TROPICAL & TRAVEL MEDICINE

## Special Issue The Memoirs of Margaretha Isaäcson

### INSIDE:

- 29 FOREWORD:  
THE MEMOIRS OF MARGARETHA ISAÄCSON (1929-2001)
- 30 EDITORIAL:  
SPECIAL ISSUES IN THE ANNALS OF THE AUSTRALASIAN  
COLLEGE OF TROPICAL MEDICINE
- 32 ISAÄCSON MEMOIRS:  
PART 1 - BUBONIC PLAGUE
- 38 ISAÄCSON MEMOIRS:  
PART 2 - MARBURG VIRUS
- 43 ISAÄCSON MEMOIRS:  
PART 3 - EBOLA VIRUS
- 51 ISAÄCSON MEMOIRS:  
PART 4 - CHOLERA

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DECEMBER 2008

## CONTENTS:

### FOREWORD:

#### *The Memoirs of Margaretha Isaäcson (1929-2001)*

John Freaan .....29

### EDITORIAL:

#### *Special Issues in the Annals of the Australasian College of Tropical Medicine*

Derek R. Smith, John M. Goldsmid and Peter A. Leggat..... 30-31

### ISAÄCSON MEMOIRS:

#### *Compiled and Edited by John Freaan*

Part 1: Bubonic Plague ..... 32-37

Part 2: Marburg Virus ..... 38-42

Part 3: Ebola Virus ..... 43-50

Part 4: Cholera ..... 51-52

**INSTRUCTIONS FOR AUTHORS**..... i

Cover Photo: The Australian Institute of Tropical Medicine in 1916 (photo courtesy of James Cook University)

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## FOREWORD:

# THE MEMOIRS OF MARGARETHA ISAÄCSON (1929-2001)



*Associate Professor John Frea*

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Emeritus Professor Margaretha Isaäcson died (aged 72) on Saturday, 20th October 2001, several weeks after surgery to remove a malignant brain tumour. Born in The Hague, the Netherlands, in 1929, Isaäcson overcame family tragedy and tremendous hardship in wartime Europe<sup>1</sup> and was later a wireless operator in the Israeli air force. She qualified in medicine relatively late in life and spent almost all her subsequent working life in the South African Institute for Medical Research (since October 2001, the National Health Laboratory Service).<sup>2</sup> Isaäcson founded and was head of the Department of Tropical Diseases in the School of Pathology of the Institute and the University of the Witwatersrand. Her higher qualifications included M.D. and D.Sc. degrees, as well as Diplomas in Tropical Medicine and Hygiene and Public Health, awarded by the University of the Witwatersrand.

Margaretha gained international recognition for her work on cholera and plague in southern Africa, and the African viral haemorrhagic fevers. Her

investigations of haemorrhagic fever outbreaks established her international reputation. The Marburg virus outbreak in Johannesburg in 1975 led to an extensive epidemiological investigation. In 1976 Margaretha was a member of the international commission assembled to investigate the outbreak, in the Zairean village of Yambuku, one of the world's most frightening viruses, Ebola. A Belgian mission hospital and the village were ravaged by the infection, with a mortality rate of more than 80%. Despite the danger of exposure to the as-yet-unknown agent, Margaretha immediately became involved in control efforts. At one point there was an acute electric power shortage; she returned to Johannesburg and flew back with a pair of large generators, acquired at short notice by the Institute's buying department.

Professor Isaäcson was a member of numerous national and international medical bodies; she served as a consultant to the World Health Organization on plague and biological warfare and was a member of the Biological Weapons Working Committee of the South African Non-Proliferation Council. She was involved in pioneering work in urban water reuse in Windhoek, Namibia. She published extensively in international scientific journals. She was a commissioned officer in the South African Citizen Defence Force, of which position she was extremely proud. This had the practical advantage of facilitating air transport to and from the plague area in Namibia, where she did extensive work. After retirement, she maintained an active interest in travel medicine and was associate editor of the international publication *The Journal of Travel Medicine*, for which she meticulously prepared journal abstracts and short literature reviews. One of her last publications, which unfortunately she was not able to see, concerned the first documented outbreak of haemorrhagic *E. coli* O157 in Africa.<sup>3</sup>

Among her many awards were an honorary fellowship of the Australasian College of Tropical Medicine, an honorary diploma of the American Veterinary Epidemiology Society for distinguished service and contribution to the progress of public health, and a Rotary International Paul Harris Fellowship. Margaretha trained in plague research in the United States under the legendary Karl Meyer, and also did the CDC's applied epidemiology and biostatistics training course there. Margaretha was a competitive individual who would never compromise her ideals, nor would she show false modesty. Some people found her abrasive and overly self-assured. Very often, I think, it was those who shared her personality traits who clashed with her. Under a tough veneer was a person with a keen sense of humour who was generous with her knowledge and experience, and whose death leaves a void in the ranks of public health experts in Africa and the world.

At the time of her death, Professor Isaäcson was busy writing her memoirs, with the intention of eventually publishing them. The account ends abruptly, reflecting the untimely death of Margaretha, who tragically left the manuscript in an unfinished form. Although incomplete, these personal writings make compelling reading, and will have a special appeal for those who knew her. While the words remain those of Professor Isaäcson herself, I have done some minor editing, provided this Foreword and arranged her writings into themes which will appear as four parts, Part 1: Bubonic Plague, Part 2: Marburg Virus, Part 3: Ebola Virus and Part 4: Cholera.<sup>4-7</sup>

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## SPECIAL ISSUES IN THE ANNALS OF THE AUSTRALASIAN COLLEGE OF TROPICAL MEDICINE

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### Introduction to Our First Special Issue

We are delighted to introduce the first "Special Issue" ever published in the Annals of The Australasian College of Tropical Medicine. This issue contains unfinished memoirs of the late Emeritus Professor Margaretha Isaäcson (1929-2001), a pioneering figure in tropical disease research who spent most of her professional life in South Africa. As Dr Frean has explained in his Foreword,<sup>1</sup> Isaäcson was originally born in the Netherlands and suffered as a child during World War Two in Europe. She later immigrated to Israel and served in the Israeli Air Force, before eventually finding her way to South Africa and a career in tropical medicine.<sup>2</sup> Isaäcson qualified in medicine relatively late in life, graduating with an M.B., Ch.B. degree in 1963, followed by a D.P.H. in 1972 and a D.Sc. (Medicine) in 1988.<sup>3</sup> She had investigated the Marburg virus outbreak in Johannesburg during 1975,<sup>4</sup> and in the 1980s, when a consultant to the World Health Organization (WHO) had sharply rejected attempts to find political meaning in the spread of cholera across South Africa.<sup>5</sup> Isaäcson was involved in the global campaign to eradicate smallpox, as well as plague research in northern Namibia.<sup>6</sup> Her experience of the emergence of Ebola virus in Zaire during 1976 provided valuable insight for managing subsequent outbreaks, such as in Kitwit in 1995.<sup>7</sup>

Isaäcson would eventually spend most of her career at the South African Institute for Medical Research, known as the National Health Laboratory Service after 2001.<sup>4</sup> She received many awards and honours throughout her professional life, including an Honorary Diploma from the American Veterinary Epidemiology Society and a Rotary International Paul Harris Fellowship.<sup>4</sup> Regarding her involvement with The Australasian College of Tropical Medicine (ACTM), Isaäcson presented the Ashdown Oration and was the recipient of the Ashdown Medal in 2001 and was awarded the ACTM Medal for Outstanding Contributions to Tropical Medicine, as well as being elected as an Honorary Fellow of the College in 2000.<sup>4</sup> At the time of her death, Isaäcson was a consultant to the WHO on biological warfare.<sup>2</sup> The South African Society of Travel Medicine now holds an annual Margaretha Isaäcson Memorial Lecture in her honour.<sup>6</sup>

The concept and realisation of our current special issue can be attributed to Associate Professor John Frean from the National Institute for Communicable Diseases, National Health Laboratory Service, and University of the Witwatersrand in Johannesburg, South Africa. In his Foreword,<sup>1</sup> Professor Frean has outlined the professional, scientific and humanitarian achievements of Professor Isaäcson and has thoughtfully arranged her memoirs into four themed sections: Part 1: Bubonic Plague, Part 2: Marburg Virus, Part 3: Ebola Virus and Part 4: Cholera.<sup>8-11</sup> Although Professor Isaäcson had intended to publish her memoirs, she passed away before they could be completed, and as such, Part 4 contains the unfinished story of her pioneering cholera research. Our current special issue helps realise Isaäcson's vision for published memoirs, and simultaneously pays tribute to her outstanding professional career and worldwide contributions to tropical medicine. The issue is also punctuated by numerous photographs which had been left to her esteemed colleague in South Africa, Associate Professor John Frean.

### Special Issues in the Scientific Literature

Special issues can be defined as an organised collection of scientific articles covering a defined topic or serving an otherwise specific purpose. The publication of special issues appears to be a relatively popular journal phenomenon nowadays, with a recent Medline search by the editors retrieving at least 2000 articles that had been indexed under this keyword. Nevertheless, when limited to our own field, only a few special issues appear to have specifically focused on such topics. Table 1 lists a selection of special issues that have previously been published in the fields of tropical or travel medicine. Perhaps the earliest special issue in tropical medicine was from 1992, which looked at leprosy and tropical skin diseases,<sup>12</sup> with the most recent special issue describing echinococcosis.<sup>13</sup> The editorial approach to special issues appears to have varied between journals however, with some covering broad topics such as tropical disease research,<sup>14</sup> while others have targeted specific, but nevertheless broad areas, such as malaria.<sup>15</sup> Interestingly, a 1999 special issue by Turtle<sup>16</sup> was dedicated to a 1898 Cambridge anthropological expedition to the Torres Strait. On the other hand, and somewhat unlike tropical medicine, where a veritable flurry of material has been published in the areas of leprosy, malaria and parasitic diseases; special issues focusing on travel medicine appear to be quite rare. In our literature search for this editorial, only two special issues appear to have been published in travel medicine, one on fecal peril<sup>17</sup> and one describing nutrition and long-term space travel.<sup>18</sup>

As described in an earlier Editorial from the Annals,<sup>19</sup> our journal has recently expanded its scope and now strives to include occupational medicine among its sphere of interest, particularly research that is concerned with the health of working populations in the tropics. Expanding our search to include special issues in the occupational health field located a large variety of topics, a selection of which are listed in Table 2. Since the 1980s, there have been many such special issues published, with diverse topics ranging from cross-cultural perspectives in occupational therapy<sup>20</sup> to occupational health psychology,<sup>21</sup> and beyond. Indeed, some individual occupational medicine journals have actually published quite a few special issues over the years, with Industrial Health for example, containing at least 18.<sup>22</sup> The publication of special issues in scientific literature appears to take on many different forms, another of which are the special issues dedicated to noteworthy individuals in a particular field. Although this is not a new concept, relatively few have been published in tropical, travel, or occupational medicine, or related fields. Our literature search for the current editorial located only four such issues, one from 1992 dedicated to Irving Selikoff,<sup>23</sup> one from 1993 dedicated to Joseph Rutenfranz,<sup>24</sup> one from 1997 dedicated to Lennart Levi<sup>25</sup> and one from the year 2000 that was dedicated to Harry Hoogstraal.<sup>26</sup> Please refer to Table 3 for further details.

From an editorial perspective, it can be suggested that the proliferation of special issues in recent years may reflect a few trends in scientific publishing. Firstly, there is the expertise and motivations of the Editor-in-Chief and / or the editorial board on a particular journal. Individuals with a personal interest in certain topics may be motivated to compile a special issue, while the interests of journal readers may encourage it to cover various aspects of the discipline which are deemed to be important. Specific authors may have a personal interest in particular topics and may be willing to collate an individual issue themselves. Publishers may encourage the formation of special issues to help boost a particular journal's position within a scientific field, and to help improve their impact factor. Review articles are known to attract a higher proportion of citations than editorials and research articles,<sup>27</sup> and for these reasons, the publication of special issues containing many literature reviews may be an effective method for improving one's coveted impact factor score. While the concept of impact factors has already been described in an earlier issue of the Annals,<sup>19</sup> it remains to be seen whether the regular publication of special issues influences these calculations on a long term basis

### Conclusions

Regardless of one's opinion on the matter, the publication of any special issue is truly a 'labour of love' for the editorial board, while its final dissemination to the scientific community is always enormously satisfying. When preparing this special issue we, the executive editorial board, would like to pay tribute to Professor Isaäcson, as well as offering our sincere thanks and congratulations to Associate Professor John Frean for providing the material and helping compile and edit it for journal consumption.

We look forward to the suggestions of readers and college members who may be interested in coordinating their own special issue of the Annals in due course.

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**Table 1.**  
Some Special Issues Previously Published in the Fields of Tropical or Travel Medicine

Author(s)	Title or Theme of the Special Issue	Journal in Which it was Published	Year
Hemphill & Kern <sup>13</sup>	Echinococcosis	Experimental Parasitology	2008
Crabb & Cooke <sup>15</sup>	Molecular approaches to Malaria	Trends in Parasitology	2004
Docampo <sup>28</sup>	Cellular biology of protozoan parasites	Microscopy and Microanalysis	2004
Gezairy <sup>14</sup>	Tropical disease research	Eastern Mediterranean Health Journal	2003
Shah <sup>29</sup>	Malaria	Journal of the Indian Medical Association	2001

**Table 1. (cont.)**  
Some Special Issues Previously Published in the Fields of Tropical or Travel Medicine

Author(s)	Title or Theme of the Special Issue	Journal in Which it was Published	Year
Anonymous <sup>30</sup>	Parasite genomes	Parasitology Today	2000
Turtle <sup>16</sup>	Anthropological expedition to the Torres Strait	Journal of the History of the Behavioral Sciences	1999
Anonymous <sup>18</sup>	Nutrition and long-term space travel	Life Support & Biosphere Science	1999
Anonymous <sup>17</sup>	Fecal peril and travel medicine	Bulletin de la Société de Pathologie Exotique	1998
Anonymous <sup>12</sup>	Leprosy and tropical skin diseases	Tropical Doctor	1992

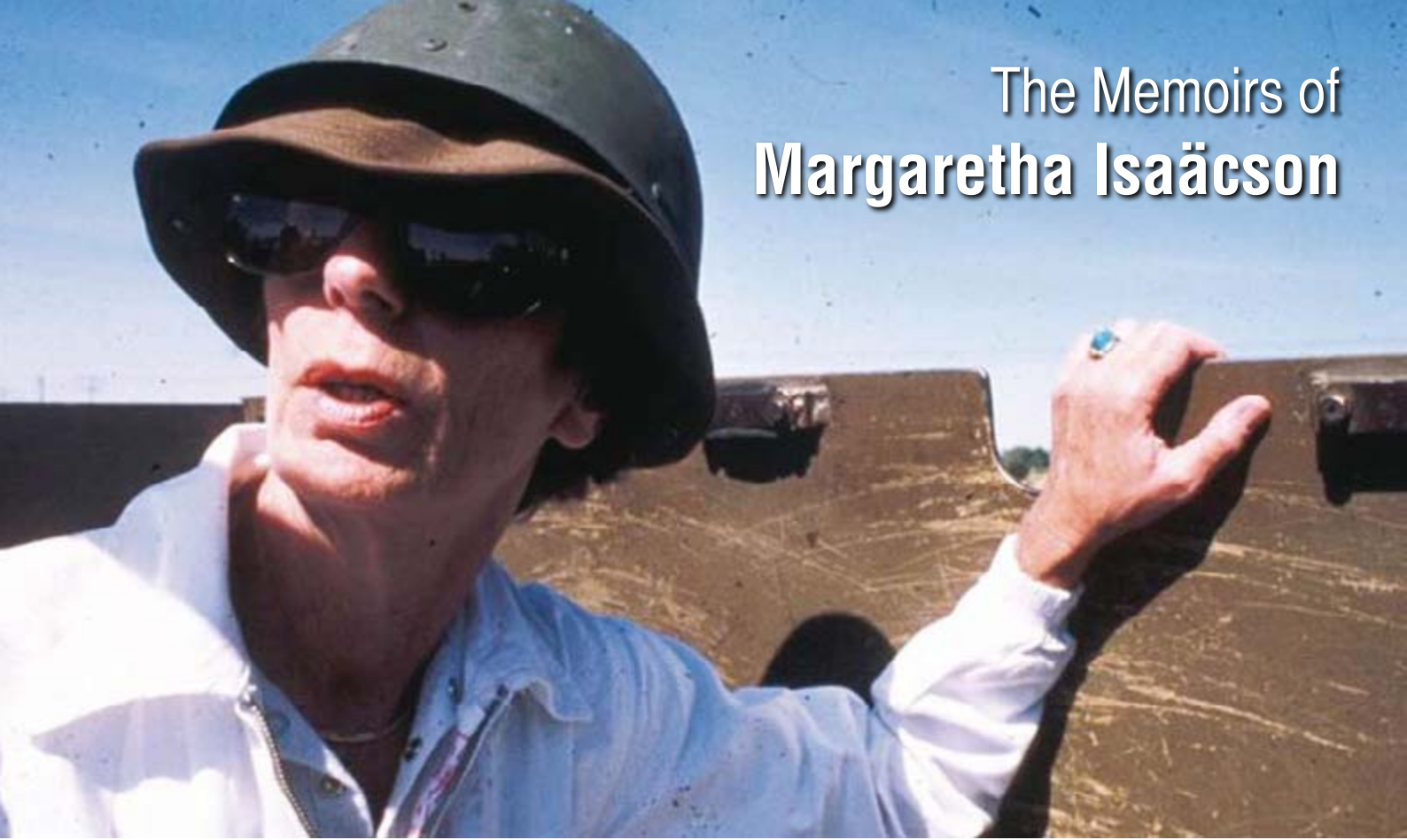
**Table 2.**  
Some Special Issues Previously Published in the Field of Occupational Health or Allied Disciplines

Author(s)	Title or Theme of the Special Issue	Journal in Which it was Published	Year
Smith et al. <sup>22</sup>	Health care workers' occupational health	Industrial Health	2007
Nester <sup>31</sup>	Vulnerable worker populations	AAOHN Journal	2005
Kovera <sup>32</sup>	Psychology, law and the workplace	Law and Human Behavior	2004
Reneman & Dijkstra <sup>33</sup>	Functional capacity evaluations	Journal of Occupational Rehabilitation	2003
Westman & Piotrkowski <sup>21</sup>	Occupational health psychology	Journal of Occupational Health Psychology	1999
Anonymous <sup>25</sup>	Future work life	Scandinavian Journal of Work, Environment and Health	1997
Anonymous <sup>34</sup>	Psychophysiology of the workload	Biological Psychology	1996
Anonymous <sup>20</sup>	Cross-cultural occupational therapy	American Journal of Occupational Therapy	1992
Winn <sup>35</sup>	Ergonomics and the older worker	Experimental Aging Research	1991
Anonymous <sup>36</sup>	Technology in occupational therapy	American Journal of Occupational Therapy	1987

**Table 3.**  
Special Issues Dedicated to Emeritus Individuals in Tropical, Travel or Occupational Medicine, or Related Fields

Author(s)	To Whom the Issue was Dedicated	Journal in Which it was Published	Year
Anonymous <sup>26</sup>	Harry Hoogstraal	Journal of Parasitology	2000
Anonymous <sup>25</sup>	Lennart Levi <sup>37</sup>	Scandinavian Journal of Work, Environment and Health	1997
Anonymous <sup>24</sup>	Joseph Rutenfranz	Ergonomics	1993
Frank <sup>23</sup>	Irving Selikoff	Environmental Research	1992

# The Memoirs of Margaretha Isaäcson



## **PART 1: BUBONIC PLAGUE** *The Vietnam Connection - The Start of the Monkey Trail*

I began my serious involvement with bubonic plague in 1967 in the San Francisco laboratories of Professor Karl F Meyer, or KF, as he was generally known. Those who knew him, and they were many, mostly loved or detested him, though all respected this great, but outspoken and overpowering scientist. KF walked in the footsteps of Robert Koch, Ignaz Semmelweis, Joseph Lister, Louis Pasteur and other trail-blazing medical investigators whose work led to the unravelling of the ways in which infectious diseases are spread and how they can be prevented. A veterinarian, KF studied various zoonoses, being infections, which under natural conditions can be transmitted from animals to humans. Thus anthrax, rabies, leptospirosis, brucellosis, botulism and tetanus were some of the many diseases to come under his scrutiny. Bubonic plague became one of his chief interests. Since his 'retirement' in 1954, KF had published more than 200 scientific papers. I first met KF in his laboratory in 1967, when he was 83 years old, still working a regular 10-hour day! His death in 1974, just 3 weeks short of his 90th birthday, resulted in an obituary in *The New York Times* which stated, inter alia: "Dr. Karl Friedrich Meyer was regarded as the most versatile microbe hunter since Louis Pasteur and a giant in public health. As a youth in Basel, Switzerland, pictures of the Black Death, or plague, so fascinated him that he became an outdoor scientist instead of following in the aristocratic business world in which he grew up. He told friends that in choosing to become a veterinarian he could 'be a universal man and study all diseases in all species.'"

At the beginning of my own odyssey in the investigation of epidemic diseases I was greatly privileged to spend several months under KF's guidance, and became one of his devoted acolytes. Our friendship and professional collaboration lasted for the remainder of his life. San Francisco, 1967, was

the centre of the universe for the hippies, the flower children, and the draft dodgers. The Vietnam War had been in progress for some years and plague had raised its ugly head once again, adding to the misery of the Vietnamese people, and a threat to US forces deployed in the region. A plague vaccine made of killed plague bacilli was in common use at that time. But, although it was moderately effective, it had to be administered as a course of three, rather painful injections. Reaction to the vaccine by recipients was often severe and even disabling. They frequently refused the second and subsequent shots and therefore developed inadequate protection against plague infection. KF had, for some years, actively investigated the development of a vaccine consisting of an attenuated strain of live plague bacilli. It was hoped that this vaccine would give good protection after a single injection without the side effects of the killed vaccine. The idea was not new. The French and the Russians had used live plague vaccines, but these had some of the same disadvantages as the killed version.

Whilst I concentrated on the basics of mastering the latest immunological techniques of investigating plague, KF continued the development and testing of his live vaccine, which he had designated EV-51f, in monkeys and other animals. Some of his monkeys had been imported from Uganda. The vaccine studies were still in progress when I returned home to South Africa, greatly enriched by the vast experience as well as the philosophies of my new mentor. Back at the South African Institute for Medical Research (SAIMR), I wasted no time introducing the new technology into our own plague research programme. I was fortunate in having Thora Crowngold as plague laboratory technologist at that time. She brought a sense of total commitment to her work. Her ability to anticipate the next step in various procedures much increased the safety of working with highly dangerous bacteria such as *Yersinia pestis*, the plague bacillus. Thora soon became proficient in the newly introduced procedures.

During August, 1967, a few months after my return, the scientific world was shaken when twenty-one laboratory workers of the Behring Werke in Marburg, Germany, became ill with a serious infectious fever. Their work

had involved contact with blood and organs of African green monkeys, which had been killed and their kidneys harvested, for the commercial production of cell lines. Such cell lines were, and still are, essential for the isolation and identification of certain viruses from sick people and animals as, unlike bacteria, viruses cannot grow on artificial culture media and need living cells for their survival. All the patients had had contact with dead monkeys or their tissues. A doctor and a nurse caring for some of these patients then became ill. Five patients eventually died. By the third week in September the epidemic seemed to be over with all the surviving patients having recovered.

At about the same time as this epidemic in Marburg, six persons, including 4 monkey handlers, a doctor and a pathology assistant, became ill with a mysterious fever at the Paul Ehrlich Institute in Frankfurt, Germany. Two of the six patients died. Concurrent with the two German outbreaks, a veterinarian and his wife came down with a similar illness in Belgrade, Yugoslavia. The Health Protection Institute employed the former where he had carried out autopsies on 5 dead monkeys. His wife, who nursed her husband during his illness, had contact with his blood. A hitherto unknown virus was isolated from patients in all three outbreaks. It was also cultured from a few of the implicated monkeys. The virus was named Marburg (vervet) virus and the disease Marburg virus disease, initially known as green monkey disease. All the animals implicated in Marburg, Frankfurt and Belgrade were traced to a single consignment of monkeys imported from Uganda where they had been trapped in the Lake Kyoga area. Immediate international reaction to these outbreaks, which had involved a total of 31 cases with 7 deaths (a 23% mortality rate), included the introduction of much more stringent controls over the importation, handling, transport, distribution, housing and quarantine of monkeys from Africa. More than 2 months after the onset of illness in the last of the Behring Werke cases in Marburg, the wife of one of the recovered employees became ill with Marburg virus disease. She was the first and only patient who had not had direct contact with infected monkey materials or with sick persons. Virus transmission by sexual intercourse was suspected and confirmed by isolation of live Marburg virus from her husband's semen.

Meanwhile, in San Francisco, KF's plague vaccine trials were yielding disappointing results. Indications were that EV 51f was not safe in African green monkeys. The trial needed to be repeated before definitive conclusions, which could lead to the vaccine being rejected for human use, could be drawn. The recent Marburg virus disaster had, however, affected the supply of African green monkeys. Moreover, monkey facilities complying with the stricter containment requirements were not available for the number of animals involved. I received an invitation from KF to join his vaccine study and to repeat the trial in South Africa, where vervet monkeys are an indigenous species and did not need to be imported. Moreover, Dr Malherbe of the SAIMR subsidiary, the Poliomyelitis Research Foundation (PRF) had shown that South African vervets seemed to be free of infection with the Marburg virus. Funds to finance the trial were to be supplied by KF. Essentially, the project was to be done in two phases, of which the first was the safety trial in which monkeys would be vaccinated with EV-51f, followed by a period of clinical observation to determine adverse effects, if any. The second phase involved infection of vaccinated and unvaccinated monkeys with plague bacilli to determine the efficacy of the vaccine. The safety trials were carried out at the PRF. For the efficacy trials, special high security monkey quarters were designed and constructed at the SAIMR. Frank Hallet, who was a zoologist doing postgraduate research on plague, Thora and I carried out the vaccine project.

In nature, bubonic plague is transmitted between animals and to humans from its wild rodent host by means of flea bites. But, if a bubonic plague patient develops the pneumonic form, one of the most serious and highly

lethal complications of this disease, the infection can spread from one person to the next by inhalation of infectious airborne particles. When plague-infected materials or animals are not handled with utmost caution, the chief danger to laboratory workers is not flea-borne or bubonic plague, but the airborne pneumonic variety. Clearly, work with experimentally infected plague monkeys is especially hazardous, as the animals cannot be controlled as easily as a culture contained inside a bottle. Monkeys jump around, generating clouds of contaminated dust particles. There is also a risk of being scratched or bitten.

The vaccine trial was instrumental in the improvement of our biohazard containment facilities and operating procedures, which enabled us to work with highly dangerous bacteria and viruses without endangering the lives of ourselves or the community. We wore protective clothing comprising gowns, gloves, masks, caps and shoe covers as well as goggles to protect our eyes. All procedures on the monkeys, such as clinical examination and drawing of blood for laboratory tests, were done under anaesthesia. There was a growing awareness in myself and in some of my colleagues that the welfare of laboratory animals in general left much to be desired. The project became instrumental in my personal decision not to use monkeys for experimental purpose again. In years to come, we established an Animal Ethics Committee at the SAIMR, one of the earliest in existence in South Africa. This committee acted as a watchdog to ensure that animal experimentation was performed only if necessary, and then only in a humane manner. Thus it contributed to a gradual decrease, and even a complete discontinuation of animal use in several departments. It is especially relevant that, as early as 1919, KF had published a report on the humane use of experimental animals. The results of our plague vaccine trial in monkeys were almost identical to those obtained by KF in San Francisco. The vaccine was indeed not safe in that several monkeys died from the effects of the vaccine alone. Furthermore, not all vaccinated monkeys were protected against subsequent plague infection, indicating its limited effectiveness. Plans to use the EV 51f vaccine in humans were abandoned and the old killed vaccine, warts and all, remained in use.



## Three Dozen White Mice (or, mouse power)

It was one of those crisp, sunny, but frosty highveld winter days in 1968 and right there on Hospital Hill in Johannesburg the icy wind whistled between the high rise buildings. The laboratories in the original building of the SAIMR, with their large airy rooms and high ceilings, designed by Sir Herbert Baker, were marvellously cool in summer. On that day, the poor heat generated by a few small, portable electric heaters, made work an act of courage and dedication. On my arrival, I saw a parcel marked with a red express label on a workbench in the in-tray of the plague laboratory. I opened it and found a note, typed on a machine that had clearly seen better days, and a few boxed tubes with blood, well wrapped in protective wadding. According to the note, the blood came from patients hospitalised at the Mohaleshoek Hospital in south western Lesotho. Diagnosis was stated to be 'typhoid fever with buboes'. The laboratory was requested to test the blood for plague antibodies. Something about that diagnosis didn't make sense. Buboes, the medical term used for enlarged, inflamed and often very painful lymph glands, typically occur in patients with bubonic plague. They are the result of bites by plague infected fleas and are certainly not found in typhoid fever. On the other hand, some of the other features of typhoid, such as high fever, generalised body aches and pains with malaise and lack of appetite occur also in plague and, indeed, in many other infections. So what was going on here?

A telephone call to Dr Nesor, the pathologist in charge of the SAIMR bacteriology laboratory in Bloemfontein, yielded a few more items of information. He informed us that a typhoid fever epidemic had been in progress for some months in south western Lesotho. The nature of this epidemic had been confirmed at an early stage of the epidemic when *Salmonella typhi*, the causative bacillus, had been isolated from the blood of several patients. Other blood tests done at the same time had shown the presence of specific antibodies against typhoid fever. No doubt about it, a diagnosis of typhoid had therefore been firmly established. Dr Nesor stated that, subsequently, more blood specimens trickled into the Bloemfontein laboratory with requests for serological tests on additional patients suspected of having typhoid fever. On the face of it the epidemic seemed to be smouldering on. A few days before the Johannesburg plague laboratories became involved, a swab and two blood samples had arrived in Bloemfontein for bacteriological examination. The label had not indicated the part of the body from which the swab had been taken but the diagnosis was filled in as being 'typhoid with buboes'.

On microscopic examination of the material on the swab the technologist had seen some small bacilli but she had apparently not succeeded in growing these on culture media. Dr Nesor wondered whether these small organisms might be plague bacilli and telephoned the Mohaleshoek hospital to try and obtain more clinical details on the patient. But, there was no further information other than that these patients, like all the previous ones, had responded very well to treatment with chloramphenicol, a broad spectrum antibiotic commonly used in the treatment of typhoid fever and many other systemic infections, including plague. In fact, both patients had meanwhile recovered and been discharged from hospital on that very morning.

Thora Crowngold, who was the chief plague technologist, and I set up a haemagglutination test for plague antibodies on the two blood samples and the following day both were positive. These results were highly suggestive of plague but in the sixties, unlike today, the technology to determine how long plague antibodies had been present, had not yet been developed. It was possible that these patients had been ill with plague at some time in the past, perhaps many years earlier, but that their current illness was due to some other infection. The positive antibody result was telephoned to the hospital, in itself a major feat in view of the telephone services of the time. The message that these two patients might have suffered from bubonic plague and not typhoid fever caused something of a stir in Mohaleshoek. Not long afterwards an official invitation arrived from the Lesotho Ministry of Health asking us to investigate what now appeared to be an outbreak of plague, rather than typhoid fever.

On Sunday, Thora and I took the overnight train to Bloemfontein. We

arrived the next morning around 4 o'clock, frozen stiff since the railway carriages weren't heated any better than our laboratories. Mr Hendriksen, a health inspector, met us and took us off for a most welcome hot breakfast followed by a briefing session at the local offices of the Department of Health. We continued our journey to Mohaleshoek by road. Not long after leaving town, we hit dirt roads and drove through clouds of red dust to the border post at Makhaleng Bridge. Another 10 kilometres or so and we entered Mohaleshoek, a small, rather dull and unappealing rural settlement. After having presented our credentials to the local Sotho Chief, who assured us of his full cooperation, we booked into a small inn where we stayed for the duration of the investigation. The following morning we went to the Mohaleshoek Hospital where we found more patients, with a revised provisional diagnosis of bubonic plague.

*What is plague, and where did it originate? Since biblical times, and probably long before, plague has been well known and greatly feared. Small mammals such as various wild rodents, hares and rabbits are considered to be its natural reservoir. From time to time, in some regions every year and in others at long intervals of a decade or more, an outbreak of plague occurs in a wild rodent population. Such an epizootic (the animal equivalent of an epidemic) usually results in the death of most members of the affected animal colony. Fleas are infected when ingesting blood from the animal hosts, on which they live and feed. Spread from sick to susceptible healthy animals or humans then occurs via infected fleabites. Whereas most plague-infected animals are fated to die, this is not the case with infected fleas, many of which can survive and remain infectious for a year or longer. Long after an animal colony has all but died out as the result of a plague epizootic, infected fleas may remain in the abandoned burrows of the almost extinct colony and keep the plague reservoir latent, but inactive.*

Sometimes, an affected colony of wild rodents, such as gerbils, is situated close to human habitation. It can then happen that infected fleas, hungry and deprived of their natural food source, find their way onto domestic rats, mice and even cats which, like the Trojan horses of Greek mythology, serve to introduce the enemy, in this case the plague bacillus, into a human community. In historical times, this scenario often affected large towns and cities. The Black Death of the Middle Ages, which claimed many millions of lives, is a good example of this. Today, with rodents being far less numerous in urban areas as a result of anti-rodent measures, and with the widespread use of insecticides, plague is rare in large urban conglomerates, but still affects rural communities in Africa, Asia and the American continent.

At the Mohaleshoek Hospital we found several plague patients in various stages of illness. When the preceding typhoid epidemic was diagnosed,

the community had been advised to treat their drinking water prior to use. This had resulted in a decline in the number of typhoid cases. This decline was obscured by a concurrent, but undiagnosed outbreak of plague. The similarity of some of the symptoms of these two diseases was responsible for the health authorities' assumption that typhoid was continuing despite appropriate control measures. The latter, mainly based on improved food and water hygiene, are great for controlling typhoid, but do nothing for plague. Whilst the plague patients in the hospital had been responding well to chloramphenicol treatment, the unsuspected epidemic continued to smoulder in the villages in the highlands of Lesotho.

We had meanwhile been joined by Dr David Davis, an ecologist and authority on animal reservoirs of disease and the mechanisms in which various diseases spread in these reservoirs. Dr Q Qhobela of the Lesotho Ministry of Health completed the team. With the plague patients clearly being correctly treated, our first priority was to assess the situation in their mountain villages. Convalescent plague patients told us that other people in their villages had become ill with swellings (buboes) in their groins or armpits and that many, sometimes whole families, had died. Even more ominous were reports of people with respiratory symptoms but no swellings, and who died very quickly, often within days of onset of illness. A full-blown plague epidemic seemed to be in progress in remote mountain villages with elements not only of bubonic plague but also of pneumonic plague, throwing an entirely different and far more serious light on this epidemic.

When bubonic plague patients are not treated promptly, plague bacilli leave the buboes and invade the blood stream, causing the rapidly fatal septicaemic or pneumonic forms of plague which spreads very quickly from one person to the next by the airborne route. Rats and fleas are no longer involved and, therefore, buboes are not seen in these patients. They are highly infectious and need to be strictly isolated. Even with antibiotic treatment, the death rate is very high because of the rapid course of illness. Were we up against a pneumonic plague epidemic? The answer came to us whilst we were still busy questioning patients at the hospital. A messenger came from one of the villages requesting transport for a teacher who had become ill that morning, shortly after arriving at the local school to teach his class. He was said to have a cough and chest pain. There were no further details. A land rover ambulance was duly despatched with a nurse to collect the teacher. The vehicle returned at about 3 o'clock that afternoon. While the nurse helped a man, whom we assumed to be the sick teacher, out of the vehicle, he coughed, collapsed and died. Only 6 hours had elapsed since the onset of his illness.

We seemed to have our answer. The symptoms and the galloping evolution of the teacher's fatal illness, given the confirmed presence of plague in

his village, could only mean that the epidemic had assumed the primary pneumonic form. Although I had dealt with plague before this was the first time, and thankfully the last, I was to see a pneumonic outbreak. Thora and I spent some time setting up our laboratory equipment. We had brought all the essentials to carry out plague diagnostic work. This included small bottles and petri dishes with special media for the growth of the plague bacillus, thin wire loops with which to plant specimens on the media and tubes containing a variety of chemicals with which to identify any bacterial growth. There were even some cages with white mice. Laboratory animals were still commonly used for diagnostic purposes and the inoculation of suspect material into animals was considered a necessary procedure for the laboratory confirmation of plague and other infections such as tuberculosis and tetanus. We were not happy about this and did not intend to use the animals if we could get the answer by growing the plague bacilli from patients' blood or other specimens on artificial culture media. Nevertheless, the animals were there and, before long, would prove to be worth their weight in gold, although not in a way we could have foreseen. To protect ourselves whilst working in the laboratory, there were surgical gowns, masks and rubber gloves as well as several disinfectants in case of accidental spills. A good supply of tetracycline, the antibiotic of choice against plague, was also included. The nurse who had accompanied the dead patient was one of the first recipients.

The Mohaleshoek Hospital allowed us to use a tiny disused brick building comprising of two rooms. It had piped water and electricity but no heating of any kind. We had brought a bottled gas supply to feed our bunsen burners which are indispensable in bacteriological work. As we did not have a portable incubator, we intended to find a safe place in the well-heated hospital where we could incubate our precious cultures. The little building, basic though it was, became a fine makeshift laboratory for the duration of our stay. Having set up our laboratory facilities, our plans to assess the extent of the problem in the affected area were unexpectedly frustrated by heavy snowfalls during the night. The following morning we made a half-hearted attempt to get into the mountains but the paths and tracks were completely obscured. Fortunately, as the snow was unseasonable, it soon thawed but this caused us to cool our heels around Mohaleshoek for a day or two, after which we were able to go with the other team members to the plague affected area. Part of the way was covered by Landrover, but the final kilometre or so to the first village to be visited, was traversed on foot, climbing and carrying our equipment.

The terrain was rocky with little in the way of trees or other vegetation. Small villages consisting mainly of sturdy, thick-walled thatched rondavels (huts) and the odd rectangular iron-roofed building were scattered up against the hillsides. Goats and chickens scratched around for something to eat.



Most of the people were wearing the typical Basotho dress, comprising a thick, colourful blanket wrapped tightly around the shoulders and pinned with a huge safety pin resembling those used by the Scots on their kilts. The unique, intricately woven Basotho hat completed the costume. Some of the men were riding the tough little Basotho ponies, the only practical type of transport in the Maluti Mountains. The scenery, though stark and bare, was majestic with distant snow-covered peaks standing out against the deep blue sky. Our guide indicated that we were approaching the first plague affected village. We stopped and waited whilst he asked the way to the house of the village Chief. Having been taken to the latter and duly exchanged greetings, we stated our business and asked for permission to question villagers and take specimens. This done, we commenced the tedious work of piecing together what proved to be a classic plague epidemic.

The epidemic affected some 15 villages in an area of about 1000 square km and with a population at risk of about 10,000. The first cases had died in Kechane as early as November 1967. Since there was no obligation on village chiefs to notify deaths immediately unless foul play was suspected, the authorities were not aware of anything unusual about these deaths. Similar accounts of sudden death after an acute short illness were obtained in other villages, in one of which 7 members of one household had died. The sad histories always included a description of patients developing buboes or a respiratory illness or both. In one village, we were told how illness had broken out after several inhabitants had attended a funeral of relatives in another village.

Bubonic plague epidemics are often preceded by large-scale rodent mortality, which in its turn tends to be preceded by a rodent population explosion. Inhabitants of rural areas are commonly quite in tune with what is happening to other elements of the ecosystem of which they are themselves a component. Thus, in rural plague endemic areas the people are often quite aware of what is happening to the wild rodent population in their area. On this occasion we obtained initially no indication of anything unusual about the local rodents. When direct questions were asked about animal population dynamics, an old man stated that, some months earlier,



there had been so many rats that they had attacked his chickens. But since then the rats seemed to have disappeared. A schoolteacher stated that, on three occasions, she had found dead rats near her house. We asked her to take us to her house. The soil around her dwelling was compacted and swept clean. Within a short time we found a deserted gerbil colony showing all the signs of inactivity - its members must have died out. Other villagers then told us of dead rodents found in or near their homes. We found the corpses of some dead rodents and scraped fleas out of the deserted rodent burrows to take back to Mhaheshoek for examination in our makeshift laboratory.

We returned at dusk and Thora and I decided to start immediately with the processing of our precious dead rats and the collection of fleas for isolation of the plague bacillus. We had also collected a number of blood specimens to be tested for plague. Having processed all this material, we walked across to the hospital to find a suitably warm place for overnight incubation of our cultures. To our dismay we were unable to find any place that was both warm enough and secure. The entire hospital was crowded with patients and staff. Only unheated areas were secure from interference. The realization that we should have anticipated this problem did not help us in our quest for safe incubation facilities. We slunk back to the laboratory for a brainstorming session. It was late in the evening and we were hungry and cold. The mice were scratching around in their cage and, while talking about our dilemma, we proceeded to water and feed the animals.

'They seem to be happy enough', I remarked, 'at least they're warm'. 'Thora, the mice are warm!' I shouted and swung round to face her. 'I heard you the first time' she answered. I went and fetched a thermometer from our equipment box and shoved it into the cage. The mercury steadily crept up and stopped at about 18 degrees centigrade. Not enough. 'Thora, please go find an old blanket at the hospital, and perhaps some newspapers. We are going to make the world's first biological incubator outside the womb'. Thora caught on to my enthusiasm. 'Just in case they ask' she said, 'what are we supposed to want the blanket for?' 'Tell them we're cold'. 'And the newspapers?' 'We are hungry for news. And talking of hungry, hurry up or we'll find ourselves without dinner when we get back to the inn'. Upon which Thora, who, tiny as she was, had an appetite for two, ran out of the door. I took a good look at the cages. There were 3 small cages with 10 mice each and there was a larger cage containing 2 guinea pigs. By the time I had finished, the guinea pigs were re-housed in a small cage each and all 30 mice were in the guinea pig cage. Thora returned, having succeeded in getting both blanket and newspapers. When she saw the new animal arrangements, she was horrified. 'You have gone and mixed up the males and the females in the same cage,' she exclaimed. 'So what, give them a break! Anyway, it may warm things up a bit more'. Together, we placed the big cage in a large carton, which we had first emptied of its contents and then placed on its side. There was now a gap of about 10 cm between the top of the cage and the top of the box. We then stuffed the gaps at the sides with newspaper and wrapped the whole contraption in the blanket, leaving a small space for air. In the space on top of the cage there was enough room for our culture media, together with the thermometer. It was around 9 o'clock before we returned to our lodgings where the others had arranged for dinner to be kept for us. Afterwards, Thora and I returned to the laboratory and checked the thermometer. It read 22 degrees Celsius. This was not the ideal temperature of 25 degrees required by plague bacilli, but we hoped for the best.

During the next few days, we visited several other villages and found some more patients whom we took to the hospital. They included a little boy, aged 4 years, who was clearly in the recovery phase without having received treatment. Together with the other team members and local health inspectors, we set up a plague control program in the affected

villages. This consisted of large-scale fumigation of affected villages with insecticides. We used DDT, which is still used in many parts of the world for plague and malaria control programmes. One of the main advantages of DDT is its residual effect, whilst the amount used in such programmes, in contrast to agricultural use, causes little or no harm to the environment. Another important component of the program was the administration of a course of oral tetracycline to all persons in the affected villages. Some of these people were probably in the incubation period of the disease and tetracycline would rapidly eliminate their infection. Two days after we had inoculated our culture media with material from rats and fleas, we sighed with relief when we found a very delicate growth of tiny colonies, typical of the plague bacillus. After transfer of the growth into the liquid reagents, and after further incubation on top of the mice, we were able to conclude that our growth was indeed the plague bacillus, *Yersinia pestis*. These positive culture results provided confirmation that plague had been the cause of the epidemic. The control programme brought the epidemic to a rapid and abrupt halt. Although the number of patients notified totalled 125 with 49 deaths, this was probably a gross under-estimation of the true extent of the epidemic, since it was likely that an unknown number of the earlier cases had been erroneously diagnosed as having typhoid fever.



## The Case of the Farmer's Cats

In November, 1972, when an elderly farmer in the Graaff Reinet district of the Eastern Cape, put out food for one of the farm cats, he noticed that all was not well with her partially-weaned kittens. They were not as active and playful as usual and seemed uninterested in their food. He thought no more of it until that evening when, on entering the shed where the cat and her brood normally lived, he found one of the kittens dead. Ollie, who, according to his wife, was concerned about all animals, large and small, scratched around till he found some sulfonamide tablets, left over from the

time a few months ago when the local doctor prescribed treatment for a sick farm labourer. He broke one of the tablets into small pieces and pushed a piece down the throat of each kitten and, for good measure, also gave some to the mother cat. She usually roamed around during the evening when she would bring back dead rats for the kittens. That evening, she had not gone out, and she too did not look her normal self. In the process, one of the kittens bit him on the thumb. Over the next two days the kittens developed what the farmer described as 'swollen heads' and soon died.

The farmer became ill two days after being bitten, by which time the small wound on his thumb had healed. Large, painful glands, surrounded by extensive swelling of the tissues, appeared under his left arm. As he was feverish and had started vomiting, he went to see his doctor, who thought that he had developed sepsis as a result of the cat bite. The doctor's alternative diagnosis was cat-scratch disease, an uncommon infection acquired from cats which, although carriers of the bacteria causing this disease, usually do not become ill. To cover either of these two possibilities, the doctor prescribed tetracycline, a broad-spectrum antibiotic, in the dosage regimen usually given for most infections susceptible to this drug. His condition improved over the next few days. Then his fever shot up, and as he had developed severe headache with confusion and delirium, he was admitted to the Provincial Hospital in Port Elizabeth. Various blood tests showed nothing abnormal except for an increase in his white cell count, indicating a bacterial infection despite the finding that a blood culture was negative. Because of his continuing fever and mental state, a lumbar puncture was performed and yielded spinal fluid that was yellowish and very clouded, indicating that meningitis had developed. The spinal fluid was also cultured for bacteria but, to everybody's horror, instead of growing meningococci or pneumococci, the two commonest causes of meningitis in adults, *Yersinia pestis*, grew in profusion. The culture was sent, post haste, to our laboratory in Johannesburg for confirmation of the diagnosis.

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# The Memoirs of Margaretha Isaäcson

## PART 2: MARBURG VIRUS

(February 5th, 1975). It was hot on the road. Michael and Diana had been walking for hours, humping their backpacks on their way south. They were tired and looking for a shady spot to rest, but were reluctant to move too far off the road where they might not be seen by some friendly driver willing to give them a ride. The two Australian hitchhikers trudged on in silence along the quiet road in Rhodesia (now Zimbabwe). Early that morning they had left Victoria Falls (known in the local language as Mosi-oa-Tunya, 'the smoke that thunders'). They had been lucky so far. There had always been a driver willing to stop and take them part of the way. That morning at Victoria Falls had been no different. One of the many touring cars gave them a ride south, but dropped them off some distance before the turn off to the Wankie (now called Hwange) Game Reserve. That had been several hours ago and the few cars going in their direction ignored their outstretched thumbs.

In the distance a filling station appeared on the other side of the road, the petrol company's logo unmistakable. As they approached, a steep hill rose up on their left, close to the road. Diana thought that they would find some shade among the trees at the bottom of the hill. The two young people increased their pace and within a few minutes reached the hill. Thankfully they shrugged out of their heavy backpacks and dropped them on the shoulder of the road. Michael led the way to a tree with roots that were exposed for a depth of about 1.5 meters, forming a kind of hollow seat in amongst them. The shade was deep and cool there. Side by side, Michael and Diana relaxed and listened to the birds. The filling station, which they could see across the road, did not seem to be very busy. Few cars stopped off and they were all going towards Vic. Falls. Diana lent her head on Michael's shoulder and closed her eyes. Suddenly Michael jerked and pulled up his tee shirt. He asked Diana to have a look at his right side where something seemed to have stung him through his clothes, and pointed to his right flank. "Here," he said, "can you see anything?" Diana saw a red flare spreading on the skin where Michael's finger pointed. She looked all over for whatever could have caused this but found nothing. No insect scurrying away, no snakes or anything else to be seen, only the birds up in the branches. "Just a red mark spreading out a bit on your skin, but nothing else," said Diana. They stood up and searched around some more, but found no sign of life amongst the roots. "Oh well," said Michael, let's get our things and start walking again." As they hoisted their backpacks, a car stopped and offered them a lift. The two got in and were on their way again.

The countdown had begun

(February 15th, 1975). At about 10 o'clock on that Saturday morning activities were hotting up in the Casualty Department of the Johannesburg General Hospital in South Africa. Most of the examination cubicles had their curtains drawn. Nurses, doctors and medical students were scurrying in and out of the cubicles, carrying clipboards, pushing instrument trolleys or carrying trays. A tall young man walked slowly through the entrance, supported by a petite blonde looking anxiously up at his face, which was grimacing with pain. A nurse quickly led the two into an empty cubicle and helped the young man onto the couch. Minutes later, an admission clerk entered with a sheaf of papers and sat down to take the patient's particulars. Diana, the girl, provided most of the information. It emerged that the young man, named Michael, was 21 years of age and a draughtsman by profession. They were both from Australia and were hitchhiking their way around the world. During the past few months they had been living in Johannesburg, which they used as a temporary base from which to make short trips through southern Africa. In fact, they had just returned from a 9 day tour through Rhodesia. Michael was then seen by one of the casualty officers who found him to have a high fever with severe muscle pains, nausea and vomiting, warranting admission as a hospital patient. Significantly, he had taken no antimalarials.

Michael's condition rapidly deteriorated and, in view of his visit to an area of Zimbabwe where there had recently been an epidemic of bubonic plague, I was called in consultation. When I saw the patient he was desperately ill. Despite his association with a plague-affected area, I did not consider this disease to rate very high on the list of diagnostic options. He had a tender skin lesion just above the right hip which, he told me, was the result of having been stung or bitten by some unidentified agent whilst travelling through Rhodesia. Despite negative laboratory tests for malaria, plague and typhoid fever, but in the absence of any other clinical diagnosis, the clinicians treated the patient with chloroquine for malaria, and with ampicillin and chloramphenicol. The latter are antibiotics known to be effective against a variety of bacterial infections, including typhoid



fever and plague. Michael's condition deteriorated rapidly. On the next day, Sunday, he developed severe diarrhoea and on Monday a generalised measles-like skin rash appeared. Underlying the individual raised small papules of the rash, the skin was a vivid red colour which blanched when I pressed it with my thumb. During the course of that day, Michael became lethargic, he started bleeding and his kidneys began to fail. On Tuesday, the haemorrhage became quite uncontrollable despite intensive treatment and his kidneys went into complete failure. He died that evening after further massive bleeding into the gastrointestinal tract and the lungs.

I participated in the postmortem examination and the most striking and alarming finding was the extreme degree of destruction of the patient's liver. This had not been apparent before his death, as jaundice, one of the common features of severe liver impairment, had been relatively mild in this case. On the day after Michael's death, Diana became ill with symptoms similar to those of Michael, but did not report these until a day later. In view of the possibility of a serious infectious disease, Diana was admitted to the Johannesburg Fever Hospital on Hospital Hill. She was nursed in strict isolation and all the nurses and doctors who had had close contact with Michael were placed in quarantine. They volunteered to look after Diana. Blood was collected from all those in quarantine and baseline laboratory tests were done. Should any of them have become ill, the results of repeat laboratory tests were to be compared with the baseline data and clearly indicate if the illness was likely to be serious. Or so we hoped!

Microscopic examination of Michael's liver tissue had shown several changes that are usually found in viral infections that cause severe liver damage. This finding, together with Diana's illness, dramatically affected the diagnostic possibilities and, for the first time since Michael had been admitted to the hospital, the possibility of a viral haemorrhagic fever, especially Lassa fever, loomed very large in the minds of the various doctors and scientists involved. Although Lassa fever had hitherto only been known to occur in West Africa, its wild rodent host, *Mastomys natalensis*, occurs throughout most of the African continent. This small animal is also the host of bubonic plague and had been implicated in a recent plague outbreak affecting the Wankie area which had been visited by the two Australians. Inevitably, the media got hold of the story and matters were getting somewhat chaotic with 35 nurses and doctors in quarantine, reporters besieging the hospital and clogging the telephone lines demanding information. Media accusations of a 'Lassa cover-up', whilst doctors were scratching their heads for a diagnosis, further aggravated the situation. A search was launched for Lassa convalescent plasma for Diana and on February 24th, Dr Lyle Conrad of the Centers for Disease Control (CDC) in Atlanta, Georgia arrived from the United States with a supply of Penny Pinneo's plasma. It was infused immediately into Diana who by then was into her 6th day of illness. At this relatively late stage we were concerned about the effectiveness of this treatment, always assuming she did have Lassa fever, still an unconfirmed working diagnosis. Meanwhile, virus studies were in progress at the Poliomyelitis Research Foundation (PRF) in Johannesburg and at the CDC in Atlanta, Georgia, on blood and other specimens from both Michael and Diana.

On Wednesday, February 26th, Sister Megan Cruickshank left her quarters in quarantine to go on duty in Diana's room. Megan had nursed Michael during the last 2 days of his illness at the Johannesburg General Hospital a few blocks away. She also assisted in the doctors' attempts at resuscitating him just before his death. Megan then sat up all night consoling Diana who, lonely and in a foreign country, had just lost her only friend and travel companion and could not stop crying. Throughout the night Megan had disposed of tissues used by Diana for blowing her nose and drying her tears. She had not hesitated to volunteer for nursing duties when Diana herself was hospitalized. Some hours after coming on duty that night of the 8th day of Diana's illness, Megan fainted briefly and then vomited. Feeling much better and not wanting to disturb her colleagues, she did not report her symptoms but finished her spell of duty. The following night Megan again went on duty but, at midnight, she went back to her room, feeling ill and suffering a backache. By the next morning she was feverish and, on examination, was found to have signs and symptoms resembling those of Michael and Diana. Worse, her blood test results on comparison with her baseline results 4 days earlier were quite abnormal and indicative of a viral infection.

Megan's condition deteriorated and she started showing signs of



impending haemorrhage. She, too, was therefore given a unit of Penny Pinneo's plasma. Two days later the CDC reported their Lassa fever tests to be negative and the following day informed us that they had found a virus, identified as Marburg virus, in our patients' specimens. This was a totally unexpected finding which hit us like a bombshell. Marburg! Where had Michael picked this up? How? When? This was bad news for the two sick girls, both of whom had received Lassa plasma. This, all of us knew, was of no value against the Marburg virus. Behringwerke in Germany, when contacted, immediately flew a supply of Marburg plasma to South Africa but, by the time it arrived, Megan's condition had begun to improve. It was decided, therefore, not to administer the plasma.

At this stage it became clear that there would be no specific treatment that could be relied on to attack and kill the virus responsible for this infection. The girls' only chance of survival would therefore depend on meticulous, ongoing monitoring of various organ functions and managing clinical problems as they presented themselves, or in anticipation. This approach required a large team in support of the core formed by the clinicians responsible for the daily evaluation, treatment and general management of the patients. The laboratory monitoring required medical specialists and technologists in microbiology, biochemistry and haematology. Although this was no different from the requirements of any other patient in intensive care, the suspected highly hazardous nature of the causative agent necessitated a great deal more than normal precautions in the processing of patients' blood and other body fluids. Although we did not know it then, the various procedures and guidelines that we (and a few other centres in the world which had to deal with similar patients) laid down by trial and error, were to form the basis for the safe handling of AIDS material during the nineteen eighties.

Lyle Conrad and I, the epidemiologists in this scenario, put our heads together. Clearly, we had a unique situation on our hands in that Michael was the first known victim of Marburg virus disease to have acquired his infection, not in a laboratory under artificial conditions like the German cases described earlier, but in nature, possibly directly from the natural reservoir host or perhaps via an insect vector or perhaps - what? We decided not to miss this opportunity to unravel the as yet unsolved questions surrounding the source and the route of transmission of the Marburg virus. Lyle scribbled on a piece of paper and came up with a graph depicting the dates of onset of illness of the three patients. "Look," he said, "Michael became ill on the 12th of February, Diana on the 19th and Megan on the 26th. That indicates a probable incubation period of one week for each of the two girls. Now all we need to know is where Michael was about one week before he became ill and 'X' marks the spot. Simple." According to Prof W Hennesen of the Behringwerke in Marburg, the incubation period of their original cases had ranged from 3 to 8 days.

It was now 15 days since the onset of illness in Diana who, fortunately, was well into her convalescent phase. Lyle and I spent many hours with Diana, going over her and Michael's travel itinerary again and again. She readily made available their photographic films, which we sent for development in the Institute's photographic department. We hoped they would yield some clues. They didn't, but they refreshed Diana's memory about events during her trip. We asked Diana where she and Michael had been on the 5th of February. Apparently, they had flown that day from Kariba to Victoria Falls where they spent the night at a rest camp/caravan park. They departed the following day and hitchhiked to Gwaai River. We decided to investigate the

Australians' entire trip through Rhodesia, but concentrate on the period surrounding the 5th of February.

It so happened that the 'sting' inflicted on Michael occurred on the day they left Victoria Falls (i.e. 6 days before onset of his illness). We prodded and urged Diana to try and remember everything she could about the circumstances surrounding the 'sting' or 'bite'. "We were sitting under a tree." "Where?" "Alongside the road from Victoria Falls." "Which road?" "The one to Bulawayo." "Whereabouts on that road?" "Somewhere near the Wankie Game Reserve." "Can you remember where exactly?" "No." "Try to remember. Was there any landmark, any building or any road sign?" Diana frowned in her concentration. "Oh, yes," she exclaimed, "there was a filling station across the road and another road that turned off there." "What did the countryside look like? Was it flat or hilly or what?" "It was hilly. There was a hill with lots of baobab trees right behind us where we were sitting in that hole." "What hole?" "Under the tree. It looked weird. The roots were bare, as if the soil had been washed away. Maybe during a storm. And we crawled in and sat among the roots." "Why?" "We had walked and walked and no car stopped to pick us up. It was the middle of the day and the sun was burning hot. There was no shade anywhere except under that tree. It was the only one along the road with really deep shade and from where we could still spot cars travelling in our direction." "What happened after you sat down there?" "Well," said Diana, "we were sitting there for a long time and suddenly Michael jumped. I asked him what the matter was and he said that something had stung him on his side. I pulled up his tee shirt and there was a large patch of red spreading on his skin." "Did you look for whatever it was that had stung him?" "Oh, yes, we both looked all over and around us but we didn't find anything." "Did you take any photographs there?" "No."

I telephoned Dr Eric Burnett-Smith, the then Secretary for Health in Salisbury (now Harare) Rhodesia, and told him the whole story as well as our strong suspicion that the virus had been picked up in Rhodesia. Dr Burnett-Smith was greatly concerned and offered official assistance in any investigation we wished to carry out. Lyle and I had discussed doing an on-the-spot investigation and Dr Burnett-Smith's offer was therefore doubly welcome. With his assistance we assembled a field team including, beside ourselves, Dr Eric Burnett Smith, Mike Crees (an entomologist), and 2 health inspectors: Piet Geldenhuys from South Africa and Jimmy Johnston, a Rhodesian. Early in March this team spent a fortnight tracing the footsteps of the two hitchhikers. We were able to confirm their itinerary accurately by checking various visitors' books and hotel registers along their route.

We were especially interested in the 'sting site' and had no difficulty identifying it from Diana's description. The hill with the baobab trees was locally known, not surprisingly, as Baobab Hill. There was a hotel on top

where we stayed during our investigation of the site. The tree was still just as she had described it. It provided more shade than any of the other trees along the road and had a deep recess in amongst its roots where the soil did indeed appear to have been washed away. Whilst we were busy inspecting the tree there was a sudden rumble and a train appeared, no more than a few meters above our heads. Diana had not mentioned any trains. We scrambled up the hillside and found a railway track running along the contour of Baobab Hill and disappearing in the distance. Subsequent enquiries revealed that the tracks forked nearby, one set going to the Wankie Collieries a little distance away, and the other going north to Victoria Falls where it crossed the Zambezi River via a bridge into Zambia.

We spent some days collecting a variety of arthropods that could potentially have served as virus transmitters. Our collection comprised various mosquitoes, biting flies, ticks, wasps and spiders. The only arthropod present in great numbers were funnel-web spiders, of which we collected no less than 140 specimens. In this locality, as well as in the various other sites visited, local people were questioned and blood samples were collected from numerous persons, ill as well as healthy. We got blood from cattle and from a lot of wild rodents that we had captured. It was of great interest to me that most of the rodents in our cages were juveniles. Having investigated the previous year's plague outbreak in the adjoining Wankie game reserve, I knew that there had been a major rodent die-off in this area due to plague but the population was evidently re-establishing itself. "Lyle, what if some insect, animal or whatever, fell or jumped off a southbound train and encountered our two hitch hikers sitting just a few feet below waiting to be bitten or stung?" I suggested. "My line of thought, exactly. Let's go find out," answered Lyle. Since the two Australians had visited Victoria Falls on the border between Rhodesia and Zambia, we set off to see what we could find there and to have a closer look at trains. Rhodesia, having defied world opinion in 1965 when Prime Minister Ian Smith unilaterally declared his country's independence was, in 1975, becoming increasingly isolated and crippled by economic sanctions. Its northern border with Zambia, formed by the Zambezi River, was heavily guarded by Rhodesian troops along the south and by Zambian troops on the opposite bank. Repeated incursions into Rhodesia by armed insurgents were associated with escalating deaths and destruction of property. The lovely old colonial Victoria Falls Hotel had remained unscathed, though at least one nearby hotel was badly damaged by mortar fire.

We used the grounds of the Victoria Falls Hotel for a preliminary inspection of the railway bridge across the Zambezi. A long freight train drew across from our side and halted on the bridge, facing Zambia. The security situation prevented anyone but train drivers from gaining access to the bridge. A Rhodesian Army spokesman had informed us that anyone else appearing from the Rhodesian side would be shot at by the Zambians. Presumably the reverse also applied. With the aid of binoculars we saw



that the wagons were heavily loaded, but it was impossible to identify the nature of the supplies which were covered with tarpaulins. Two men climbed out of the locomotive and started walking back into Rhodesia. We continued watching the train through binoculars. There was no movement. It was hot and humid, and the shrill, high-pitched chirp of cicadas mingled with the sounds of hundreds of birds restlessly darting from tree to tree. Upstream of the bridge, across its width of almost one and a half kilometres, the Zambezi River crashed more than 100 meters over the edge of the gorge, providing a thunderous backdrop of noise to the orchestra of bird and insect sounds immediately around us. A permanent cloud of water droplets, thrown up high into the sky, could be seen from a long distance away.

Suddenly, out of the bush on the Zambian side, a troop of chacma baboons skipped and ran onto the bridge and, quick as a flash, jumped onto the freight cars. They tugged and tore at the tarpaulins and grabbed handfuls of what we were now able to identify as yellow maize. With both hands they stuffed the maize into their mouths until their cheeks bulged. Obviously, the baboons had become accustomed to 'unloading' the freight cars for their own benefit and we wondered why the train was left unattended on the bridge. The time had come to talk to the Rhodesia Railway officials. As we left, the baboons were running freely between Rhodesian and Zambian territories. The following morning, Mike located the local railway office and found a most obliging official who offered to assist us. The official told us that the trains ran regularly with goods, mainly maize, from South Africa to Zambia and on to 'other countries up North'. This was interesting, since both Rhodesia and South Africa were subject to trade sanctions by members of the OAU (Organization of African Unity).

"Do the trains carry freight on the return trip?" Lyle wanted to know. "No, they always come back empty," was the reply. "Do you have a returned train somewhere around here for us to have a look at?" I asked. "Sure, one got in earlier, want to come now?" We accepted enthusiastically and set off for the railway siding where the train in question was parked. Lyle and I climbed into several freight cars and looked around. The floors were covered with thick layers of dust and broken maize kernels. In the dust were numerous animal footprints, as well as rodent and other droppings and traces of what looked like nesting materials. As we had suspected, animals besides baboons evidently frequented these trains. My question if the trains were cleaned out on their return was answered in the negative. "So much for disinfection of aircraft from Nairobi and Kinshasa," I remarked. "With the trains bringing in who knows what in the way of disease vectors, why worry about aircraft?"

When we raised the matter of trapping and bleeding baboons and monkeys on the bridge, we learnt that this would require the joint approval and assistance of the Railway Police, the Rhodesian Army and the Nature Conservation people. The Rhodesian members of the team, under the leadership of Dr Burnett-Smith as Secretary of Health, soon arranged the collaboration of all concerned. In fact, they were a little too helpful for my liking. "Why trap the baboons?" commented a wildlife representative. "We'll shoot them for you - much quicker and simpler." "You're not serious," I said, aghast. As discussed earlier, I had enough monkeys on my conscience and I wasn't about to add to my burden of guilt. "It's no problem, we'll gladly do it, there are too many of them and they've become a nuisance, raiding and looting the trains" "There is to be no shooting," I said, "we will trap, bleed and release". "Margaret," said Eric seriously, "it would really be a lot safer to take their advice. Remember, this is a war zone and trapping operations will take a lot more time and increase the danger of attack." "No shooting," I repeated obstinately. I was adamant and no amount of argument could change my mind. In the end, and to my great relief, my colleagues gave in.

Someone in the party wondered aloud why the trains were just abandoned to the baboons, obviously for hours on end. Mike Crees, as always, knew somebody with answers and went off to make enquiries. He returned before dinner and told us a rather hilarious story. "It appears," he said, "that there is an unwritten agreement between the two countries that, sanctions or no sanctions, the food shortage in much of sub-Saharan Africa is such that the importation of cheap South African produce is absolutely essential. It was decided that as long as it was done discreetly, the trains would continue to run with the quiet connivance of all countries concerned in the deal. There would be no people on board other than the two engine drivers

needed to operate the train. The idea was for the South African railway men to be relieved by Rhodesians on the South Africa/Rhodesia border and for the Rhodesians to be relieved in their turn by Zambians, on reaching Zambian territory," Mike said as he upended his beer can. "All went well for a while until suddenly, one fine day, when the train reached Zambian territory the Rhodesians were roughly hauled off the train and thrown into a Zambian jail. Rhodesia immediately stopped the transport of produce until further notice and demanded the release of the two men. Furthermore, they conveyed to the Zambian authorities that no more Rhodesian railway staff would be allowed to take trains into Zambia. Zambia suggested, via the grapevine, that maybe the trains should, in future, be fetched from Rhodesian territory by their own men. Negative, was the Rhodesian response. Stalemate! With evident relish, Mike took another swig from his beer and settled himself more comfortably.

"To solve the problem," he said, "the railway authorities of both sides devised a scheme that would be acceptable to both Zambians and Rhodesians. A white line was to be painted across the exact centre of the bridge and Rhodesian train drivers would in future reverse the train up the bridge until some of the cars were on the Zambian side of the white line. Without having to cross into Zambian territory, the drivers would then be able to uncouple the locomotive and take it back into Rhodesia. That done, a Zambian engine driver was to connect a locomotive to the Zambian end of the string of freight cars and haul the whole lot off the bridge into Zambia. That was the basic theory. In practice, a Zambian locomotive was not always immediately available and the freight cars often stood on the bridge, unattended, for many hours. This is where the baboons entered the picture. They quickly got wise to the fact that there was food for Africa to be looted."

Primate trapping cages were provided and, fortunately, we had brought a supply of Sernylan, a veterinary tranquilizer suitable for monkeys, as well as all the other equipment needed to take blood from animals. The following morning we obtained permission to go onto the near side of the bridge, which was normally, a restricted area. The train had disappeared during the night. A couple of game rangers assisted in the trapping of the baboons, whilst a platoon of soldiers kept watch. With the aid of a sliding partition in the cages, the occupants were brought up tight against the front of the cage and quickly injected with Sernylan. The tranquilizer acted rapidly and injected animals soon flopped down and lay motionless in the cage. They were then taken out of the cage, placed on top and I would draw a sample of blood from a vein at the front of the elbow, much the same as in humans. Having done this, we placed the animals on the ground in the shade of a large tree and stayed with them until the effects of the drug wore off. When the baboons had fully regained their senses, they calmly walked onto the bridge and clambered down its massive steel supports.

Suddenly we saw several human shapes in camouflage uniform spread out and take up positions along the opposite bank of the Zambezi. They were armed and, when an armoured troop carrier made an appearance, we judged the time ripe for a strategic withdrawal. We hastily beat a retreat into the bush with our blood samples and equipment. That afternoon, Mike Crees came back from the railway office with another tale. A Zambian railway official had telephoned his Rhodesian counterpart and asked what we had been doing to their (sic!) baboons. He suspected us of having fitted them with radio equipment and of using the baboons for spying on Zambia. The Rhodesians had a difficult time convincing the Zambians that we had done nothing of the sort but, to our relief, the Zambians decided to let the matter rest. The next morning we left the Victoria Falls area where we were rapidly outstaying our welcome with our kind Rhodesian hosts.

We made for Gwaai River and Kyle Dam National Park, which were another two stops on the Australians' itinerary. At Gwaai River, the two had spent the night on the lawn of the local hotel which was situated about 200 meters from the river. We had a look around, but found nothing unusual other than a tame zebra grazing on the lawn. From there we proceeded to the Kyle Dam National Park where Michael and Diana had visited a small private game reserve. For the last part of their way, Paul Bosman, who at that time was associated with the running of the reserve, had given Michael and Diana a ride. Paul took pity on the pair and offered them a hot meal on their arrival at his home in the reserve. The meal included venison in the form of eland steaks. The eland is the largest African antelope and may have horns measuring more than one meter in length. In some parts of the world they

have been domesticated like cattle. Could the eland have been the source of Marburg virus disease? We rejected the idea almost immediately. After all, Paul and a friend had shared the meal. Moreover, Paul and his staff had dressed, cut up and frozen the carcass. If anybody were to become infected by the meat, Paul would have been a prime candidate. Nevertheless, we took a sample of his blood and of the frozen eland meat still remaining in the deep freezer, just in case.

Before dinner, Paul had taken his two young guests on a short tour of the reserve and Diana had told us about a tame civet cat that was kept in a wire-fenced enclosure. Both she and Michael had been close to the animal. Although they had not touched it, they had touched parts of the enclosure and the animal had come close to them on the other side of the wire. We asked to see the civet, which was a large animal, more than a meter in length from nose to tail tip. Beautifully marked in black, grey and white, it came quite close to us and seemed unafraid. Civets, contrary to their common name, are not cats, but belong to the mongoose family. They don't even look like cats, having a long body with short legs and an almost dog-like face, like most mongooses. Paul told us that his dog had suckled the civet in its infancy, together with two orphaned vervet monkeys.

We decided to obtain blood from all these animals. After some discussion we felt it wiser not to use Sernylan on the civet. Animal species vary tremendously in their reaction to drugs and a tranquilizer that is safe for one may well kill another. We just did not know how the civet would react, but this one, having been hand reared since infancy, should be quite amenable to having its blood taken. Asked if it would be possible to hold the animal securely while we took a blood sample from a vein, Paul did not think this would present any problems. Little did he know! A couple of game rangers wrapped the civet in an old blanket as protection against its formidable, curved claws and I quickly found a prominent vein on a front leg. Before I even touched the skin with the needle, the animal jerked away its paw and started up a deafening screeching that I was sure could be heard within a radius of a hundred miles. Successive attempts to grip the limb resulted in more pitiful yowling, screeching and yelping which did nothing for my composure. Sure enough, within minutes, tourists came running to investigate the cause of the racket. Their curiosity changed to indignation at what they perceived to be cruelty to an animal. Fortunately, at that moment I managed to keep a tight hold on the civet's furry paw and slip the needle into a prominent vein. Within seconds I drew a small amount of blood into the syringe and withdrew the needle. The game rangers released the animal, which ambled off as if nothing had happened. Paul explained matters to the small crowd that had gathered around us. Their anger quickly changed to fascinated interest as they heard about our investigation. We played down the severity of the infection, as we wanted to avoid an exodus of terrified tourists. We then proceeded to tranquilize the two monkeys and to take blood from the game rangers, the monkeys and Paul's dog, a friendly black and white Jack Russell terrier. The dog made my day by licking my face as I drew its blood.

From the reserve we proceeded to the camp at the Kyle Dam National Park where Michael and Diana had spent the night in a chalet. The chalet showed signs of being frequented by bats. We found that the camping

area and the toilets were submerged in water following recent heavy rains. The swimming pool had apparently also been submerged and was badly cracked as a result. The last item on the hitch hikers' itinerary was the Zimbabwe ruins which they visited on their way back to Johannesburg. We were unable to find anything of significance when we, in turn, paid a visit there. Lyle, Piet and I returned to Johannesburg with two cool boxes packed with 178 serum samples on ice. Most of these sera were of human origin. In addition we had the funnel web spiders which we carried frozen in a liquid nitrogen container. We had made arrangements with Jimmy Johnston to collect more sera for us and during April and June a further 356 human sera and 157 from animal, mostly rodents, arrived in the Institute. Marburg virus or antibodies to this virus were not found in any of the material we had collected.

Many years later, when Paul Bosman had already gained world wide fame for his stunning paintings of African wildlife, I visited him at his home in the scenic Hartebeespoort Dam area due west of Pretoria, where he had moved with his wife and small daughter. I recalled the civet incident and asked what had become of the animal. "Come," said Paul, getting up, "I'll show you." He led me to another room where, on the floor in front of the French doors leading into a sun drenched garden overlooking the quiet waters of the dam, lay the civet's skin, beautifully preserved and mounted. I had a vivid sensory image of the civet's vibrant paw in my hand and felt a twinge of sadness. "What happened?" I asked. "One day it just lay there in its enclosure. I think it died of old age", Paul answered. A black and white Jack Russell terrier, arthritic with age, limped into the room and lay down beside the civet skin. The image of a cracked and twisted swimming pool in a Rhodesian landscape ravaged by the forces of nature flitted into my memory. I smiled and gave the skin a lingering look, thinking back over the years to Michael and Diana and wondering what undetected role, if any, the civet might have played in the Marburg mystery.

More specimens of human and animal blood were collected during June and, early in February, 1976, we revisited all the sites again in the expectation that the same general ecological conditions would prevail as existed during Michael and Diana's trip. After all, the activity of the causative agent of Marburg virus disease might be seasonally determined.

No serological evidence of Marburg virus ever emerged.

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# The Memoirs of Margaretha Isaäcson

## PART 3: EBOLA VIRUS

### *Mayinga's Story*

A highly fatal epidemic of unknown origin was rumoured to have been in progress for some time in Yambuku in the Equateur province, northern Zaire (now the Democratic Republic of the Congo), when Sister Mayinga fell ill in the capital Kinshasa, with headache, fever and severe muscle pains. She was employed at the Clinique Ngaliema, a private hospital where she had helped in the care of two sick nuns who had come from Yambuku in the company of a priest, Father A.S., who was also not feeling too well. One of the nuns, Sister Myriam, had died 12 days before Mayinga became ill. At that stage the cause of illness was unknown but the doctors thought it might be malaria or typhoid fever, both of which were very common infections in Zaire. It was hoped that the nuns' tales about 'hundreds of people dying from some mystery illness' would, as is often the case, prove to be grossly exaggerated. Two days after Mayinga became ill, Sister Edmonda, the other nun from Yambuku, also died. Some post-mortem liver tissue, taken from Sister Myriam, had already been sent to the Prince Leopold Institute for Tropical Medicine in Antwerp, Belgium. The medical staff at Ngaliema anxiously awaited the results of laboratory tests on this tissue. Once these became available they would know what had killed the nuns and the correct treatment to be given to Sister Mayinga, whose illness was similar. Furthermore, a firm diagnosis would also enable the health authorities to take appropriate measures to prevent further cases. Meanwhile, a health official had been dispatched to Yambuku to find out the true state of affairs concerning the rumoured epidemic.

Yambuku is a small but lively Catholic mission, more than a thousand kilometers northeast of Kinshasa as the crow flies, and almost a hundred kilometers north of Bumba, which is situated on the northern bank of the great Congo River at a point where it reaches its northernmost position before curving southwest. A thousand kilometres: not an insurmountable distance these days, easily reached by road in two days, by air within two hours. Except that there were no roads, not even a main national artery in Zaire. Unless an uneven, muddy dirt track, frequently crossing little streams, which became roaring torrents when it rained, can be classified as such. Mobutu Sese Seko, self-styled president since 1965, had forcibly

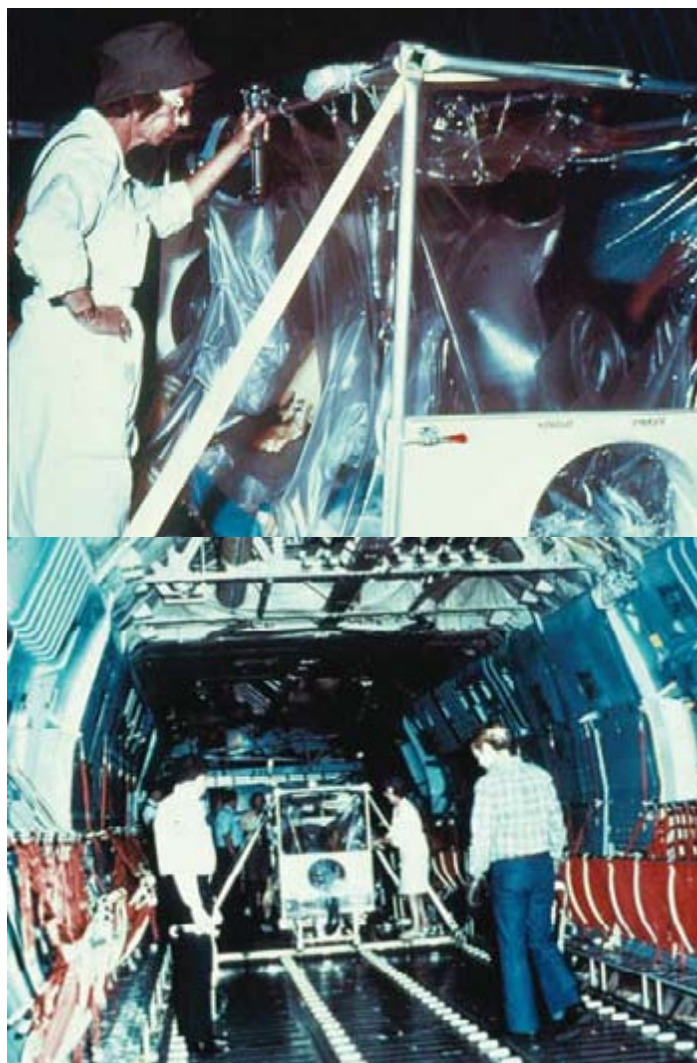


moved whole communities out of the interior of the forest to these ribbons of mud, to live and maintain the track or be without supplies. The villages in this part of the African interior were picturesque with their low rectangular dwellings surmounted by great, overhanging thatch roofs. But the scenes were also those of incredible poverty and hardship. The missionaries seemed to be the sole source of education, health care and, through religion, the illusion of a better life in the hereafter. I had no problem with this. Hope for a better future, whatever its source, had to be better than utter hopelessness.

Immediately behind the dwellings, which were ranged in a single line, also ribbon like, along both sides of the track, the impenetrable rainforest was the ultimate ruler of peoples' lives. No more than 10 or 20 meters into the dense forest, out of sight of government inspectors, stills had been constructed ingeniously, albeit illegally, out of assorted enamelled and galvanised iron kitchen containers and bamboo piping, passively supported by the patient giants of the forest. Plantains formed the basis of the potent local brew, which was consumed on ritual occasions and for relaxation. Many decades ago, Catholic missionaries had arrived with the Belgian colonial rulers in Yambuku where they built a hospital, a school, a convent and a church. The nuns, those with some basic nursing training, battled against malaria, sleeping sickness, yellow fever, loiasis or eye worm (in which the parasitic worms could be seen wriggling their way across the cornea), river blindness (a far worse parasitic disease, responsible for total blindness of 30% or more of the population in endemic regions), and a host of other scourges. The sisters introduced childhood vaccination and taught the villagers a healthier life style. In the school, the teaching nuns

battled ignorance and illiteracy. At the time, South Africa's apartheid policies had already caused enforcement of complete or partial sanctions by members of the Organization of African Unity (OAU). Some form of contact by various African governments nevertheless occurred on a very clandestine basis as certain medical and other forms of expertise and resources were often obtainable from South Africa more quickly and more cheaply than from any other source. Politically, South Africa exploited crisis situations in poverty stricken African countries by making available her advanced resources free of charge, in an attempt to gain Brownie Points. Such assistance was frequently accepted unofficially and on the understanding that South Africans, while present in OAU member states, would maintain a very low profile.

About mid-October I received a telephone call from the Department of Health enquiring whether we had any Marburg convalescent plasma available. I replied in the affirmative and asked what the enquiry was all about. I was intrigued, but not altogether surprised to hear that the party on the other end of the line had merely been instructed to locate a source, if any, of such plasma. I was, however, told to expect a call from the Department of Foreign Affairs. Sure enough, within a very short time, the Foreign Affairs official was on the line. They asked me to confirm the availability of the plasma and whether it could be supplied to Zaire where there appeared to be an outbreak of Marburg virus disease somewhere in the rainforests of the Congo River basin in the equatorial region. The 'most urgent' request had apparently originated in the President's office. No further details were available. By that time I had collected exactly six units of Marburg plasma from Sister Megan Cruickshank, one of our recovered Marburg patients, and I was not about to let go of these on the basis of vague, unconfirmed stories, even if the request did come from the President of Zaire.



I informed the Foreign Affairs official that Marburg plasma is rarer than hen's teeth and that I was quite willing to make it available provided I took it myself to ensure its appropriate use. This proposal was readily accepted by the Zairean government, apparently in view of my previous experience with containment of this disease which, it was felt, would also be useful. Accordingly, on the 16th of October I set off on an Alitalia flight and, after about three and a half hours, arrived at Kinshasa's Njili Airport. When the aircraft door was opened prior to disembarkation, two officials in business suits boarded the aircraft and spoke briefly to the chief purser who then called out my name. With some difficulty, due to a heavy polystyrene cool-box containing the Marburg plasma, I made my way forward through the passengers who tightly packed the aisle, as they had not been given the go ahead to disembark. The two officials, who proved to be Protocol Officers, greeted me and preceded me down the steps at the bottom of which was a black, chauffeured limousine. So far, so good. 'Some low profile', I thought to myself as several hundred passengers' eyes were out on stalks, visibly wondering what that was all about. The limousine drove up to a door in the main airport building through which I was ushered down a corridor and into a very comfortably furnished and air conditioned VIP lounge. A tray with coffee and cakes sat on a low table and my escorts proceeded to make small talk whilst we enjoyed the refreshments and watched the offloading of the plane from South Africa. The contents included crates of onions, marked with a well known South African brand name burnt into the rough, slatted wooden crates. So much for sanctions! Dozens of wire cages containing white rabbits, happily munching carrots and seemingly none the worse for their flight followed the onions. I wondered what fate awaited the rabbits in Mobutu's Zaire. Onions and rabbits - rabbit stew for a special presidential function?

My passport was taken away from me to be returned, so I was told, on my departure from Zaire. After about 20 minutes, a porter entered the lounge with my baggage. The Protocol Officers took me to the waiting limousine where they wished me a pleasant stay in Zaire and instructed the driver to take me to the FOMETRO (Fonds Médicale Tropicale) head office in Kinshasa. On arrival, I was warmly welcomed by Drs Jean Ruppol, Jean Burke, Gilbert Raffier and several other Belgian colleagues, as well as Dr Pierre Sureau of the Pasteur Institute in Paris, France. Dr Ruppol showed me to the room where I would be staying while in Kinshasa. The room was air conditioned, comfortably though staidly furnished with heavy, dark, Belgian furniture - a rather masculine room, I thought. Later I learnt that this was the room of the Belgian Royal Prince, Stephane d'Arenberg, who was also a doctor and the founder of FOMETRO. A great honour, indeed.

*[Margaretha instituted proper patient care and infection control measures at the Clinique Ngaliema, which ended the outbreak there. The crisis triggered a concerted international response, which materialised in the form of a commission to investigate and control the disease-JF]*

The International Medical Commission (IMC) was established with Dr K Nguete, the Zaire Minister for Health ('Commissaire de la Sante Publique') as Chairman and Dr Karl Johnson [chief of the Special Pathogens section, CDC, Atlanta] as coordinator of its activities. Ten Land Rovers, one Alouette and one Puma helicopter and a C130 Hercules transport aircraft were put at the IMC disposal, together with crews, by FOMETRO, WHO and the Zairean Air Force. The air force crews flew when and where it suited them, which rarely coincided with the needs of the IMC. Ludicrous excuses such as a pilot's legs being too short to reach the controls were sometimes given. This resulted in the piling up of essential food, fuel, spare parts and other materials and equipment in Kinshasa and our intermediate base of Bumba. Sadly, the Alouette eventually crashed in dense jungle outside Yambuku, killing all on board. Peter Piot, who was supposed to have been on board,

had refused fly on this occasion as, in his opinion, a threatening thunderstorm made flying an unnecessarily hazardous venture.

The surveillance teams comprised Zairean doctors, medical assistants and nurses who, with the assistance of expatriate epidemiologists, did sterling work tracing contacts of Ebola victims. Initially (in Kinshasa), we distinguished between primary and secondary contacts. Primary contacts were defined as healthy persons who had face-to-face contact with, or lived in the same dwelling as an Ebola patient. Such primary contacts were rounded up and quarantined. Healthy persons who had similar contact with healthy primary contacts were considered secondary contacts and were confined to their own homes where they were visited daily for 21 days. Some 300 secondary contacts were identified in Kinshasa. Subsequently it became clear that all the known Ebola cases had been primary contacts and the tracing and confinement of secondary contacts was discontinued. Just as well, as the sheer numbers of secondary contacts would have made their surveillance an impossible task. Kinshasa was declared free of Ebola infection on November 10th.

At the same time [as the Zairian epidemic], two similar outbreaks occurred in Nzara and Maridi (180 km east of Nzara) in southern Sudan, with 67 and 213 cases, respectively. The Nzara outbreak was centred on a large cotton factory, and the Maridi outbreak on the large local teaching hospital. The overall mortality was 53%. Starting in June in Nzara it spread from there to Maridi, Tembura (1 case from Nzara, 3 secondary cases who nursed the first one), and Juba (4 cases from Nzara and Maridi gave rise to only 1 secondary case). Three of the primary cases in Juba were subsequently flown to the capital, Khartoum (1200 km north of Juba), but no secondary transmission occurred in Khartoum. Thus it was shown here also that actual contact with a case was necessary for transmission. Passers-by, contacts of contacts and even children sleeping in the same room as a case, did not become ill. There was no evidence of airborne transmission. In the vast majority of cases, nursing was a requirement for infection - or,

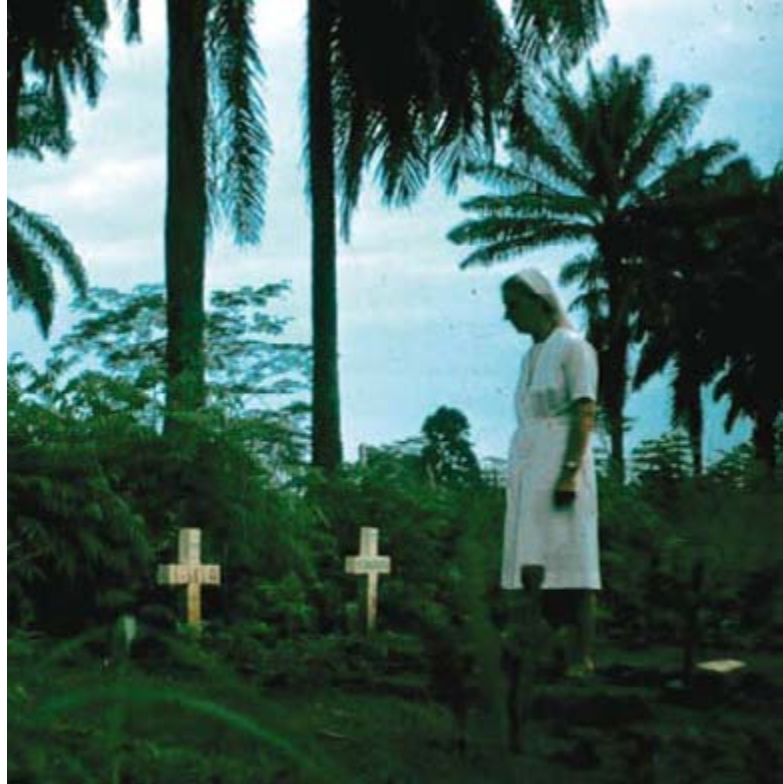


as in the case of Yambuku, actual injection by re-use of inadequately decontaminated hypodermic needles.

Sooner or later I would have to visit the Mama Yemo, Kinshasa's large, new, academic hospital, named after President Mobutu Sese Seko's mother. It was there that the blood transfusion service was located and I was to visit its head, a charming haematologist from the Caribbean whose name escapes me. I'll call him Dr Pedro. Our American colleagues and I had brought equipment with us to enable a plasmapheresis programme to be set up. We had not included a refrigerated centrifuge, as we were all pretty sure that we would find one in Kinshasa, as indeed we did at the Mama Yemo. The plasmapheresis programme and a portable virology laboratory would have to be taken to Yambuku, complete but for a refrigerated centrifuge. Karl Johnson contacted the CDC with an urgent request for such a machine to be flown out. However, there was none available at a moment's notice. The best they could do was 'we will fly one out as soon as possible but it may take a week or 10 days.' We didn't have a week or 10 days to spare with people dying every day. I contacted the Minister of Health, Dr Nguete, who informed me that the only refrigerated centrifuge in existence in Zaire was located at the Mama Yemo blood bank. Enter Dr Pedro. He was reluctant, to say the least, to part with the centrifuge, but we came to an agreement. It would take us another 3 days before we could leave for Yambuku, during which time Dr Pedro would mount an immediate emergency blood donation campaign and stock his blood bank to bursting with blood. In three days' time he would give us his centrifuge and, in return, he would receive a new, state of the art machine when it arrived at Njili Airport from the States.

The deal was struck shortly after lunch and Dr Pedro invited me to accompany him to the market. My rather puzzled look prompted him to tell me that, yes, it was all part of the job (of a haematologist at Mama Yemo) and I would understand later. He did not take off his white hospital coat and I was, as usual, dressed in one of the SAIMR technologists' white uniforms which I found much more comfortable in the hot, steaming Zairean climate than street clothes covered by a long sleeved hospital coat. Off we went to the principal market somewhere in Kinshasa. The place thronged with colourful crowds, mostly of women and children, carrying baskets. Many of the young women sported the Sputnik hairstyle so popular in Zaire and which consisted of a score or more, short, stiff plaits of hair spiking in all directions from the scalp. Suddenly I stopped in horror when we came to several long trestle tables, some covered with what looked like white sheets, others with large banana leaves. On the sheets and the leaves was row upon row of what looked for all the world like dead, newborn babies. Dr Pedro saw my concern and hastened to assure me that these were not human babies but skinned monkeys, a delicacy in Central Africa. The resemblance to human babies was uncanny, the tiny delicate hands and fingers of these creatures were stretched out as in mute appeal.

"What are we doing here?" I asked of Dr Pedro, now angrily. "Not far now," he answered and sure enough, a few stalls further on we came to a table where several, almost new microscopes were displayed. "What the hell?" I thought, but said nothing. The stall owner warmly greeted Dr Pedro and the two started bargaining in French about a price for the instruments. I inspected them a little more closely and saw that they were almost new, and of a very high quality with a well known brand name. Not long afterwards the men had come to an agreement and Dr Pedro paid over the equivalent of something like ten US dollars each. A couple of street kids were instructed to carry the microscopes to Dr Pedro's car. I could not help remarking that, obviously, the microscopes must have been stolen. Even so, the price seemed rather low for such good quality, almost new items. Dr Pedro looked at me and said 'those are the blood bank's microscopes and when you have to buy them back every couple of months, it does



mount up, you know!' He proceeded to tell me that most of his colleagues were regular customers at the market for their own equipment. The traders had a regular income and, if not happy, everybody at least appeared to be resigned to the situation. My thoughts went back to some of the patients at Mama Yemo who told how they had to bribe ward maids to bring them a bed pan and how orderlies would not fetch blood from the blood bank for seriously ill patients until a relative paid them the going rate. The country was rife with corruption, but then, nobody was paid their wages, so bribery was considered nothing less than the collection of one's due pay.

Meanwhile, the President was in Switzerland together, so it was said, with a large retinue comprising his family, friends and enemies. "Enemies?" I asked, amazed. "The only way to prevent your enemies from staging a coup d'etat in your absence is to take them with you wherever you go. That's how Mobutu has stayed in power as long as he has." "What am I doing here in this hell?" I thought once again. But when I was with the patients, and when I saw the nurses and other employees slaving away for little or no material reward, those thoughts would clear like mist under the rising sun. I planned to return to South Africa on 5 November to collect information, equipment and drugs urgently needed by the IMC. Easier said than done! I was delayed at the hospital, from where I went straight to the airport, wearing my white uniform and carrying just a small overnight bag. On my arrival at Njili Airport, I checked in, got my boarding pass and went to Passport Control. I reminded the Immigration Official that they had taken my passport on my arrival in Zaire and they were to please to return it - like right now. They checked through the drawers in the counter, without success. Was I sure that I had not received it back? I was very sure and reminded him also that I was supposed to be a VI Persona Non Grata, and the unofficial, clandestine guest of the Zairean Government. All of which did nothing to resurrect my passport. OK, I told the Immigration Official, I would go back without my passport. "Oh, no, you cannot do that" he said, "the South Africans won't let you in without a passport". I was furious and replied, "You take care of your end and I'll handle the South African officials." With which I swept out of the departure hall, past a policeman who, having watched the altercation, thought better of confronting this angry, but Very Important Persona non-Grata without a passport, but with a boarding pass.

I marched across to the waiting Alitalia flight and boarded the half-empty aircraft. I had three seats all to myself and looked out of the window, keep-

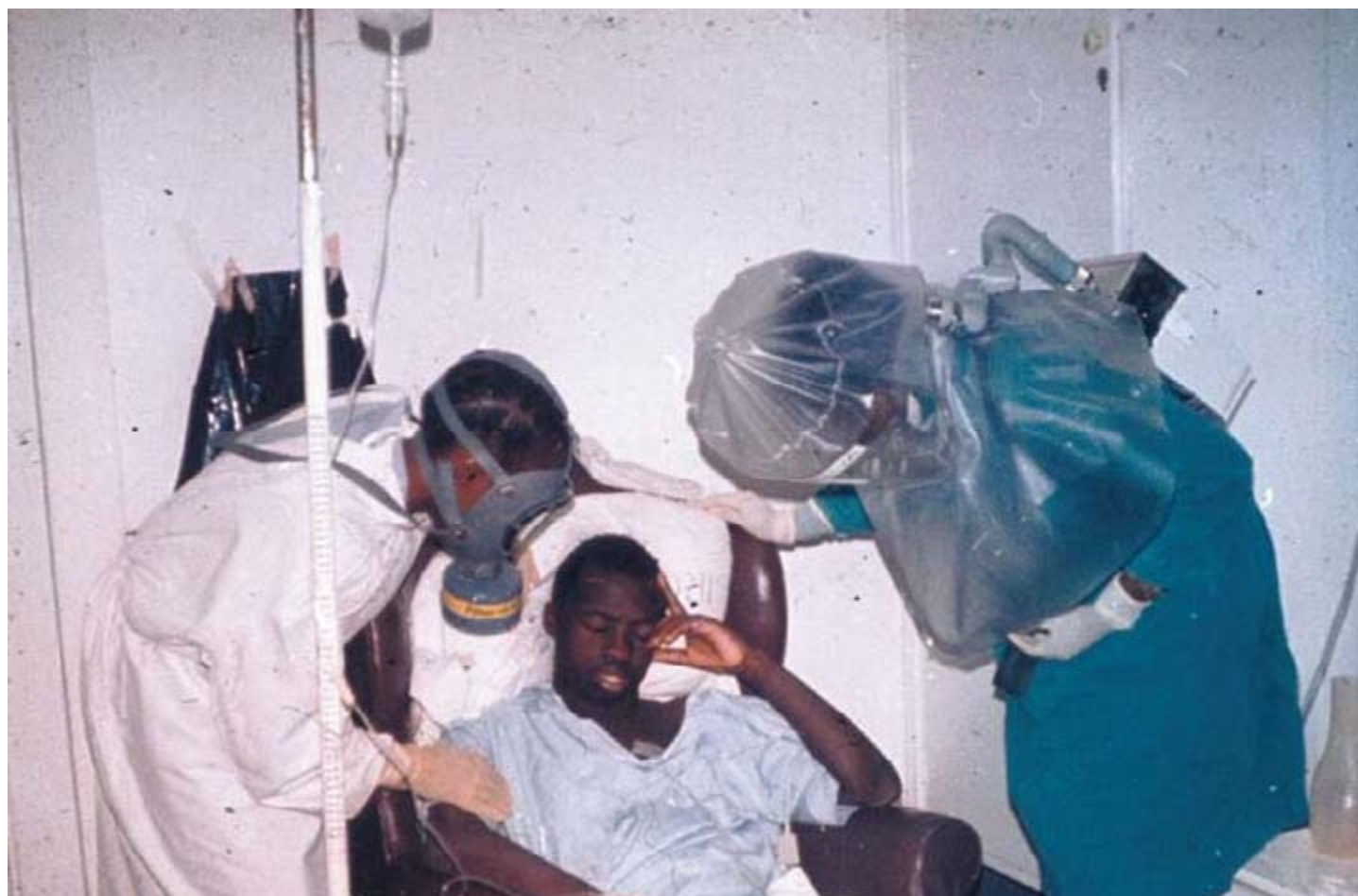
ing my fingers crossed that I wouldn't be hauled off the flight. But I need not have worried, no sooner was I settled in and the doors were locked, the boarding stairs rolled away and the aircraft taxied to the runway. As soon as the 'Fasten Seatbelts' signs went off after takeoff, the cabin crew started taking orders for refreshments. I was still turned away, staring out of the window and planning a strategy for entry at Jan Smuts Airport where, as I well knew, the South African Passport Control officials would play the game according to the book. A voice brought me back to the here and now; "Good afternoon, Reverend Mother, can I get you something to drink?" I looked around as I had not seen any nuns when I boarded, but when I saw the steward giving me a friendly smile, I realised that he had mistaken me in my white hospital garb for a nun. I hastened to set the record straight - no way was I going to miss out on that badly needed gin and tonic! After a pleasant but uneventful flight we landed at Jan Smuts Airport. I sauntered into the Arrival Hall and made a beeline for the office of the Medical Officer of Health, hoping fervently that I would know whoever was on duty. As I knew most of the staff there, I was not surprised when I was greeted by name. From there it was a simple matter to phone Foreign Affairs in Pretoria where immediate arrangements were made with the airport immigration office to issue a set of temporary travel documents. After all, it was Friday and I was booked to return to Zaire on Sunday on the same Alitalia flight.

## ***No Room at the Inn***

Del Conn was one of our genuine volunteers. Not like some of us who didn't really know what we were letting ourselves in for when we rushed out to Zaire. And not like some we recruited and who were paid for their work. Del joined us some days after it became public knowledge that all the wild rumours of hundreds dead in Yambuku were actually true. He had been working in Zaire as a Peace Corps volunteer when Ebola struck. A histologist by profession, he was trained to diagnose disease by microscopic examination of body tissues taken during life, or after death. We

were glad to have him. Guido Vandergroen, who had set up our field virology laboratory, was especially delighted to have an extra pair of laboratory trained hands. Del soon got the hang of the, for him, unfamiliar virological techniques and became an indispensable member of the IMC. Histologists usually work with tissues that have been preserved in a chemical such as formalin as this tends to firm up the material and preserve its appearance, especially its microscopic structure. As an extra bonus, formalin also kills most pathogenic micro organisms. I had a session with Del before he started work with the Ebola material in the laboratory. In microbiological laboratories, you don't want to kill viruses or bacteria; on the contrary, you need to encourage them to stay alive and multiply in order to get enough virus material to enable their identification and other studies. Microbiological work, therefore, is associated with constant danger of infection to the laboratory worker.

I had drawn up a strict protocol for the protection of IMC members. Although we were dealing with an unfamiliar virus, the general principles of infection prevention and control are applicable to any epidemic situation. Vaccination and drug prophylaxis, common and effective measures against many other infectious diseases, could not be practiced in this epidemic - there was no vaccine and there was at that time no effective drug against viruses. It was not until several years later that Joe McCormick, working on Lassa fever in Sierra Leone, was able to show the usefulness of ribavirin in preventing, and curing, that particular viral haemorrhagic fever. Interferon, a protein substance [produced by the body's lymphocytes] known to interfere (hence the name) with viral multiplication, has not lived up to initial expectations for the treatment of viral infections. No drugs and no vaccine - we had to fall back on physical barriers to prevent ourselves from becoming infected. Normally, the choice of physical barrier/s depends on the mode of transmission of the micro organism involved. There are basically four different ways in which spread can take place, any or all of which may operate with any given micro organism. For example, plague can be



acquired by a fleabite (vector-borne) or by inhalation (airborne), cholera by ingestion (food and water-borne) and AIDS by sexual intercourse (sexually transmitted) or by needle-stick (blood-borne). What about Ebola?

We did not know the source of this virus, let alone how it was transmitted from the source to humans. There was no certainty until much later during our studies that airborne transmission did not play an important role with the Ebola virus. We suspected early in our investigations that person-to-person transmission occurred and that this was accomplished via direct contact with blood and other body fluids, and could occur also by the use of contaminated syringes and needles. We believed this to be the principal route of transmission but couldn't be sure until all the data had been collected and analysed. By that time the epidemic would be over - we hoped. The vector-borne route seemed unlikely but the airborne route could not be altogether excluded. Physical barriers were therefore indicated mainly to prevent direct contact or accidental injection with infectious materials, or their inhalation. Essentially, this boiled down to a need for protective clothing. Having anticipated this before leaving South Africa, I had brought a large supply of all kinds of disposable protective clothing, including surgical gowns, gloves and masks. I had also brought a few respirators of the 'gas mask' type, fitted with cartridges designed for protection in bacteriological warfare situations. The American contingent brought further large supplies of protective clothing and a variety of other equipment. All IMC members were requested to wear protective clothing when working with patients or with infectious materials in the laboratory. In addition, they were issued with thermometers and instructed to take their temperatures daily and, most important of all, report any kind of illness at the earliest opportunity to myself or Karl.

Of course, any one of us could come down with an illness unrelated to the Ebola epidemic, such as 'flu, gastroenteritis, typhoid, malaria and various other tropical infections. Some of these would be easily and quickly differentiated from Ebola, others very difficult or time consuming. It was therefore important to minimize also, as far as possible, the risks of acquiring other infections, especially those with symptoms similar to those of Ebola. Malaria and typhoid, being endemic in Africa and with symptoms and signs closely resembling those of Ebola virus diseases in its early stages, were especially important in this regard. Prophylactic antimalarial drugs were therefore issued to those IMC members who did not already take them. We also took precautions to ensure the safety of food and water so as to minimize the risks of typhoid and similar infections. All this seemed to work quite well and for some 6 weeks there were no incidents of illness in the teams. Before we left Kinshasa for Yambuku we were informed that Geoff Platt had become ill in England. Geoff was a scientist working at the high security virology laboratory at Porton Down in England. Some of the material from the Zairian and Sudanese patients had been sent there, as well as to the CDC in Atlanta, for diagnostic purposes. During the morning of November 11th, at the Clinique Ngaliema, I received the following telex from Professor Jack Metz, then Director of the SAIMR in Johannesburg:

***'Worker in UK pricked finger while working with infected material from patient with Ebola disease ex Sudan. You will receive request for convalescent serum via British embassy, Kinshasa.'***

I had only just started the plasmapheresis programme in Kinshasa as it had taken some weeks for the IMC field teams to identify and confirm recovered cases of EVD in the Yambuku area. Further delays were caused in arranging for some of these convalescents to be flown to Kinshasa but two, Sukato and Sophie, had fortunately arrived some days before the rerouted message from Porton Down, UK. Sukato, a male nurse from the Yambuku mission hospital, had recovered from his Ebola infection on October 12th and I had already obtained several units of blood from him. Sophie was the widow of the Yambuku index case (Antoine) who had lost both her husband and one of her 8 children to the Ebola virus. To save time, I immediately established that the next flight to Europe would leave Kinshasa's Njili Airport that evening and, anticipating agreement by the other IMC members wrote a covering letter to go with the plasma. Towards midday, Karl Johnson and some of the others returned to FOMETRO and we discussed the telex from Dr Harris, the then Director of the high security Microbiological Research Establishment (MRE) at Porton Down. It was agreed by all that the plasma should be made available, and the cooler box containing Sukato's plasma was rushed to the airport to catch the evening flight. The British Embassy had meanwhile also made contact with us, but they had little to add to our information.

Later, it became evident that the infected MRE staff member had become ill on that same day, having infected himself six days earlier. He was placed in a Trexler isolator where he was nursed throughout his illness. As it was possible that our convalescent plasma still contained a few viable virus particles, I informed Dr Harris that the IMC recommended that, in order to kill any virus present, the plasma should be heated at 60°C for 30-60 minutes before administering it to Geoff, their patient. This was done and one unit of plasma was infused on October 13th, and a second unit three days later. The possible presence of Ebola virus was, however, not the only reason we





suggested heating the plasma. There was a high carriage rate of hepatitis B virus in the healthy African population and heating would also take care of this as well as any other micro organisms that might be present. AIDS (Acquired Immune Deficiency Syndrome) was unknown in 1976. It was only in 1981 that AIDS was first recognised. It took another 4 years before tests became commercially available to identify HIV (Human Immunodeficiency Virus, the cause of AIDS), and antibodies against this virus. Sera, collected by the IMC during the Ebola outbreak in 1976, were, during the nineteen eighties, subjected to HIV testing and some were found to be positive for HIV antibodies. Therefore, heating of the Ebola convalescent plasma before its use proved, in retrospect, to be a sound precaution.

Clinically, the plasma infusion did not result in any noticeable improvement in Geoff's condition. If anything, it deteriorated and a second unit of plasma was administered on the fourth day of illness. Recovery only set in from the tenth day of illness. Notwithstanding the apparent lack of clinical response, the number of Ebola virus particles in Geoff's blood had dropped dramatically from its pre infusion level of about 30000 to fewer than 10 per millilitre on the day after the first plasma infusion. Although the patient had also received interferon, which was then an experimental antiviral drug, it was generally believed that the reduction in virus particles was a response to the plasma rather than to the interferon. The British health authorities traced all Geoff's contacts, which included his wife and children, fellow workers at the MRE and members of a sports club that he had visited during his incubation period. All these people were strictly isolated in their own homes where they were subjected to medical surveillance twice daily for 21 days. No secondary transmission from this single case occurred in the UK.

Sukato and Sophie were very unwilling to remain in Kinshasa for more than one week as they had domestic responsibilities back home in Yambuku. The urgency is well illustrated by the case of Sophie who, having lost her

husband and one child, had another 7 children to care for. Our original plans made provision for flying any recovered patients from Yambuku to Kinshasa where they could be plasmapheresed. We had not reckoned with the reluctance of the patients, most of whom gave us several good reasons why they could not, or would not leave to go on a wild goose chase to Kinshasa, a thousand kilometers and more from home. If the mountain would not come to Mohammed, Mohammed would have to go to the mountain, necessitating radical re-planning. For the plasmapheresis programme to be a success it became clear that it would have to be moved to Yambuku. A quite sophisticated laboratory, complete with enclosed working cabinets, fluorescent microscope, laminar flow facilities and electronic blood testing apparatus and a refrigerated centrifuge were flown, together with a Landrover or two, on board our Hercules to Bumba. At the Yambuku mission, where the equipment was to be used, an additional power supply was needed for which two large generators were purchased, with funds from USAID, in South Africa during my short return visit. The generators, which were also on board, were subsequently installed by two Zairean electricians who also rewired the entire Yambuku hospital. The electricians were so anxious to return to Kinshasa that they completed the job in two days, a feat that must surely be unique.

Yambuku hospital was the 'epicentre' of the Ebola epidemic, which involved more than 50 villages in an area of some 10,000 km<sup>2</sup> around Yambuku. Ten IMC surveillance teams had interviewed about 33000 families in 530 villages before declaring the epidemic to be over. Life was hard for the IMC in Yambuku. We started work early in the mornings, largely to escape the worst heat and incredibly high humidity of the Congo River basin. We had none of the comforts that we took for granted at home. Our living quarters were adequate, thanks to the hospitality of the nuns of the mission. As the only female doctor, I was given a room in the convent that had belonged to one of the dead nuns. This, too, was more than adequate. We had our



meals with the nuns who were accustomed to having their main meal at midday. The hot and heavy, though tasty Belgian meals took some getting used to in that climate. I think the nuns welcomed our presence, which to some extent took their minds off the enormous tragedy that had befallen their small community. At meal times and after work, we temporarily filled the gaps around the large wooden refectory table. Despite the warm hospitality extended to us, it did not take long for boredom to set in during leisure hours. Most of us occupied ourselves updating our records or reading the few paperbacks that circulated. And always, we speculated about the source and natural transmission cycle of the Ebola virus.

*[Del Conn and Margaretha both became ill in Zaire with fever and rash, and they were evacuated to South Africa, the only country willing to accept patients who might have the deadly infection; hence the title of the chapter. She wrote to Dr Lyle Conrad, the CDC epidemiologist who had helped with the Marburg investigation in South Africa and Zimbabwe-JF]*

'5 December, 1976

Dear Lyle,

*I hope I made some sense during our telephone conversation last Wednesday (December 1). Having had virtually no sleep since the previous Sunday (November 28th). Since then I developed symptoms similar to those of Del Conn, my white blood count took a nosedive and lymphocytes went up and, in the absence of a second isolator, the full gas mask routine was introduced. I doubt that it is the virus probably something else, maybe Marburg Mark III? At any rate, Del is making good progress, so am I but am very vexed by this enforced idleness. Sorry, I never got around to photographing his rash, but somebody else did and I'll try and get you a copy. However, it was identical to that of Megan's, very florid, and blanching on pressure. The trip from Yambuku to Johannesburg was a nightmare; herewith the details.*

*You may have gathered already from Karl Johnson that we were in a quandary as to whether the medevac plan should be set in motion. It was really Professor Courtois, our French haematologist, who looked at the question very objectively and caused us to make the right decision. This was at 07.30 on Monday (November 29th). The decision to evacuate Del was automatically linked to the necessity to administer convalescent plasma. Initially, when I microscopically examined the blood from the donors, almost all the samples contained microfilariae of the *Loa loa* parasite. We also suspected that a substantial number would be positive for the hepatitis B virus. Finally, we could not be sure that the convalescent plasma did not still contain live Ebola virus and that Del ac-*

*tually suffered from this disease. The possibility therefore existed that, by giving Del the convalescent plasma, we might infect him with the Ebola virus. For all of these reasons, the plasma should be heated to destroy any disease causing microorganisms without damaging the antibodies.*

*This can be accomplished by heating the plasma at 56 °C for one hour. I had brought a temperature adjustable water bath from South Africa and spent Sunday evening regulating the water temperature to 56 °C. Of course, on immersing two units of frozen plasma on Monday morning, the temperature dropped and took a while to return to 56 °C. The whole heating process therefore took till about 9 o'clock and, on removing the bags from the water bath, they contained a lot of coagulated material. As we had no facilities for filtration, the bags had to be centrifuged and the clear plasma transferred to new bags. I felt frustrated at having to do all this in a Mickey Mouse fashion. While the bags were spinning at high speed in our looted centrifuge, the generator packed up. Restoration of power and subsequent centrifugation took another half-hour. Once the clear plasma was transferred into new bags, it looked beautiful.*

*[Margaretha and Del Conn were admitted to the Rietfontein Tropical Diseases Hospital in Sandringham, Johannesburg. Investigations proved that neither had contracted Ebola virus, and arboviruses, generally mild pathogens transmitted mainly by mosquitoes, were thought to be the most likely cause of their illness-JF]*

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# The Memoirs of Margaretha Isaäcson



## PART 4: CHOLERA

### *Carrots and Cholera*

Wednesday, the 11th of December 1985, was one of those days when the highveld sun shone brightly in a clear and deep blue sky after early morning rains. Countless water droplets on plants and trees sparkled like diamonds in the sun. The traffic moved smoothly, cars looking shiny bright after the rain had washed off the red dust. I arrived at the Institute where the gardens were a riot of colourful flowers. The scent of roses filled the air and a pair of Cape wagtails with their greyish brown plumage and white

bibs were busily walking along the lawns, every now and then tugging insects out of the grass. This was not a day for work. After parking the car I took the lift to the fourth floor. In the office I checked my diary - no appointments, no lectures and no meetings. So far, so good. It was early and no one else had arrived as yet. I became engrossed in a small pile of current medical journals. About ten minutes later the rest of the staff started arriving and the usual sounds of daily activities increased. Emily arrived with a bright greeting and went off to get us some tea. Lorraine, the chief technologist, came to report on the previous day's laboratory results.

It must have been about half past nine when the door to the outer office opened and a heavily built, moustached man walked in. He was dressed in a white safari suit and carried a coolbox. 'Health inspector' was my diagnosis as I glanced up from my desk and through the connecting door. I returned to my journals but was interrupted by Lorraine who asked if I would talk to Mr X, a health inspector ('told you so', I told myself) who, she said, had a rather unusual problem. 'Sure' I said, 'ask him to come right in and join us'. Mr X gave me a bone crunching handshake and removed the lid from his coolbox. Looking inside I saw several bunches of baby carrots, obviously freshly harvested as muddy clods of soil were still clinging to the carrots. They didn't smell so good, though. I looked up at Mr X who had a very anxious look on his face and I wondered what could be so tragic about a bunch of carrots. It transpired that the carrots belonged to a market gardener who had on several occasions complained to the health department of the municipality on the outskirts of which his farm was situated. The source of his gripe was a small municipal sewage pumping station, which, according to the vegetable farmer, had leaked sewage onto his land on more than one occasion. Mr X said that the pump had been repaired. Early that morning he had once again received a call from the farmer who threatened to take the council to court. Why so?

Apparently, the pump had broken down during the night and had not just leaked onto his land, but flooded an extensive area with sewage. Mr X went out to the farm from where he had just returned and confirmed the farmer's allegations. The latter had fenced off the affected area, and instructed his labourers not to enter this field. According to Mr X, the farmer was furious and stated that he was ruined if his carrots were contaminated with anything that might make his customers ill. The council, in its turn, did not need a lawsuit, nor the attendant adverse publicity and, through Mr X, requested full bacteriological testing of the carrots plus advice as to what, if anything, was to be done about the contaminated carrot field. After the departure of Mr X, minus coolbox, Lorraine and I discussed the case and decided to process the carrots for any disease-causing bacteria that may be found in sewage. The infections they can cause include typhoid fever, dysentery, gastroenteritis, food poisoning, cholera and several others.

The following morning, Lorraine entered my office, looking uncharacteristically serious. "About those carrots," she said. "Yes?" "You remember the carrots?" she asked. "Do I look senile? What about the carrots?" "They've got cholera." "You're pulling my leg!" "No, seriously, we grew *Vibrio cholerae* O1, El Tor, Inaba," she added, specifying the exact identification of the particular biotype and serotype of the strain she had grown. We went to the laboratory where Lorraine demonstrated her findings. No doubt about it, those were cholera bacilli. Before we could telephone the laboratory results, Mr X walked in. He looked a lot happier than the previous day. "Just thought I'd drop by and see if you got anything for me yet," he said, half asking. "Well, yes, as a matter of fact we do. Let's go to my office and have some coffee." Coffee, the universal tranquilizer. Indispensable when breaking the news to health officials about carrots that have a bout of cholera. "About those carrots," I said. Mr X leant forward eagerly, looking at Lorraine and myself in turns. "Yes, about those carrots, did you find anything?" he asked. "Yes, we did. We found cholera." "Cholera!" "Cholera." "But there hasn't been any cholera in the country for several years now. Where would it have come from?" "A healthy carrier probably contaminated the sewage," I answered. "Perhaps a refugee or a visitor from up north somewhere. There is still plenty of cholera there." Mr X looked very anxious again and I suggested: "If you like, let's go and look at the farm together and we can decide what to do when we have seen the site and the circumstances." "Good idea, when would you like to go?" asked Mr X. "The sooner, the better, before this cat gets out of the bag," I answered. Lorraine went back to the laboratory and I left with Mr X, taking a box with specimen collection equipment.



Excerpt from the Annual Report of the South African Institute for Medical Research, 1985.<sup>14</sup>

*'The silent presence of Vibrio cholerae in the environment was dramatically demonstrated when part of a municipal sewerage system on the Witwatersrand burst during December, resulting in the accidental inundation of part of a vegetable farm with raw sewage. The affected soil with its carrot crop was 'quarantined' while microbiological tests were conducted to determine whether the land was safe for replanting. V. cholerae was isolated from the sewage, the contaminated soil and from carrots. Subsequent monitoring showed a decrease in the extent of cholera contamination, probably due to a flushing effect by heavy rains. The last batch of soil samples to yield V. cholerae on culture was obtained 10 days after the contamination had occurred. Water used for irrigation of the vegetable crop was found to be free from cholera.....Farm workers, a nearby prison and a sanatorium for mentally handicapped persons were all asked to report recent or current diarrhoeal illness, but none had occurred. Under the circumstances it was decided that prophylactic treatment was not indicated for anyone in the area, but the affected land was to remain out of bounds until clear of cholera.....After three successive batches of soil samples had become negative, permission was granted to the farmer to work the land again. Although the clinical incidence of cholera in South Africa has decreased markedly, these findings clearly show that cholera transmission continues to take place, probably in a cycle between subclinically infected people and the environment.'*



*[Margaretha Isaäcson's reminiscences end abruptly here because, sadly, she became ill and a malignant brain tumour was diagnosed (see Foreword in this issue). She had been extensively involved in cholera work since 1970, when the 7th pandemic first reached South Africa and thousands of cholera cases were confirmed in her laboratory. No doubt she would have described all her work in cholera, as well as a pioneering water reclamation project in Windhoek, Namibia, had it not been for her untimely death in 2001-JF]*

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