AD-A259 524

AD_____

GRANT NO: DAMD17-90-Z-0005

TITLE: DIAGNOSIS AND CHEMOTHERAPY OF HUMAN TRYPANOSOMIASIS AND
VECTOR ECOLOGY OF RIFT VALLEY FEVER AND CONGO-CRIMEAN
HEMORRHAGIC FEVER IN KENYA

PRINCIPAL INVESTIGATOR: J. K. Omuse, Ph.D.

CONTRACTING ORGANIZATION: Kenya Trypanosomiasis Research
Institute
P.O. Box 362
Kikuyu, Kenya

REPORT DATE: November 6, 1991

TYPE OF REPORT: Midterm Report

PREPARED FOR: U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release;
distribution unlimited

The findings in this report are not to be construed as an
official Department of the Army position unless so designated by
other authorized documents.

93-00402

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION	1b. RESTRICTIVE MARKINGS
Unclassified	

2a. SECURITY CLASSIFICATION AUTHORITY	3. DISTRIBUTION/AVAILABILITY OF REPORT
	Approved for public release;
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE	Distribution unlimited

4. PERFORMING ORGANIZATION REPORT NUMBER(S)	5. MONITORING ORGANIZATION REPORT NUMBER(S)

6a. NAME OF PERFORMING ORGANIZATION	6b. OFFICE SYMBOL (If applicable)	7a. NAME OF MONITORING ORGANIZATION
Kenya Trypanosomiasis Research Institute		

6c. ADDRESS (City, State, and ZIP Code)	7b. ADDRESS (City, State, and ZIP Code)
P.O. Box 362 Kikuyu, Kenya, AFRICA	

8a. NAME OF FUNDING/SPONSORING ORGANIZATION U.S. Army Medical Research & Development Command	8b. OFFICE SYMBOL (If applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER Grant No. DAMD17-90-Z-0005

8c. ADDRESS (City, State, and ZIP Code)	10. SOURCE OF FUNDING NUMBERS			
	PROGRAM ELEMENT NO.	PROJECT NO. 3M1	TASK NO.	WORK UNIT ACCESSION NO.
Fort Detrick Frederick, Maryland 21702-5012	62787A	62787A870	AN	014

11. TITLE (Include Security Classification)
Diagnosis and Chemotherapy of Human Trypanosomiasis and Vector Ecology of Rift Valley Fever and Congo-Congo-Crimean Hemorrhagic Fever in Kenya

12. PERSONAL AUTHOR(S)
J. K. Omuse

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Year, Month, Day)	15. PAGE COUNT
Midterm Report	FROM 11/15/89-5/14/91	1991 November 6	

16. SUPPLEMENTARY NOTATION

17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB-GROUP	RA I; Volunteers; Hemorrhagic Fever; Vectors; Trypanosomiasis; Rift Valley Fever; Lab Animals; Monkey
06	03		
06	13		

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

This activity is principally centered around work with the KETRI Vervet Model and the Alupe Human Sleeping Sickness Referral Hospital at Busia.

Over the last ten years, KETRI has been able to develop a primate model that closely mimicks late stage human sleeping sickness. Application of this model for development and refinement of diagnostic and chemotherapeutic regimens is now in progress. By mid-term of this project, five potential compounds from Walter Reed Army Institute had been screened. Three of the compounds proved to have an efficacy that merits further investigation.

Although no funds were specifically allocated for combination therapy the project reviewers recommended that the synergism reported between suramin and other drugs by other workers be investigated in the KETRI Vervet model. This work has started especially using DFMO and a combination of other drugs.

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21. ABSTRACT SECURITY CLASSIFICATION
☐ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT. ☐ DTIC USERS	Unclassified

22a. NAME OF RESPONSIBLE INDIVIDUAL	22b. TELEPHONE (Include Area Code)	22c. OFFICE SYMBOL
Mrs. Virginia M. Miller	301-619-7325	SGRD-RMI-S

DD Form 1473, JUN 86   *Previous editions are obsolete.*

The year 1990 saw a major outbreak of human sleeping sickness on the Kenya-Uganda border whereby up to 90 (ninety) people were seen by mid 1990. The majority of the cases were from one focus and had late stage disease. Prompt action was taken to treat people and to control the flies through spraying. Although the situation was brought under control, active surveillance along the border, in concert, with the Ugand side, is now in progress so as not to have a repeat of the same.

In the area of Rift Valley Fever, studies under this project have been able to show models for predicting likely breeding sites for mosquitoes and as such the likelihood of getting outbreaks of the disease. It is now possible to use this information to design specific pilot strategic control programmes.

Work on Congo-Crimean Hemorrhagic Fever has not progressed as fast as the other two. However, collection of ixodid (soft) ticks has commenced. The ticks collected are sent to Fort Detrick for testing. It is hoped that on ixodid tick distribution map can be worked out so as to use as a means of carrying further epidemiological studies on this condition.

For the future, the project hopes to vigorously pursue work in diagnosis of human trypanosomiasis, particularly so the use of antigen ELISA techniques. Work will also continue in the area of chemotherapy particularly in developing more efficacious regimens using existing drugs and a search for new drugs to be used alone or in combination with the existing drugs.

In the area of Rift Valley Fever, efforts will now be intensified in piloting possible strategic control strategies and in the area of Congo Crimean Hemorrhagic Fever, work will continue in collecting and testing soft ticks from different parts of the country so as to understand better the epidemiology of this disease.

DTIC QUALITY INSPECTED 3

FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.

_____ Where copyrighted material is quoted, permission has been obtained to use such material.

_____ Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.

__X__ Citations of commercial organizations and trade names in this report do not constitute an official Department of the Army endorsement or approval of the products or services of these organizations.

__X__ In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council (NIH Publication No. 86-23, Revised 1985).

__X__ For the protection of human subjects, the investigator(s) have adhered to policies of applicable Federal Law 45 CFR 46.

_____ In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

PI Signature   Date 14/11/91

I Diagnosis and Chemotherapy of Human Trypanosomiasis

a. Screening of WRAIR trypanocides

<u>Background</u>

About 50 million people on the continent of Africa are currently at risk from the two forms of Sleeping Sickness, caused by <u>Trypanosoma b. gambiense</u> in West and Central Africa and <u>Trypanosoma b. rhodesiense</u> in Eastern and Southern Africa. The gambiense disease is usually chronic, leading over months or years to invasion of the central nervous system by trypanosomes, resulting in a fatal encephalitis if not treated. The rhodesiense disease, on the other hand, may be acute and rapidly fatal from pancarditis or more slowly from encephalitis. Treatment of trypanosomiasis is limited at present to the use of 3 or 4 drugs. The early disease may be treated with suramin or, in the case of <u>T. gambiense</u> infection, pentamidine. The late encephalitic form of the disease is treatable only with melarsoprol, an arsenical compound, which itself may result in encephalopathy in 10% of treated cases; 1-6% of these are fatal. Administration of these drugs requires hospitalisation and is difficult. In addition, it has long been recognized that some strains of trypanosomes are refractory to treatment. Recently the use of DFMO has shown promising results in cases of <u>T. gambiense</u> infection in Sudan and other areas. The position with <u>T. rhodesiense</u> is less encouraging.

The objectives for the trypanosomiasis component of this project were firstly, to examine the therapeutic properties of compounds from the Division of Experimental Therapeutics, WRAIR, against *Trypanosoma brucei brucei* and *Trypanosoma brucei rhodesiense* infections in mice and vervet monkeys. Secondly to explore the efficacy of combination therapy in encephalitic *T. rhodesiense* infected vervet monkeys.

<u>Introduction</u>

The chemotherapy division at KETRI has developed a protocol for testing novel compounds with trypanocidal activity in *T. b. brucei* and *T. rhodesiense* murine and primate models of human sleeping sickness. More recently this has been extended to include a trypanosome culture system. Together these systems, which include both the acute and the meningoencephalitic stages of trypanosomiasis, permit a full assessment of the potential of novel compounds or revised treatment regimens to be made prior to clinical trials.

The focus of attention for studies in the murine and primate models of *T. rhodesiense* at KETRI has recently been directed towards a more detailed understanding of the behaviour of melarsoprol, of eflornithine (DFMO - Omidyl^R, Merrell Dow), and towards the evaluation of treatment regimens utilizing combinations of drugs already registered for use in humans, rather than towards experimental compounds. There continues to be an urgent need for new compounds for *T. rhodesiense* infection but there may be little hope of commercial manufacture or field use in the immediate future.

Previous studies in the vervet trypanosomiasis model indicated that combination therapy involving suramin and an experimental nitroimidazole from Merck Sharpe and Dohme, MK436, cured four of five encephalitic cases, thus giving the next best cure rate to melarsoprol. Although another nitroimidazole from Hoffman La Roche, Ro15-0216, did not give satisfactory results alone (2 cures in 14 treatment courses) or in combination with suramin (1 cured in 4 treatment courses) in the early phase of the vervet model, it has been shown to have a synergistic effect with other trypanocidal compounds, particularly DFMO, against *T. brucei brucei* in culture and in mouse and sheep models of the acute disease.

Encouraging results (4 out of 5 non-encephalitic vervet cases cured) were achieved with suramin in combination with the arsenical Mel Cy or cymelarsen which is now being developed by Rhone Poulenc for *T.evansi* therapy in camels and horses.

It has also been demonstrated in encephalitic vervet cases, that dosages of melarsoprol lower than those recommended for routine use in human cases of both Gambian and Rhodesian sleeping sickness were effective and might therefore constitute a lowered risk from arsenical toxicity. A double blind clinical trial in patients at Daloa was initiated as a result of these findings. This has not been completed, however, because there is a strong suspicion amongst those running the trial that there is a greater than expected number of relapse in patients selected. Independent statistical analysis of the results of some 60 cases did not support this view but, because the confidence of the clinicians concerned had been undermined, completion of the trial was delayed.

The exact nature of the adverse reaction reported after treatment with melarsoprol in 1-15% of patients continues to be ill defined. Studies have been pursued in mice at Glasgow and to a limited extent at KETRI to explore the aetiology of these reactions and to devise preventative therapeutic measures.

In encephalitic vervet monkeys infected with *T. rhodesiense* KETRI 2537, although far from ideal, melarsoprol continues to be the superior drug studied to date.

The limited number of reports of DFMO treatment of *T. rhodesiense* patients indicate variable responses to the drug while DFMO is successfully used in *T. gambiense* human patients refractory to melarsoprol. The reasons for this difference in response to the drug have yet to be explained, but the finding in mice that *T. rhodesiense* isolates exhibit a wide range of sensitivities to DFMO is important.

The results of extensive eflornithine (DFMO) treatment trials in *T.rhodesiense* KETRI 2537 infected encephalitic vervet cases indicated that the drug was not curative at any of the dosages or in any of the combinations tested. It was been encouraging therefore to confirm the value of this drug used orally in Sykes monkeys *Cercopithecus mitis* and one vervet, all with encephalitic changes due to *T.gambiense* KETRI 2347 and 2569. In contrast to the *T.rhodesiense* KETRI 2537 cases, there was rapid and total remission of clinical signs and trypanosomes could not be detected.

Progress Report

1. Experimental compounds with trypanocidal activity from Walter Reed Army Institute of Research (WRAIR)

Five compounds were sent by Dr Willis Reid from a series that had been shown by scientists from the WRAIR Division of Experimental Therapeutics to possess trypanocidal activity in *T. rhodesiense* infected mice (Table 1). Since small quantities only were available, studies were initially confined to mice. However we were informed that at this stage in development there is no likelihood of further supplies of these compounds being synthesized. Three of the compounds (3,4, &5 in Table 2) were extremely effective in the mouse model and merit further investigation in the vervet model.

1. **BN BK 46353** (1245S ORIG) $2C_{19}H_{24}N_4O_4 \cdot 4HCl.H_2O$
   WR 250.385AA
   QQ Ash Stevens DJD-04-59
   Source: Ash Stevens
   Quantity remaining: 0.1322g

2. **BN BL 00076** (1259S ORIG) $2C_{21}H_{25}N_6.2Br.2HBr.3H_2O$
   WR 253.984AA
   Sundberg V-68-GM
   Source: Sundberg, Univ of Virginia
   1,3-dimethyl-2-(4'-formylphenyl)imidazo[1,2-A]pyridinium N,N
   tetramethyleneguanylhydrazone dibromide SES
   Quantity remaining: 0.5615g

3. **BN BL 21593** (1259S ORIG) $C_{17}H_{21}N_6.Br.HBr.H_2O$
   WR 255.765AA
   Sundberg II-27-A
   Source: Sundberg, Univ of Virginia
   1,3-dimethyl-2-(4'-formylphenylethenyl)imidazolium N-(2-
   imidazolinyl)hydrazone dibromide hydrate
   Quantity remaining: 0.2857g

4. **BN BK 64897** (1259S ORIG)
   $C_{17}H_{19}N_6.C_7H_7O_3S.C_7H_8O_3S$
   WR 249.928AB
   Sundberg II-31-GM
   Source: Sundberg, Univ of Virginia
   2-/4.-formylphenyl/-1,6-dimethylimidazo/1,2-A   pyridiniumguanyl hydrazone
ditosylate
   or 1,6-dimethyl-2-(4'-formylphenyl)imidazo[1,2,-A] pyridinium   guanylhydrazone
ditosylate
   Quantity remaining: 0.3670g

5. **BN BL 06961** (1259S ORIG) $2C_{18}H_{21}N_6O.2Br.2HBr.5H_2O$
   WR 254.523AA
   Sundberg V-88-GM
   Source: Sundberg, Univ of Virginia
   1,6-dimehtyl-2-(4'-formyphenoxymethyl)imidzo[1,2-A]   pyridinium
guanylhydrazone dibromide 2.5hydrate
   Quantity remaining: 0.7355g

Results of toxicity and mouse treatment trials:

Table 2 Compounds submitted to KETRI/USAMRU-K: mice infected with KETRI 1416 (*Trypanosoma brucei brucei*) were treated by subcutaneous injection and followed for 60 days after infection.

Drug	Dose	Deaths Toxicity	Deaths non-tryps	Relapsed	Efficacy
1. **BN BK 46353**	62.5	2	0	0	8/8
WR 250.385AA	31.25	0	0	0	10/10
	15.125	0	0	1	9/10
	7.5625	1	2	2	5/10
		0	0	7	3/10
2. **BN BL 00076**	3.91	5	0	0	5/5
WR 253.984AA	1.955	1	0	2	7/10
	0.9775	3	0	5	2/10
	0.48875	0	0	10	0/10
3. **BN BL 21593**	62.5	4	0	0	6/6
WR 255.765AA	31.25	0	0	0	10/10
	15.125	0	1	0	9/9
	7.5625	1	2	0	7/7
4. **BN BK 64897**	62.5	4	0	0	6/6
WR 249.928AB	31.25	0	0	0	10/10
	15.125	0	0	0	10/10
	7.5625	0	0	1	9/10
5. **BN BL 06961**	31.25	3	0	0	7/7
[WR 254.523AA]	15.125	0	0	0	10/10
	7.5625	0	2	0	7/7
	3.78125	0	2	1	7/7

b. chemotherapy of human African trypanosomiasis using the KETRI vervet model.

Introduction: Although not funds were not specifically allocated under this project, it was recommended by the project reviewers that the synergism reported by other workers between suramin and other compounds such as DFMO and melarsoprol be investigated further using the KETRI vervet model.

The standard protocol for the CSF and encephalitis phases of the vervet trypanosomiasis model was followed in all trials.

In summary, the early CSF phase is used for fundamental testing of compounds between 30 to 50 days after intravenous inoculation of 10^3 *T. rhodesiense* KETRI 2537. Animals in the late or encephalitic phase are used for trials after successful completion of the CSF phase. The late or encephalitic phase is derived by sub-curative treatment with diminazene aceturate between 30 to 40 days after inoculation of the trypanosomes; this is followed by temporary parasitic and clinical remission. Later trypanosomes reappear and signs of encephalitis develop at which time the test drug is applied. The criteria adopted for confirmation of the onset of encephalitis are as follows:

1. changes in CSF:
   - increase in white cell count above 15 cells/mm^3 (normally <10 cells/mm^3)
   - increase in total protein (normal <25mg/dl)
   - presence of trypanosomes in CSF (these are present in all cases from 7 to 14 days onwards following infection.

2. Clinical signs indicating neurological involvement include: depression, somnolence, ataxia, tremors, paralysis, central blindness, excess vocalization or other behavioural changes.

Three animals are allocated to each dosage group. The follow-up period after apparent successful treatment is six hundred days, in the absence of any other more reliable method to detect cryptic infections. This period is currently being reviewed in the light of results from analysis of an antigen trapping ELISA applied to the many stored samples of serum and CSF from monkeys which were successfully treated and those which relapsed. Preliminary results suggest that it may be reduced below 400 days.

Routine monitoring of all cases prior to and following treatment includes twice daily visual assessment, daily blood collection of ear tip capillary blood for trypanosome detection. Each animal is anesthetized every fourteen days for a detailed physical examination, blood and CSF collection, and electrocardiography.

Blood is subjected to haematological examination and serum separated for protein assay and storage at -20°C. The number of white cells are counted in CSF which is examined for trypanosomes by direct microscopy and by a concentration technique and is stored. Blood chemistry is to be introduced shortly. The animals are given full supportive care when under trypanocidal therapy, such as extra warmth, intravenous and oral fluid and electrolytes, control of secondary infection, high potency vitamin injections and oral or parenteral feeding.

Any case which does not respond to therapy is humanely destroyed. When trypanosomes relapse after an initial treatment course, cases are allocated to the next most appropriate trypanocidal treatment group currently under investigation. At the successful termination of a treatment course including a period of 600 days of follow up, the monkeys are examined post mortem for vestigial changes in organs particularly heart and brain. Some examples of the protocols used for trials of combined drug therapy are given in Table 3.

Table 3: Six examples of treatment protocols applied to the vervet trypanosomiasis model.

	DRUGS route	DOSAGE RATES	DAILY PROTOCOL
1.	SURAMIN iv [S]	20mg/kg sid x1	day |1|2|3|4|5|6|7|8|9|10|11|12|13|14|15| |S|/|/|/|/|/|/|/|/|/|/|/|/|/|/|
2.	SURAMIN iv [S]	20mg/kg sid x5	day |1|2|3|4|5|6|7|8|9|10|11|12|13|14|15| |S|/|S|/|/|S|/|/|/|S|/|/|/|/|S|
3.	SURAMIN iv [S] +DFMO oral [D]	20mg/kg sid x1 400mg/kg qid x14	day |1|2|3|4|5|6|7|8|9|10|11|12|13|14|15| |S|/|/|S|/|/|/|S|/|/|/|/|S| |/|D|D|D|D|D|D|D|D|D|D|D|D|D|
4.	SURAMIN iv [S] +DFMO oral [D] +NIFURTIMOX oral [N]	20mg/kg sid x5 400mg/kg qid x14 15mg/kg tid x14	day |1|2|3|4|5|6|7|8|9|10|11|12|13|14|15| |S|/|S|/|S|/|/|/|S|/|/|/|/|S| |/|D|D|D|D|D|D|D|D|D|D|D|D|D| |/|N|N|N|N|N|N|N|N|N|N|N|N|N|
5.	MELARSOPROL iv [M] +DFMO oral [D]	0.3 mg/kg sid x4 400mg/kg qid x14	day |1|2|3|4|5|6|7|8|9|10|11|12|13|14|15| |M|/|/|/|M|M|M|M|/|/|/|/|/| |/|D|D|D|D|D|D|D|D|D|D|D|D|D|
6.	SURAMIN iv [S] MELARSOPROL iv [M]	20mg/kg sid x5 0.1mg/kg sid x4	day |1|2|3|4|5|6|7|8|9|10|11|12|13|14|15| |S|/|S|/|/|S|/|/|/|S|/|/|/|/|S| |/|M|M|M|M|/|/|/|/|/|/|/|/|/|

iv = intravenous, sid = once daily, tid = three times daily, qid = four times daily

STUDIES ON DIFLUOROMETHYLORNITHINE (DFMO) IN THE VERVET TRYPANOSOMIASIS MODEL

In contrast to the successful use of DFMO in *T. gambiense* human patients refractory to melarsoprol, the very few reports of DFMO treatment of *T. rhodesiense* patients indicate variable responses to the drug. The reasons for this difference in response to the drug have yet to be explained. Five aspects of the therapeutic use of DFMO were investigated:

   i. Culture of a selection of the *T. rhodesiense* stocks from the KETRI Trypanosome Bank for drug testing

   ii. Drug trials in acute infections of mice with the same *T. rhodesiense* stocks as those studied in culture.

   iii. pharmacokinetics of DFMO in blood and CSF from uninfected vervet monkeys

   iv. Therapy trials in the vervet monkey model of *T. rhodesiense* encephalitis using oral DFMO alone.

   v. Trials in the vervet monkey model of *T. rhodesiense* encephalitis where one or more drugs was tested in combination with DFMO.

The latter relates to the present project particularly.

TREATMENT OF ENCEPHALITIC VERVETS WITH DFMO ALONE AND IN COMBINATION WITH OTHER TRYPANOCIDAL DRUGS

In view of the problems associated with DFMO treatment of human cases of melarsoprol refractory *T. rhodesiense*, it was decided to examine the potential of drug synergism or potentiation. This has been described by several scientists who demonstrated synergism in trypanosome culture, acute mouse or CNS affected mouse models when DFMO was administered in combination with one of a number of drugs, for instance bleomycin, diminazene, nifurtimox, suramin, melarsoprol, trimelarsen, cymelarsan or nitroimidazoles.

Thirty vervets were allocated to the following DFMO trials: various doses of DFMO alone, in combination with melarsoprol, in combination with suramin, in combination with both nifurtimox and suramin.

The trials were designed in the belief that DFMO would have a similar effect on the *T. rhodesiense* used for the vervet model as on *T. gambiense* human cases that had been the subject of many reports of successful treatment. Thus the decision was made to omit the first part of the standard vervet trypanosomiasis model protocol, namely, the early testing in CSF phase vervets, and to proceed immediately to encephalitic cases. Three animals were allocated to each dose group. Dosages were extrapolated from the human DFMO protocol, while the doses of drugs to be used in combination with DFMO were derived from the results of previous trials in vervets.

The potential of these combinations to treat encephalitic vervet monkeys was examined . Typical protocols f >r combined drug therapy are shown in Table 3.

(1) ORAL DFMO ALONE - MINIMUM CURATIVE DOSE (MCD)

The dosages of oral DFMO administered to *T. rhodesiense, KETRI 2537*, infected encephalitic monkeys are summarised in Table 4. There was no dose at which trypanosomes were eliminated for longer than eight days from blood nor longer than 13 days from CSF.

(Sampling of CSF of course is a fortnightly procedure). There was a high mortality rate. The incidence of side effects included diarrhoea and increased depression.

Table 4: Treatment of encephalitic *T. rhodesiense*, *KETRI 2537* infected vervets with DFMO administered orally four times daily, every six hours (qid). The interval in days to detectable trypanosome relapse in blood and CSF is shown for each case.

DRUG	DOSE mg/kg qid xdays	CASES TREATED	CASES DIED*	CASES CURED	DAYS TO RELAPSE AFTER TREATMENT	
					BLOOD	CSF
DFMO	25 x14	1	1	0		
	50 x14	1	0	0	8	8
	100 x14	2	2	0		
	200 x14	3	2	0	1	7
	400 x14	2^	0	0	7,0	10,9
	400 x21	1	0	0	0	0
	800 x14	1	0	0	4	13
	TOTAL	11	6	0		

* = cases which died during or within 3 days of treatment
"0" DAYS TO RELAPSE = denotes a case which was never free of trypanosomes
^ = early cases, not yet encephalitic

(2) DFMO IN COMBINATION WITH INTRAVENOUS MELARSOPROL

The dose rates used for treatment of *T.rhodesiense*, *KETRI 2537*, encephalitic cases and the results of this trial are summarised in Table 5. When melarsoprol is used alone for four days, doses of $0.6^{mg}/kg$ and below have resulted in relapse, while $0.8^{mg}/kg$ has variable results (see Table 9). The combination of DFMO and melarsoprol did not eliminate trypanosomes permanently from both blood and CSF at any of the doses tested. More than 50% of the animals in this trial died during or immediately after treatment (within three days).

Table 5: Treatment of encephalitic *T.rhodesiense*, *KETRI 2537*, infected vervets with DFMO administered orally four times daily every six hours (qid) in combination with intravenous melarsoprol once daily. The interval in days to detectable trypanosome relapse in blood and CSF is shown for each case.

DFMO mg/kg TREATMENT qid xdays	MELARSOPROL mg/kg xdays	CASES TREATED	CASES DIED*	CASES CURED	DAYS TO RELAPSE AFTER BLOOD	CSF
200 x14	0.3 x4	1	1	0		
200 x14	0.6 x4	2	1	0	44	44
400 x14	0.3 x4	1	0	0	2	6
800 x14	0.3 x4	3	2	0	5	14
800 x14	0.6 x4	1	1	0		
800 x21	0.1 x4	2	1	0	5	15
800 x21	0.3 x4	1	1	0		
TOTAL		11	7	0		

* = cases which died during or within 3 days of treatment

(3) ORAL DFMO IN COMBINATION WITH SURAMIN

The dose rates used for treatment of encephalitic cases and the results of this trial are summarised in Table 6. There was no case in which trypanosomes were permanently eliminated from both blood and CSF but in one animal the period to detectable relapse was prolonged.

Table 6: Treatment of encephalitic *T.rhodesiense*, *KETRI 2537*, infected vervets with DFMO administered orally four times daily every six hours (qid) in combination with intravenous suramin once daily. The interval in days to detectable trypanosome relapse in blood and CSF is shown for each case.

SURAMIN mg/kg TREATMENT xdays	DFMO mg/kg qid xdays	CASES TREATED	CASES DIED*	CASES CURED	DAYS TO RELAPSE AFTER BLOOD	CSF
10 x1	400 x14	2	0	0		
20 x1	800 x14	1	1	0		
20 x1	200 x14	2	1	0	14	20
20 x1	200 x21	2	0	0	13,0	14,9
20 x1	800 x21	2	0	0	21,0	21,2
20 x5	400 x14	2	0	0	31,83	23,208
	TOTAL	11	2	0		

* = cases which died during or within 3 days of treatment
"0" days to relapse = denotes a case which was never free of trypanosomes

(4) DFMO AND NIFURTIMOX (Lampit^R - Bayer) COMBINED WITH SURAMIN

Lampit was found to be an extremely unpalatable and upsetting drug for vervets. Dosing three times daily was possible by means of a large syringe and special metal oral catheter. A multiple combination of DFMO, suramin and Lampit at doses shown in Table 7. Results were disappointing.

Table 7: Treatment of encephalitic *T. rhodesiense* infected vervets with DFMO administered orally four times daily every six hours (qid) in combination with intravenous suramin once daily and oral nifurtimox (Lampit) three times daily (tid)

DFMO RELAPSE	SURAMIN	LAMPIT	CASES	CASES	CASES	DAYS TO	
mg/kg TREATMENT qid	mg/kg	$^mmg/kg$	TREATED	DIED*	CURED	AFTER	
xdays	xdays	xdays				BLOOD	CSF
400 x14	20 x5	15 x14	3	3	0		
800 x14	20 x5	15 x14	1	0	0	41	7
* = cases which died during or within 3 days of treatment							

There were no cures amongst the five animals treated with this combination, three died during treatment. One showed a remission of parasitaemia for 41 days but trypanosomes were detected in CSF seven days after treatment.

(5) ORAL DFMO THERAPY OF ADDITIONAL *T.RHODESIENSE* STOCKS.

In the standard vervet trypanosomiasis model which employs KETRI 2537, DFMO was ineffective at any dose from 50 to 800^{mg}/$_{kg}$ every six hours. Subsequently, the stock KETRI 2537 was found in mouse and culture experiments to be one of the more refractory strains in our collection, even though it has never previously been exposed to DFMO. Other more sensitive stocks are therefore required to pursue further studies on DFMO treatment of *T.rhodesiense* infections.

Two groups of three vervets were inoculated with 10^4 trypanosomes from stocks of *T.rhodesiense* which are more sensitive to DFMO than KETRI 2537. Those chosen for these additional models, were KETRI 2545 and KETRI 2772. The former has proved difficult due to a peracute relapse following diminazene treatment which killed two of the three. The third monkey was treated with DFMO on development of encephalitis. Clinical improvement and disappearance of parasites from both blood and CSF resulted rapidly but the follow up period is only 21 days so far.

None of the group infected with KETRI 2772 has relapsed after supposedly subcurative treatment with berenil (70 days). Further stocks KETRI 2562 and 2708 will be tested. Unfortunately each stock has to be fully explored, through lengthy studies on all aspects of the disease course and pathology, to confirm its mimicry of the human disease and drug sensitivity patterns.

(6) ORAL DFMO THERAPY OF *T.GAMBIENSE*:

Five cases (four Sykes and one vervet) have been treated. Although for one the follow up period is less than 250 days, all have remained free of trypanosomes to date.

c. Division of Human Trypanosomiasis-Alupe

Introduction:

The KETRI hospital at Alupe admits sleeping sickness cases either from their routine clinic referrals from other health facilities or from active surveillance.

The fact that the Kenya Government attaches so much importance to a disease of little importance numerically while at the same time facing many other urgent health problems is because of the potential danger of a sleeping sickness epidemic, since the neighbouring countries are heavily affected.

Activities, Materials and Methods:

(a) ACTIVE SURVEILLANCE

We carry out active surveillance in those areas where cases of sleeping sickness have been reported. We go in a team of six technical staff, one clinician (Doctor or Clinical Officer) and one driver. We screen people using blood obtained by finger prick using the "buffy coat" examination technique.

(b) FOLLOW-UP OF TREATED CASES:

On admission the particulars of each patient is taken carefully so that we know the administrative area (location, sublocation and village) where the individual comes from.

Through the village elders with whom we work in close cooperation we are able to reach each individual when his/her time for follow-up has come. Some of these patients are well informed and they come for follow-up without us going for them. These are few and far in between.

c) ROUTINE CLINIC

We have a routine clinic where we see patients routinely. The patients who attend these clinics either suspect themselves to have sleeping sickness or have been 'bitten' ("stung") by an unidentified insect. We do get positive cases from this hospital in Alupe and sometimes it is here that we detect that there is an epidemic or an impending epidemic in a given area.

(d) TRYPANOSOMIASIS CONTROL

In terms of Trypanosomiasis control we liaise with the Ministry of Livestock Development who concern themselves with tsetse and animal Trypanosomiasis control.

(e) DIAGNOSIS

The diagnostic techniques are the conventional ones recommend by WHO: Examination of blood from finger prick either as a wet smear preparation, thin and thick film. "Buffy coat" examination or animal inoculation.

(f) CHEMOTHERAPY

We have been using a dosage schedule with a more slowly increasing rate of drug administration compared to the currently recommended Melarsoprol therapy of late stage Trypanosomiasis.

Results:

1990: - This is the year of the sleeping sickness epidemic in Apatit South Teso location in Busia District. The Table below shows the number patients admitted to Alupe in 1990 by location and sex:

LOCATION	MALES	FEMALES	TOTAL
SOUTH TESO	36	32	68
BUKHAYU	2	4	6
SAMIA	6	8	14
SOUTH NYANZA	0	2	2
UGANDA	3	0	3
TOTAL NUMBER	47	46	93

1991: We have admitted only four cases, one from Marachi and three from Samia. Ever since the advent of this epidemic we have carried out a regular sleeping sickness surveillance programme.

We have covered Samia, of South and West Teso locations of Busia District. We have had small campaigns in Bukhayo and Marachi locations where the disease is in low endemicity level.

We have 193 follow-up cases in our list from Busia and South Nyanza Districts.

Due to our vigorous recording of patients addresses, we have lost only a few in our follow-up. This will allow us to write a good review of the patients we have treated in Alupe.

MELB TREATMENT

Of all the 97 cases treated in 1990 and 1991 (up to September 1991) 22 of them had early stage of sleeping sickness and 75 had late stage of the disease. The 75 with late stage disease were treated with Suramin and MelB. Six of them had toxic encephalopathy and four died.

The percentage of toxic encephalopathy (8%) and mortality (5%) associated with treatment are similar to those reported in other studies

Conclusions:

Our treatment regime with MelB is similar to those of other workers in terms of results. MelB has been used for the last forty years as the drug of choice for late stage sleeping sickness despite the high morbidity and mortality rate associated with its use.

It is necessary that we look for alternative drugs of equal efficacy but reduced side effects to replace MelB in the treatment of late stage sleeping sickness.

We need to include an immunodiagnostic method in our diagnostic arsenal. We prefer to have an antigen ELISA type of technique. Of late we have been experimenting on a transport media developed by USAMRU-Kenya for transportation of Malaria parasites from the field to the laboratory. We have found this adaptable to transportation of trypanosomes from the field to the laboratory. Further research is needed in this as its success will reduce our expenditure in surveillance programmes.

II. Studies of Rift Valley Fever virus ecology in Kenya

BACKGROUND

In 1981 a collaborative research project was initiated between Kenyan, USAMRU-Kenya, and USAMRIID scientists to study RVF in Kenya. Significant data has been accumulated on this important human and animal pathogen.[1-10] A paper presented at the 7th Annual Medical Scientific Conference of the KEMRI/KETRI summarized the major results achieved, including the demonstration of a close link between the endemic cycle of RVF virus, Aedes mosquitoes, and specific types of mosquito breeding habitats known as dambos.[11] However, almost all studies have been confined to a relatively small geographical area in Kenya. Virtually nothing is known about the role of ground pool Aedes mosquitoes and dambos in RVF maintenance and transmission in other parts of Kenya, even though RVF is known to be widespread,[12] with the highest RVF antibody prevalence rate in humans in Kenya found in the northwest in Turkana District[13]. Rift Valley Fever is an important human and livestock disease which cannot be controlled at this time. There is no licensed human vaccine available, and the livestock vaccine, producing up to 30-40% abortions, is not widely used.

Detailed studies have been conducted in the laboratory to investigate vector competence of many species. Some of the species tested are considered to be likely secondary vector species; however, because the important ground pool breeding Aedes spp. have not been colonized, only very limited vector competence (both horizontal and vertical) studies have been made of the primary maintenance vectors.

Using the National Oceanographic and Atmospheric Administration's (NOAA) satellite data, the potential for predicting outbreaks of RVF in Kenya has been demonstrated.[14] A paper on this subject was presented at the Organization of African Unity Symposium on viral diseases in Africa, held in Nairobi in May-June 1986.[15] The prediction of outbreaks, however, needs refinement and validation. In addition, other high resolution remote imagery techniques, such as LANDSAT, SPOT, METEOSAT, or SAR radar imaging need to be evaluated in the detection of dry and flooded dambos.

Estimates of a recent (October-December 1987) serious RVF epidemic/epizootic in the Senegal River basin in Mauritania and Senegal indicate that more than 20,000 people were infected (45% attack rate in some areas), and that up to 90% of the livestock were infected. Human disease in this area had never previously been reported, even though antibodies had been detected. There is suggestive evidence that the epidemic was precipitated by the construction of dams designed to maintain water level in the river to allow for the development of rice and other agricultural crops. The ecology of the area and the utilization of irrigation schemes is similar to the situation found in some areas in Kenya, in particular the Tana River Project. Cattle have been found to have RVF virus antibody in these regions in Kenya.[12] The potential for occurrence of RVF epidemics caused by alterations in the natural ecology of such areas has not been assessed in Kenya. Studies on the geographic distribution of maintenance and secondary mosquito vectors and their potential breeding habitats could provide the information needed to assess the RVF threat both to the human and domestic animal population.

The unique relation between vectors, dambos, rainfall, and RVF makes the disease a likely candidate for control targeted against mosquito vectors and their habitats. Currently available safe insecticides or biological control methods might be efficient in controlling or eliminating RVF virus disease. No information is available concerning the efficacy of these insecticides in the dambo habitats.

INTRODUCTION

Rift Valley fever (RVF) is an important disease of man and domestic animals in much of Africa. Daubney, et al. established that a virus was the causative agent of RVF during an epizootic in Kenya in 1930[Daubney, 1931 #4]. Since then, periodic outbreaks of RVF have occurred in Kenya as well as other African nations [Logan, 1991 #56; Yedloytschnig, 1981 #130; Hoogstraal, 1979 #34; Walsh, 1988 #120; McIntosh, 1983 #66; Meegan, 1981 #128]. RVF causes clinical disease in man and most domesticated ungulates. An outbreak of RVF in Egypt during the years 1977-1978 demonstrated the potential for the virus to cause high morbidity/mortality in humans [Imam, 1979 #259; Meegan, 1981 #128; Laughlin, 1979 #43].

Mosquitoes are the primary vectors of RVF virus [Hoogstraal, 1979 #34; McIntosh, 1983 #66; Linthicum, 1985 #50]. There is strong evidence for transovarial transmission of the virus in *Aedes mcintoshi* [Linthicum, 1985 #50]. Sand flies and ticks have been experimentally infected with RVF virus and have been implicated as potential vectors of RVF [Turell, 1990 #116; Linthicum, 1989 #54].

In 1981, scientists from Kenya, USAMRU-Kenya and USAMRIID established a collaborative research project to study RVF in Kenya. Extensive research since then has provided considerable information about the ecology of RVF and its vectors. RVF outbreaks are often associated with unusually heavy rainfall that fills streamless depressions known as dambos [Davies, 1985 #184; Linthicum, 1988 #45]. Flooded dambos serve as breeding habitat for *Ae. mcintoshi* and for numerous other mosquito species that can serve as amplifying vectors of the virus during outbreaks of RVF [Linthicum, 1983 #48; Linthicum, 1984 #47; Linthicum, 1984 #49]. There is also evidence that natural lakes, marshes and irrigated land may provide suitable breeding habitat for potential mosquito vectors of RVF virus [Logan, 1991 #56; Logan, Submitted #58][Logan, 1991 #56].

Successful RVF vector abatement and RVF vaccination programs in Kenya will require identification of potential endemic areas of the virus. The use of remote sensing data from earth orbiting satellites and data from airborne imaging radar may provide a means to quickly and economically map dambo habitats and to predict their flooding [Linthicum, 1987 #46; Linthicum, 1990 #135; Linthicum, #134; Pope, submitted #255].

RVF control strategies have been directed at the control of *Ae. mcintoshi*, the presumed reservoir for the virus. *Ae. mcintoshi* is one of the first mosquito species to emerge from flooded dambos. It produces one generation, disappears and is replaced by other mosquito species [Linthicum, 1983 #48; Linthicum, 1984 #47; Linthicum, 1988 #45]. The majority of eggs in the soil hatch after initial flooding with very little hatching during subsequent floodings[Logan, 1991 #57]. Abatement efforts directed at this species may prevent or greatly reduce the severity of epizootics because of these characteristics in *Ae. mcintoshi* biology. Several studies have demonstrated that pretreatment of dambos with a sustained-release formulation of methoprene prior to flooding effectively reduce or eliminate *Ae. mcintoshi* populations [Linthicum, 1989 #55; Logan, 1990 #260].

OBJECTIVES:

1. Identify critical ecological factors which influence fever (RVF) in Kenya,
2. Determine the geographical distribution of floodwater *Aedes* species which are suspected enzootic vectors and reservoirs of the RVF virus and evaluate RVF vector abatement strategies.

Abstracts and summaries of papers resulting from research during this report period are included in the appendix.

CURRENT RESEARCH:

We are currently directing RVF research efforts at vector control, laboratory colonization of RVF *Aedes mcintoshi* and RVF/vector ecology at Lake Naivasha and elsewhere in Kenya. We will also continue to refine techniques using remote satellite imagery to predict vector habitats as well as environmental conditions favoring RVF outbreaks.

III. TICK-BORNE VIRUSES

Introduction:

Ixodid ticks are thought to be the primary vectors of Crimean-Congo hemorrhagic fever (CCHF), Dugbe, Thogoto, Bhanja and Jos viruses [Wood, 1978 #261]. Linthicum, et al. provided evidence that ticks may also be able to transmit Rift Valley fever virus [Linthicum, 1989 #54].

CCHF virus has not been isolated from vertebrates in Kenya. However, limited surveys have demonstrated antibodies to the virus in humans and cattle [Hoogstraal, 1979 #144; Johnson, 1980 #147; Johnson, 1983 #39; Watts, 1988 #166].

Ticks in the genus *Hyalomma* appear to be the primary vectors of CCHF. Six *Hyalomma* species have been collected in Kenya [Walker, 1974 #165]. Three of these, *Hy. impeltatum, Hy. rufipes* and *Hy. truncatum*, serve as invertebrate hosts of CCHF virus in Senegal.[Camicus, In Press #138]. Ticks in this genus are generally restricted to arid and semi-arid habitats and do not survive in areas where there is high humidity and abundant rainfall [Watts, 1988 #166; Wilson, submitted #179; Camicus, In Press #138].   Logan et al. demonstrated transtadial transmission of CCHF virus *Hy. truncatum* and horizontal transmission by feeding adults. He was unable to demonstrate transovarial transmission of the virus.

Little is known about the distribution and epidemiology of other tick-borne viruses in Kenya. Steele and Nuttall compared the vector competency of *Amblyomma variagatum* and *Rhipicephalus appendiculatus* and found that *Am. variagatum* was a competent vector of Dugbe virus and that *Rh. appendiculatus* was not [Steele, 1989 #263]. However, Linthicum et al. experimentally infected *Rh. appendiculatus* ticks with Dugbe virus, and these successfully transmitted the virus to susceptible hamsters [Linthicum, 1989 #176].

Current Research:

We are currently collecting ixodid ticks and vertebrate host sera from throughout Kenya testing them for tick-borne viruses at Fort Detrick, Maryland. Tick collections also provide information on tick species geographical and seasonal distribution, as well as host preference.

APPENDIX

GRANT PUBLICATIONS

1989 - present

**Logan, T.M., K.J. Linthicum, F.G. Davies, Y.S. Binepal and C.R. Roberts. 1991.
Isolation of Rift Valley fever virus from mosquitoes (Diptera: Culicidae) collected
during an outbreak in domestic animals in Kenya. J. Med. Entomol. 28(2): 293-295.**

ABSTRACT: During an outbreak of Rift Valley fever (RVF) in livestock near Lake
Naivasha, Rift Valley Province, Kenya, 61,347 mosquitoes (1287 pools) collected in
CO_2-baited light traps yielded seven viral isolates. Five isolates of RVF virus were
recovered from 18,831 *Culex zombaensis* Theobald and one from 14,439 *Mansonia
africana* (Theobald). One of isolate of a Bunyamwera group virus was recovered
from 1175 *Aedes quasiunivittatus* (Theobald).

**Logan, T.M., K.J. Linthicum, P.C. Thande, J.N. Wagateh, G. Nelson and C.R. Roberts.
1991. Egg hatching of Aedes mosquitoes during successive floodings in a Rift Valley
fever endemic area in Kenya. J. Am. Mosq. Contr. Assoc. 7(1): 109-112.**

ABSTRACT: Floodwater *Aedes* breeding habitats in central Kenya were
sequentially flooded to determine the amount of egg hatch that occurred during each
flooding. Approximately 90% of the total number of larvae sampled during four
floodings emerged during the initial flooding. The number of *Aedes* eggs hatching
during the second flood was lowest of all 4 floodings and no significant differences in
the amount of egg hatching during floodings 3 and 4 were seen. Unhatched *Aedes*
eggs were present in soil samples collected after the final flooding. The possible
implications of these findings with regard to rift Valley fever virus control are
discussed.

**Logan, T.M., K.J. Linthicum, P.C. Thande, J.N. Wagateh and C.R. Roberts.
Mosquito species collected from a marsh in western Kenya during the long rainy
season. submitted to J. Am. Mosq. Contr. Assoc.**

ABSTRACT: A total of 476,656 mosquitoes representing 10 genera and 43
species were collected from a marsh in the western Kenya highlands. *Culex
pipiens* was the most common species, totalling 91.3% of the collection
followed by *Cx. zombaensis* (2.1%), *Anopheles coustani* (1.1%), *An. squamosus*
(0.8%), *Mansonia uniformis* (0.6%), *Ma. africana* (0.4%), *Coquilletidia aurites*
((0.4%) and *Uranotaenia mashonaensis* 0.3%). *Aedes quasiunivittatus* was the first
floodwater species to emerge from newly flooded areas and was the most abundant
Ae. spp. collected representing 88% of all *Ae.* specimens. *Culex guiarti* and *Cx.
zombaensis* colonized newly flooded areas soon after the areas became flooded.

**Linthicum, K.J., T.M. Logan, P.C. Thande, J.N. Wagateh, C.W. Kamau, C.W. Bailey,
F.G. Davies and J.P. Kondig. 1989. Efficacy of a sustained-release methoprene
formulation on potential vectors of Rift Valley fever virus in field studies in Kenya. J.
Am. Mosq. Contr. Assoc. 5(4): 603-605.**

ABSTRACT: Dambos were artificially flooded and treated with Altosid
pellets applied at a rate of 5.6 kg/ha. One dambo was treated the day after
flooding, and one was treated 3 days after flooding. An untreated dambo was
used as a control. There was 100% mortality of both *Aedes* and *Culex* pupae in
treated dambos during week 2 of the study. This was significantly higher than in the

control (untreated) dambo. There appeared to be some residual effect for *Culex* pupae for up to 3 weeks following treatment.

Logan, T.M., K.J. Linthicum, J.N. Wagateh, P.C. Thande, C.W. Kamau and C.R. Roberts. 1990. Pretreatment of floodwater Aedes habitats (dambos) in Kenya with a sustained-release formulation of methoprene. J. Am. Mosq. Contr. Assoc. 6(4): 736-738.

ABSTRACT: Effectiveness of sustained-release Altosid pellets (4% AI methoprene) against floodwater mosquitoes in dambos treated a 5,3, and 1 week before and 1 day after flooding was determined. Only 2% of *Aedes* pupae (primarily *Aedes mcintoshi*) survived to adults in an area treated 5 weeks preflood, and no adult mosquitoes emerged from an area treated 1 day after flooding. In contrast, 12 and 16% of *Aedes* pupae successfully survived to the adult stage in areas pretreated 3 and 1 week, respectively, preflood. The effectiveness of the Altosid declined against *Culex* spp. (primarily *Cx. antennatus*) collected from dambos 15-31 days after flooding. The potential for using preflood treatment with methoprene to control *Aedes* vectors of Rift Valley fever virus in endemic areas is discussed.

Linthicum, K.J., C.L. Bailey, C.J. Tucker, K.D. Mitchell, T.M. Logan, F.G. Davies, C.W. Kamau, P.C. Thande and J.N. Wagateh. 1990. Application of polar-orbiting, meteorological satellite data to detect flooding of Rift Valley fever virus vector mosquito habitats in Kenya. J. Med. Vet. Entomol. 4: 433-438.

ABSTRACT: Measurements of green leaf vegetation dynamics recorded by the *advanced very high resolution radiometer instruments* onboard National Oceanic and Atmospheric Administration satellites 7 and 9 were used to derive ground moisture and rainfall patterns in Kenya and monitor resultant flooding of mosquito larval habitats (dambos) likely to support Rift Valley fever virus vector mosquitoes (*Aedes* and *Culex* spp.). Satellite-derived data from mid-1981 to December 1988 have been analyzed with corresponding rainfall, flooding and vector population data as they relate to Rift Valley fever virus ecology. Single (7X& km) and multiple grid-cell image analysis (200X300 km) in small localized areas and large geographical regions, respectively, of vegetation data were used to quantify the potential for flooding of mosquito breeding habitats. The ability to detect accurately parameters, such as ground moisture, that determine flooding could provide local officials with sufficient warning to *allow for implementation of specific mosquito* control measures before a disease outbreak.

Linthicum, K.J., D. Angleberger, D. Ashby, G. Nelson, R. Whittle, J.N. Wagateh, P.C., P.C. Thande and C.W. Kamau. an automated technique to map mosquito-breeding habitats in Kenya. In preparation.

ABSTRACT: The flooding of mosquito-breeding habitats known as dambos has been associated with epizootics and epidemics of Rift Valley fever (RVF) virus in sub-Saharan Africa. Identification and mapping of these habitats are critical to the identification of foci of disease outbreaks and implementation of vaccination and vector control programs. An automated technique was tested for its ability to map dambos with existing LANDSAT Thematic Mapper satellite data. Multivariate statistical techniques were used on a wet season (1987) and a dry season (1984) data set for a 135 square km test area (150,000 pixels) in central Kenya. Principal component analysis of all 14 available satellite bands found that most of the variation in the data was contained in the first 3-4 linear combinations of the original bands. Cluster analysis of the components was used to remove clouds and cloud shadows. Linear discriminant analysis was performed on the band data by using a

training dambo data set previously identified and confirmed. Dambo habitats were accurately identified with a quantifiable degree of precision.

Pope, K.O., E.J. Sheffner, K.J. Linthicum, C.L. Bailey, T.M. Logan, E.S. Kasischke, K. Birney, A.R. Njogu and C.R. Roberts. Identification of central Kenya Rift Valley fever virus vector habitats with Landsat TM and evaluation of their flooding status with airborne imaging radar. In preparation.

ABSTRACT: This study demonstrated the potential for using LANDSAT satellite data to predict dambo habitats. It also demonstrated the potential for using aircraft mounted synthetic aperture radar (SAR) data to show dambo flooding.