AD		

DTIC

ELECTE FEB 2 2 1994

AD-A277 725

ANNUAL PROGRESS REPORT

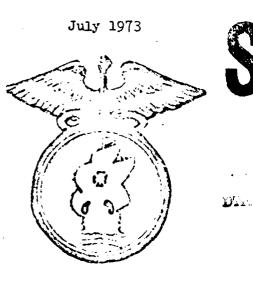
RCS MEDDH-288 (R1)

1 July 1972 - 30 June 1973

U.S. Army Medical Research Unit, Fanama

Box 1809

APO New York 09826





Approved for public release, distribution unlimited

9472 18 169

DISCLAIMER NOTICE UKILITUN ~1EK هوالالالم

THIS DOCUMENT IS BEST QUALITY AVAILABLE. THE COPY FURNISHED TO DTIC CONTAINED A SIGNIFICANT NUMBER OF PAGES WHICH DO NOT REPRODUCE LEGIBLY.

ANNUAL PROGRESS REPORT

ΑÚ

RCS MEDDH-288 (R1)

1 July 1972 - 30 June 1973

U.S. Army Medical Research Unit, Panama

Box 1809

APO New York 09826

. :

Project No. 3A061102B71Q, Task 00, Work Units 110, 419, 421

July 1973

Approved for public release; distribution unlimited

i

US ARMY MEDICAL RESEARCH UNIT - PANAMA

.

1

6

under technical direction of

WALTER REED ARMY INSTITUTE OF RESEARCH

.

an operating agency of

•-

US ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND

is co-located with the	
	Accesion For
MIDDLE AMERICA RESEARCH UNIT Ancon, Canal Zone	NTIS CRA&I
and administratively supported by	By Di. tab: tio::/
	Avhiability Codes
US ARMY FORCES SOUTHERN COMMAND	Dist Avail a dijor Special
	A-1

ii

SUMMARY

The research program of UNAMEN-P is devoted to the study of infectious diseases military injectance in Latin America. The investigations reported are primarily concerned with American leishmaniasis, a disease which continues to affiliet US Forces personnel.

A study of the effect of chamotherapy on serum antibody was made to determine if serologic testing would be of value in judging treatment efficacy. Although few patients reverted to seronemativity, there was a demonstrable effect in most cases, and the rate of treatment failure was inversely correlated with diminution of titers. In one espundia case declining titers paralleled clinical improvement and an increase in titer accompanied an explosive recrudecence.

Follow-up of patients treated with actualidate in the Canal Zone and Republic of Panama medical facilities demonstrated conclusively that this drug is of no value.

A vero cell experimental infection to tell for antideishmanial drug screening was developed which permits exposure of intracellular amastigotes to drug for up to 10 days. However, no effect on the parasites could be demonstrated with this system using a clipically effective drug, methyl glucamine antimoniate.

An incidental finding was made of the first human liver fluke (<u>Amphimerus sp</u>.) infection in Panama, which constitutes only the third report from the Western Hemisphere.

Normal hematologic values for the colonized cotton rats (<u>Sigmodon</u> <u>hispidus</u>) used for experimental infection studies were derived from monthly samples over a 6-13 month period.

The life-cycle of <u>Angiostroncylus conterioensis</u> was established in the laboratory and experimental infections studied in several species of wild rodents and 2 species of sub-human primates, which showed monkeys develop a disease picture resembling that of humans.

A 2 year study of breeding populations of phlebotomine sandflies and local environmental effects on these populations was completed. The species complement is divided into 2 major consociations, one dominated by anthropophilic species and the other by moophilic species. The species complement includes 6 major species of which 4 are anthropophilic and have been implicated in transmission of American leishmaniasis. The effect of clinatologic, hydrologic, phytologic, and edaphic factors on sandfly distribution was studied. Mass rearing techniques using stendard Laboratory plassware were developed which produced improved yields over traditional methods, with greatly reduced expenditure of man hours. Wild caught females were placed in culture preparations in which eggs were laid, hotched and immature stage development progressed with essentially no attention or care, which constitutes an important first step to colonization.

y

<

iν

FORWARD

The research program of the U.S. Army Medical Research Unit, Panama is devoted to the study of infectious diseases and their vectors of military importance in Latin America.

The research projects were carried on under the following project and task number:

3A061102B71Q, Task 00, Work Units 110, 419, 421

In conducting the research described in this report, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care", as promulgated by the Committee on the Guide for Laboratory Animal Resources National Academy of Sciences - National Research Council.

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.

v

TABLE OF CONTENTS

		P	AGE NO.
WORK UNIT	421	Studies on Parasitic Infections in Latin America	1
WORK UNIT	110	Studies on Arthropods of Medical Importance in Latin America	14
WORK UNIT	419	Pathology and Pathogenesis of Naturally Occurring Infections in Latin America	30
DISTRIBUTI	ION LI	ST	43
DOCUMENT C	CNTRO	L DATA (DD FORM 1473)	44

ANNUAL PROGRESS REPORT

PROJECT NO.	3A061102B71Q :	Comm	unicable Disease and Immunology
TACK NO.	00 :		ogy and Control of Disease Vectors Reservoirs
WORK UNIT	421 :		ies on Parasitic Infections in in America
REPORTING INSTALLATI	CON ? :	Box	Army Medical Research Unit, Panama 1809 New York 09826
PERIOD COVERED BY RE	PORT ·	l Ju	ly 1972 - 30 June 1973
PRINCIPAL INVESTIGAT	OR :	Bryc	e C. Walton, COL, MSC
ASSOCLATE INVESTIGAT	OR :	Larr	y D. Hendricks, CPT, MSC
ASSISTANTS	:	Irma	ael E. Hajduk, SFC, AMEDS Arjona o J. Fuentes

REPORTS CONTROL SYMBOL: RCS-MEDDH-288 (R1) SECURITY CLASSIFICATION: UNCLASSIFIED

14

. /_

l

T FTLETOCK				Jan Cal at		12 - 45			47.447 A.R.H.SH
	4. KIN'SS SAGE		in a second						. LEVEL OF SUN
72 00 30	H. Terminat:	10n U	1 U	316	<u>NL</u>		20 yes - 1.	1.0	A VORE LH.T
10 40 00.	PROGRAM CLIMENT			TASK APEA HUNBL	P		WORK UNT	NUM T	P
A. PEUMARY	G. Low Fr	12012 2012		<u>رن</u>			121		
U. CONTRIG TONS		್ ತಾ ನಟಣಾ	- 1	00					
	1.0203 3.224(3.)								
IS TITLE , MAR IA HAN	Seturite Contentorflue Code	,*							
(U) Etulie:	s of Earloitic	e bilonde i	'n Let'e F	terica (PLI	PZ)				
2. 54124 716 2 140 12									
002600 Stol	10/7/010100 M	ierc' log		Clining Medi	icin	<u>.</u>			
ISTAN' LAIS		14. ES	etter filosofie et tel Till	IS FURLING AGENCY			IS. PERFORM	NCE ME	1+.00
64 07		73 05 30		<u>P4</u>			<u>"Ç" –</u>	<u> IN H</u>	0003
IT. CONTHACT CHANT	ot applicable					A PROFESSIO	NAL MAN YRS	2.00	NDS fin Bleusandes
& DATES/CFFECTIVES	oo appersate	EXPIRATION		I'NE - EUIF 4				1	
L NUMBER:*				FISCAL 72	1		2		55
G TYPS:		& ANO-INT:		YEAR LOOPLNY					
E KIND OF A LAPLE		f. CRM. AMT.		73	1		1 1/2		55
O. RESPONSILLE DING	ORGANIZATION		- 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997	20 PEHIORING ORGI	ANIZATI	Эн	7	سميدين مشيره	
NAME:*				HAME TIC AND		·· -	• • • • • • • • • • • • • • • • • • •		
US Arm	w Medical Res	search Unit	, Panala	US ATT					it, Panam
ADDRESS.* BOX 3	1809 APO New Y	lork 03826		ADDRESS.ª BOX	1808	, APO .	llew Yor	rk 09	826
				PRINCIPAL INVESTIGA		mish stan #	11 8 Arada-1-	tos/10-11-	-
				NAME . Walto					Y
RESPONSIBLE INCOVICU					-	•	• , 001		
NAME Walton, Bryce C.				TEL: PHONE: 82-3017					
						MUMORE			
TELEPHONE 82-				SOCIAL SECURITY A		NUMBER			
TELEPHONE 82-				ASSOCIATE INVESTIGA	TORS			- T	
TELEPHONES 82- 11. general usc	-3017	"destates		ASSOCIATE INVESTIGA NAMP: HERIGY	toas cicks	s, Larr			
TELEPHONG 82- II. GENERAL USC "FOREIGH III	-3017 TELLIGENCE CC			ASSOCIATE INVESTIGA	toas cicks	s, Larry	J., MA	J	
TELEPHONY, 82- 11. general usc "FOREIGN II. 2. revalation worse	-3017 NTELLIGENCE CC	carron (+ 'e)		associate investiga name: Heridr mane: Acker	ricks man	s, Larry , Larry (U)	J., MA Leptos	J piro:	
TELEPHONY, 82- N. GENERAL USC "FOREIGN II: E. REVALACT/MOREIGN (U) Parabit	-3017 MTELLIGENCE CC EACH DE STORE COMMUNICATION tic Disease (L	ana an J) Leishnan	Nirajs (J)	Associate investica HAMP: Hendr HAMP: Acker	ricks rman	s, Larry , Larry (U) J) Sero	J., MA Leptos logy (U	J piro:) Li	ver fluke
TELEPHONY 82- U. GENERAL USC "FOREIGN IN E. REVERDED, PARASIT (U) Parasit D. TECHNICAL CALLOR	-3017 ITELLIGENCE CC EACH HAT STORAGE COMMUNICATION LIC DISCUSSE (U	ceron (c. le) J) I (ci shiaan Phoas (st (comist (ndist al paragraphie i	Associate investiga HAMP: Hendr HAMP: Acker Chemotherapy	ricks	s, Larry , Lerry (U) J) Sero	J., MA Leptos Losy (U	J piro:) Li ⁻	ver fluke
TELEPHONY 82- "FOREIGN IN KEYNDROTOPHONE (U) Paradit D. TECHNICAL COLLOC 23. (U) The	-3017 ITELLIGENCE CO EACH HAS SHOWN COMMON tic Disease (U Type," 24 APPROACH, 25 e acquisition	diora (4) J) Josishnam Phose as formed (Of dota co	ndisi al peregressie MCCMILLS I	Associate investica HAMP: Hendr WANT: Acker Chemotherapy deminied to non ber. Press prevalence an	ricks rman . r (l	s, Larry (U) <u>(U)</u> <u>(U)</u> Sero	J., MA Leptos Lory (U unv classifie tion of	J piro:) Li 	ver fluke •.) asitic
TELEPHONY 82- "FOREIGN IN (U) Paradit (U) Paradit 23. (U) The diseases in	TELLIGENCE CO EACH	Color Color J) Joishnan PROSE SS (Jerner) Of dota co Sa; recogni	ncoming p tion of pu	Associate investica HAMP: Hendr WANT: Acker Chemotherapy dentified is comber. Press prevalence an ablic health	ricks man (I v (I v (I v (I) v	5, Larry (U) <u>(U) Sero</u> Istribu	J., MA Leptos Lory (U tion of f actua	J piro:) Li pari l or	<u>ver fluke</u> *, asitic potentia
TELEPHONY 82- U. GENERAL UIG U. FOREIGN III E. REVALACION FROM (U) Parabit 23. (U) The diseases in military in	-3017 TELLIGENCE CO EACH	J) Leishnan Paose Stateman Of deta co ea; recogni prease of k	ncoming p tion of pu nowledge of	Associate investica HAMP: Hendr WANT: Acker Chemotherapy denuise transfer pre- prevalence an ablic health of reservoirs	ricks man (I v (I v (I v (I) v	5, Larry (U) <u>(U) Sero</u> Istribu	J., MA Leptos Lory (U tion of f actua	J piro:) Li pari l or	<u>ver fluke</u> *; asitic potentia
TELEPHONY 82- "FOREIGN IN (U) Parabit D. TECHNOL CALER 23. (U) The diseases in military in of diagnosi	TELLIGENCE CO EACH HES STORE COMMUNICATION tic Disease (U Twe," 24 APPROACH, 25 e acquisition in Latin Americ sportance; inc is, treatment	J) Joishnan Paos Strummu of deta co ea; recogni crease of k and contro	ncoming p tion of pu nowledge of 1 of these	Associate investiga Hawr: Hendr WART: Acker Chemotherapy dentified to on her Press prevalence an ablic health of reservoirs e diseases.	(L man) (L)(L)(L)(L)(L)(L)(L)(L)(L)(L)(L)(L)(L)(s, Larry (U) J) Sero Istribu Distribu Diems o I vecto	J., MA Leptos lory (U tion of f actua rs; and	J piro <u>Li</u> par l or imp:	ver fluke asitic potentia rovement
TELEPHONY 82- "FOREIGN IN "FOREIGN IN "FO	TELLIGENCE CC EACH HIS SUMPLIE tic Disease (University Communi- tic Disease (University Communi- Communi- Communi- Communi- Communi- Communi- Communi- Communi- Commu	J) Jeishnan Of deta co ea; recogni rease of k and contro nemotherapy	nowning p tion of pu nowledge o 1 of these on sorum	Associate invession waw: Hendr waw: Kendr waw: Acker Chemotherapy denuted transfer Free prevalence an ablic health of reservoirs e diseases. antibodies c	(Unit of the second sec	s, Larry (U) <u>J) Sero</u> Istribu Dlems o l vector	J., MA Leptos <u>lory (U</u> tion of f actua rs; and with p	J piros <u>J</u> Li pars l or imp: rima:	ver fluke ,, asitic potentia rovement ry cutan-
TELEPHONY 82- "FOREIGN IN (U) Parabit (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ	TELLIGENCE CO EXCHANTINGENCE CO EXCHANTING tic Disease (L Exc. 24 APPROACH 24 e acquisition h Latin Americ sportance; inc ls, treatment e effect of ch can leichmanis	J) Jeishman Prostation of deta co ea; recogni crease of k and contro nemotherapy asis and wi	ncorning p tion of pu nowledge of 1 of these on strum th seconds	Associate invession waw: Hendr waw: Acker Chemotherapy denuised to an her. Free prevalence an ablic health of reservoirs e diseases. antibodies o ary succoutar	ricks man (I a und prob s and of pa neous	s, Larry (U) <u>1) Sero</u> Istribu plems o l vecto: atients s diseau	J., MA Leptos lory (U min channe tion of f actua rs; and with p se was	J piro: <u>Li-</u> par: l or . imp: rima: stud:	ver fluke asitic potentia rovement ry cutan- ied with
TELEPHONY 82- "FOREIGN IN (U) Parabit (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec	TELLIGENCE CO Extension Communication tic Disease (L type: 24 Apendate 24 e acquisition in Latin Americ sportance; inc is, treatment e effect of ch can leichmanis et Fluorescent	J) Jeishman of deta co ea; recogni crease of k and contro hemotherapy asis and wi c Antibody	ncorning p tion of pu nowledge of the second the second test. The	Associate investica HAMP: Hendr WANT: Acker Chemotherapy derivation by pro- prevalence an ablic health of reservoirs e diseases. antibodies of ary mucocutar e series incl	ricks man r (l prob s and of pe luded	s, Larry (U) <u>J) Sero</u> Istribu Diems o l vecto atients s disea l patie	J., MA Leptos losy (U min channe tion of f actua rs; and with p se was nts tre	J piro: <u>Li:</u> par: l or . imp: rima: stud: ated	ver fluke asitic potentia rovement ry cutan- ied with with
TELEPHONY 82- "FOREIGN IN (U) Parabit (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil	TELLIGENCE CC <u>Extension comm</u> tic Disease (L type, 24 APPROACH 25 e acquisition h Latin Americ nportance; inc is, treatment e effect of ch can leichmanis et Fluorescent L pamoate, two	J) Jeishman of deta co ea; recogni crease of k and contro hemotherapy asis and wi contibody o aif.erent	ncorning p tion of pu nowledge of of those on scrum th seconds test. The penterale	Associate investica NAME: Hendr WANT: Kendr WANT: Acker Chemotherapy denote to an ber Prese prevalence an ablic health of reservoirs e diseases. antibodies of ary mucocutar e series incl ent antimonia	(1 man) (1) (1) (1) (1) (1) (1) (1) (1) (1) (1	s, Larry (U) <u>J) Sero</u> Istribu Distribu Diems o l vecto atients s diseau l patien and wi	J., MA Leptos losy (U min channe tion of f actua rs; and with p se was nts tre th amph	J piro:) Li para l or imp: rima: stud: ated oter.	ver fluke asitic potentia rovement ry cutan- ied with with icin B.
TELEPHONY 82- "FOREIGN IN (U) Parabit (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil The efficac	TELLIGENCE CO EACH DESIGN CE CO EACH DESIGN COMMUNICATION tic Disease (U NVE, 24 APPROACH 25 e acquisition in Latin Americ inportance; inc is, treatment e effect of ch can leichmanis of Fluorescent l pamoate, two by of metranid	J) Jeishman of deta co ea; recogni crease of k and contro nemotherapy asis and wi c Antibody o aif.erent iazole for	nowning p tion of pu nowledge of of those on scrum th seconds test. The pentovale the treats	Associate investica NAME: Hendr NAME: Hendr NAME: Acker Cherotherapy corevalence an ablic health of reservoirs e diseases. antibodies of ary succoutar e series incl ent antimonia aent of cutan	(1 ricks rman r (1 prob a not prob a not p prob a not prob p	s, Larry (U) J) Sero Istribu Dlems o l vecto atients s diseas and with and with	J., MA Leptos logy (U min comme tion of f actua rs; and with p se was nts tre th amph can lei	J piro:) Li par: l or . imp: rima: stud: ated oter: shma:	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis
TELEPHONY 82- "FOREIGN IN (U) Parabit (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil The efficac was studied	TELLIGENCE CC EXCRANSION COMMUNICATION tic Disease (L NVE, 24 APPROACH, 24 e acquisition h Latin Americ sportance; inc is, treatment e effect of ch can leichmanis et Fluorescent L pamoate, two by of metranid i by follow-up	J) Jeishnan of deta co ea; recogni rease of k and contro nemotherapy asis and wi c Antibody o aiflerent iazole for o of patien	nowning p tion of pu nowledge o l of these on scrum th seconds test. The test. The the treats	Associate invession waw: Hendr waw: Hendr waw: Acker Chemotherapy orevalence an ablic health of reservoirs e diseases. antibodies of ary mucocutar e series incl ent antimonia anti of cutan d with this d	(I man prot and di prot and di prot and di prot and tuded also, ineous luded	s, Larry (U) 1) Sero Istribut	J., MA Leptos lory (U tion of f actua rs; and with p se was nts tre th amph can lei ocal me	J piro:) Li: pari l or imp: rima: stud: ated oter: shma: dica:	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis l facilit
TELEPHONE 82- "FOREIGN IN "FOREIGN IN "FOREIGN IN "FOREIGN IN "FOREIGN IN "TECHNICAL CALLOR 23. (U) The diseases in military in of diagnosi 24. (U) The eous America the Indirec cycloguanil The efficac was studied A tissue cu	TELLIGENCE CO EXAMINED CONTRACT tic Disease (University Contraction is acquisition in Latin America sportance; includes the effect of children en leichmania of Fluorescent 1 pamoate, two by of metranic i by follow-up alture drug so	J) Jeishman of deta co ea; recogni crease of k and contro memotherapy asis and wi c Antibody o aiflerent iazole for o of patien creening sy	nowning p tion of pu nowledge o 1 of these on scrum th seconds test. The pentevale the treats its treats	Associate invession waw: Hendr waw: Hendr waw: Acker Chemotherapy demuted to an her Free prevalence an ablic health of reservoirs e diseases. antibodies of ary mucocutar e series incle ent antimonia ant of cutan d with this d cried as a me	(I man ricks man r (I prot s and of prot s and of prot s and luded als, ineous luded als, ineous luded als,	s, Larry (U) 1) Sero Istribut plems of atients atients s diseas and with and with a Americ in 3 lo of in 3	J., MA Leptos lory (U time comment tion of f actua rs; and with p se was nts tre th amph can lei ocal me vitro d	J piro) Li par l or imp: rims stud ated oter shma dica eter	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis l facilit mination
TELEPHONY 82- "FOREIGN IN (U) Parabit (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil The efficac was studied A tissue cu of anti-lei	TELLIGENCE CO TELLIGENCE CO TAGAINE STORY COMMON tic Disease (L tic Disease (L treation America acquisition a Latin America aportance; inco is, treatment e effect of ch can leichmanise t Fluorescent l pamoate, two by of metranica i by follow-up ulture drug so ishmanial acti	J) Jeishman of deta co ea; recogni crease of k and contro hemotherapy asis and wi t Antibody o affierent iazole for o of patien creening sy wity again	ncorning p tion of pu- nowledge of on scrum th seconds test. The pentovale the treats the treats star vas t star vas t	Associate invession waw: Hendr waw: Kendr waw: Acker Chemotherapy prevalence an ablic health of reservoirs e diseases. antibodies of ary mucocutar e series incl ent antimonia ant of cutan d with this d cried as a me cellular amas	(I man r (I prol s and of prol s and of prol s and luded als, neous luded als, stigo	s, Larry (U) J) Sero Ustribut blems o l vector atients s diseau and wite and wite in 3 lo of in 3 btes,	J., MA Leptos logy (U min comme tion of f actua rs; and with p se was nts tre th amph can lei ocal me vitro d The Hem	J piro) Li par l or imp: rima: stud ated oter shma: dica eter olyt:	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis l facilit mination ic Lepto-
TELEPHONY 82- "FOREIGN IN (U) Parabit (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil The efficac was studied A tissue cu of anti-lei	TELLIGENCE CO EXAMINED CONTRACT tic Disease (University Contraction is acquisition in Latin America sportance; includes the effect of children en leichmania of Fluorescent 1 pamoate, two by of metranic i by follow-up alture drug so	J) Jeishman of deta co ea; recogni crease of k and contro hemotherapy asis and wi t Antibody o affierent iazole for o of patien creening sy wity again	ncorning p tion of pu- nowledge of on scrum th seconds test. The pentovale the treats the treats star vas t star vas t	Associate invession waw: Hendr waw: Kendr waw: Acker Chemotherapy prevalence an ablic health of reservoirs e diseases. antibodies of ary mucocutar e series incl ent antimonia ant of cutan d with this d cried as a me cellular amas	(I man r (I prol s and of prol s and of prol s and luded als, neous luded als, stigo	s, Larry (U) J) Sero Ustribut blems o l vector atients s diseau and wite and wite in 3 lo of in 3 btes,	J., MA Leptos logy (U min comme tion of f actua rs; and with p se was nts tre th amph can lei ocal me vitro d The Hem	J piro) Li par l or imp: rima: stud ated oter shma: dica eter olyt:	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis l facilit mination ic Lepto-
TELEPHONY 82- "FOREIGN IN (U) Parabit (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil The efficac was studied A tissue cu of anti-lei spiral (HL)	TELLIGENCE CO TELLIGENCE CO TAGAINE STORY COMMON tic Disease (L tic Disease (L treation America acquisition a Latin America aportance; inco is, treatment e effect of ch can leichmanise t Fluorescent l pamoate, two by of metranica i by follow-up ulture drug so ishmanial acti	J) Jeishman of deta co ea; recogni crease of k and contro hemotherapy asis and wi contribody o afficerent dazole for o of patien creening sy wity again cablished t	ncerning p tion of pu nowledge of on scrum th seconds test. The pentovale the treatm the treatm the treatm the treatm of intra-co	Associate invession waw: Hendr waw: Kendr waw: Acker Chemotherapy Grevalence an ablic health of reservoirs e diseases. antibodies of ary succoutar e series incl ent antimonia anti of cutan d with this d cried as a me cellular amas a tool to ma	(International states) (International states) (Inter	s, Larry (U) 1) Sero Ustribut blems of l vector atients s diseas and wit and wit in 3 lo of in 3 otes.	J., MA Leptos locy (U min comme tion of f actua rs; and with p se was nts tre th amph can lei ocal me vitro d The Hem veillan	J piro) Li par l or imp: rima: stud ated oter shma: dica: eter olyt: ce f	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis l facilit mination ic Lepto- or
"FOREIGN 62- "FOREIGN IN (U) Parabit (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil The efficac was studied A tissue cu of anti-lei spiral (HL) leptospiral	TELLIGENCE CO Extension Communication tic Disease (L tic Di	J) Jeishman of deta co ea; recogni crease of k and contro hemotherapy asis and wi contribody o aiflerent iazole for o of patien preening sy wity again cablished t tong U.S. F	nearning p tion of pu- nowledge of of those on scrum th seconds test. The test. The the treats the treats the treats ast intra- o provide orces per	Associate investica NAME: Hendr NAME: Hendr NAME: Acker Chemotherapy prevalence an ablic health of reservoirs e diseases. antibodies of ary mucocutar e series incle ent antimonia aent of cutan i with this d cried as a me cellular amas a tool to ma connel. Cons	(1) (1) (1) (1) (1) (1) (1) (1) (1) (1)	s, Larry (U) J) Sero Istribution Istributi	J., MA Leptos lorv (U the comment tion of f actua rs; and with p se was nts tre th amph can lei ocal me vitro d The Hem veillan ervices	J piro piro par l or imp rima stud ated oter shma dica eter olyt ce for	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis l facilit mination ic Lepto- or
"FOREIGN 62- "FOREIGN IN (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil The efficat was studied A tissue cu of anti-lei spiral (HL) leptospiral of unusual	TELLIGENCE CO Extension communication tic Disease (L tic Di	J) Jeishman of deta co ea; recogni crease of k and contro hemotherapy asis and wi contribody o afferent iazole for o of patien creening sy wity again cablished t tong U.S. F Sections wa	nowned proving p tion of pu- nowledge of 1 of these on scrum th seconds test. The test. The the treats the treats the treats the treats of the treats of the treats of the treats of the treats test intra- of provide orces persons provided	Associate investica NAME: Rendr NAME: Rendr NAME: Acker Cherotherapy corevalence and ablic health of reservoirs e diseases. antibodies of ary succoutar e series incle ent antimonia tent of cutan d with this d cried as a me cellular amass a tool to ma sonnel. Cons i to local me	(I man) (I m) (I m) (I m) (I m) (I m) (I m) (I man) (I (I man) (I (I (I man) (I (I (I (I (I (I (I (I (I (I (I (I (I	s, Larry (U) J) Sero (U) J) Sero (U) Sero Sero Sero Sero Sero Sero Sero Sero	J., MA Leptos logy (U the comment tion of f actua rs; and with p se was nts tre th amph can lei ocal me vitro d The Hem veillan ervices litics.	J piro:) Li par l or imp: rima: stud: ated oter shma: dica: eter olyt: ce for	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis l facilit mination ic Lepto- or diagnosi
"FOREIGN 62- "FOREIGN IN (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil The efficae was studied A tissue cu of anti-lei spiral (HL) leptospiral of unusual 25. (U) A d	TELLIGENCE CC Extension communication tic Disease (L Net: 24 APPROACH 24 e acquisition h Latin America sportance; inc is, treatment e effect of ch can leichmania of Fluorescent L pamoate, two cy of metranic i by follow-up ulture drug so ishmanial acti) test was est L infection an parasitic inf listinct respo	J) Jeishman PROFESSION OF deta co ca; recogni rease of k and contro nemotherapy asis and wi c Antibody o afflerent iazole for o of palien recenting sy vity again cablished t tong U.S. F Sections was onse of ser	newruing p tion of pu nowledge o on sorum th seconds test. The the treats the treats the treats the treats of provide forces pure s provided un antil of	Associate investica waw: Hendr waw: Hendr waw: Acker Chemotherapy corevalence an ablic health of reservoirs e diseases. antibodies of ary mucocutar e series incl ent antimonia anti of cutan d with this d cried as a me cellular amas a tool to ma connel. Cons i to local me lies to drug	(I ricks rman) (I prob s and of pa luded also luded also stigo ainto sulta edica trea	s, Larry (U) 1) Sero (U) 1) Sero (U) 1) Sero (U) 1) Sero (U) 1) Sero (U) 1) Sero (U) 1) 1) Sero (U) 1) 1) Sero (U) 1) 1) Sero (U) 1) Sero	J., MA Leptos logy (U the comment tion of f actua rs; and with p se was nts tre th amph can lei ocal me vitro d The Hem veillan ervices lities. was obs	J piro:) Li par l or imp: rima: stud ated oter shma: dica eter olyt: ce for for	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis l facilit mination ic Lepto- or diagnosi d in most
"FOREIGN 62- "FOREIGN IN (U) Parabit (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil The efficae was studied A tissue cu of anti-lei spiral (HL) leptospiral of unusual 25. (U) A d cases of le	TELLIGENCE CO TAGANESSICE CO TAGANESSICE CO TAGANESSICE CO TAGANESSICE CO TAGANESSICE CO TOTALOS CONTACT A APPROACE SE acquisition h Latin America aportance; inc is, treatment e effect of ch can leichmania of Fluorescent 1 pamoate, two cy of metranic i by follow-up ulture drug so ishmanial acti) test was est 1 infection am parasitic inf listinct responses.	J) Jeishman Of deta co ca; recogni crease of k and contro hemotherapy asis and wi controlerapy asis and wi asis and wi controlerapy asis and wi asis asis asis asis asis asis asis asis asis asis asis asis asis asis asis	noevalag tion of pu- nowledge of nowledge of lot these on scrum th seconds test. The pentevale the treats the treats the treats the treats of pentevale of pentevale	Associate invession waw: Hendr waw: Hendr waw: Acker Chemotherapy orevalence an ablic health of reservoirs e diseases. antibodies of ary mucocutar e series incle ent antimonia ant of cutan d with this d cried as a me cellular amas a tool to ma ionnel. Cons i to local me lies to drug ntage reverte	(I ricks rman) (I ricks rman) prob s and of pa and of pa luded als, ieous luded als, isouta stigo ainto sulta edica tread	s, Larry (U) 1) Sero (U) 1) Sero (U) 1) Sero stribut olems o 1 vecto atients s diseas and with s Americ in 3 lo of in 3 otes, ain sur- ative st attent vo	J., MA Leptos lorv (U tion of f actua rs; and with p se was nts tre th amph can lei ocal me veillan ervices lities. was obs egativi	J piro:) Li par l or imp: rims: stud: ated oter shma: dica eter olyt: ce for for crve(ty,)	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis l facilit mination ic Lepto- or diagnosi d in most but some
TELEPHONY 82- "FOREIGN IN (U) Parabit (U) Parabit (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil The efficac was studied A tissue cu of anti-lei spiral (HL) leptospiral of unusual 25. (U) A d cases of le predictive	TELLIGENCE CO TELLIGENCE CO TAGANESSION COMMUNICATION tic Disease (L tic Disease (L televelocition a acquisition a latin America aportance; inc is, treatment e effect of ch can leichmanias of Fluorescent l pamoate, two by follow-up alture drug so ishmanial acti) test was est l infection am parasitic inf istinct responses of shamaniasis. value for rec	J) Jeishman of deta co ea; recogni crease of k and contro hemotherapy asis and wi controlerapy of patien iazole for of patien cof patien cong U.S. F fections wa onse of ser Only a sm currence of	ncerning p tion of pu- nowledge of nowledge of the these on scrum th seconds test. The pentryale the treats the treats the treats the treats of pentryale of the treats star was t ist intra- o provide forces per s provide the antil of hall percer lecions w	Associate invession waw: Hendr waw: Hendr waw: Acker Chemotherapy Grevalence an ablic health of reservoirs e diseases. antibodies of ary mucocutar e series incl ent antimonia dent of cutan d with this d cried as a me cellular amas a tool to ma connel. Cons i to local me lies to drug ntage reverte vas shown for	(I realized to realized to	s, Larry (U) J) Sero (U) J) Sero (U) Istribu- plems o less o less o atients and with a America of in 3 le of in 3 le otes. ain sur- ative s ative s atiment to peron cologic	J., MA Leptos losy (U the comment tion of f actua rs; and with p se was nts tre th amph can lei ocal me vitro d The Hem veillan ervices lities. was obs egativi monito	J piro piro par l or imp rima stud ated oter shma dica eter olyt ce for for erve ty, l	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis l facilit mination ic Lepto- or diagnosi d in most but some
"FOREIGN 62- "FOREIGN IN (U) Parabit "Advances of diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil The efficac was studied A tissue cu of anti-lei spiral (HL) leptospiral of unusual 25. (U) A d cases of le predictive Metranidazo	TELLIGENCE CO TELLIGENCE CO TELIGENCE CO TELLIGENCE CO TELLIGENCE TELLIGENCE CO TELLIGENCE CO TELLIGENCE CO TELLIGENCE	J) Jeishman of deta co ea; recogni crease of k and contro hemotherapy asis and wi contherapy asis and asis asis and asis asis and asis asis asis asis asis asis asis asis asis	ncorning p tion of pu- nowledge of on scrum th seconds test. The pentovale the treats the treats the treats the treats of pentovale of the treats of pentovale of the treats of pentovale of the treats the treats the treats the treats of pentovale of pentovale of pentovale of pentovale of the treats the treats the treats the treats the treats of pentovale of the treats of pentovale of the treats of the treats the tre	Associate investica waw: Hendr waw: Kendr waw: Acker Chemotherapy prevalence an ablic health of reservoirs e diseases. antibodies of ary mucocutar e series incl ent antimonia tent of cutan d with this d cried as a me cellular amas a tool to ma connel. Cons i to local me lies to drug ntage reverte vas shown for of no value i	(I man ricks man r (I prob s and of prob s and and and and and and and and and and	s, Larry (U) J) Sero (U) Il Sero Il Sero Il vecto atients atients and with and with a facility attent of a facility attent of a facility attent of a facility attent of a facility attent of a facility attent of a facility attent of a facility atte	J., MA Leptos logy (U the comment tion of f actua rs; and with p se was nts tre th amph can lei ocal me vitro d The Hem veillan ervices lities. was obs egativi monito tment o	J piro piro piro par imp imp rima stud ated oter shma dica dica dica for cryce for f Am	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis l facilit mination ic Lepto- or diagnosi d in most but some erican
"FOREIGN 62- "FOREIGN IN (U) Parabit (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil The efficac was studied A tissue cu of anti-lei spiral (HL) leptospiral of unusual 25. (U) A d cases of le predictive Metranidazo leishmanias	TELLIGENCE CO Extension Communication tic Disease (L tic Di	J) Jeishman of data co ea; recogni crease of k and contro hemotherapy asis and wi contherapy asis and control asis asis asis and wi contherapy asis and asis asis asis asis asis asis asis asis and wi contherapy asis asis asis asis asis asis asis asis asis asis	ncerning p tion of pu- nowledge of nowledge of the treat the seconds test. The pentryale the treat the treat of the treat of the treat of the treat of the treat of the treat of the treat of the treat	Associate invession way: Hendre way: Kendre way: Acker Chemotherapy Grevalence an ablic health of reservoirs e diseases. antibodies of ary mucocutar e series incle ent antimonia ant of cutan d with this d cried as a me cellular amas a tool to ma connel. Cons i to local me lies to drug ntage reverte yas shown for of no value i	(I real real real real real real real real	s, Larry (U) 1) Sero (U) 1) Sero (U) 1) Sero attients of an so attients and wi and wi attients of in sur- attive sur attient of osciologic attient of osciologic attient of attient attie	J., MA Leptos lory (U the comment f actua rs; and with p se was nts tre th amph can lei ocal me vitro d The Hem veillan ervices lities. was obs egativi monito tment o f infec	J piro piro piro par imp rimat stud ated oter shmat dicat dicat eter olyt: ce for crved for ty, l	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis l facilit mination ic Lepto- or diagnosi d in most but some erican cells to
"FOREIGN 62- "FOREIGN IN (U) Parabit (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil The efficat was studied A tissue cu of anti-lei spiral (HL) leptospiral of unusual 25. (U) A d cases of le predictive Metranidazo leishmanias test compou	TELLIGENCE CO Extension communication tic Disease (L tic Di	J) Jeishman of deta co ea; recogni rease of k and contro hemotherapy asis and wi contributy o aiflerent iazole for o of palien preening sy wity again cablished t tong U.S. F fections was onse of ser Only a sm currence of sively sho culture so 10 days w	neerning p tion of pu- nowledge of a of these on scrum th seconds test. The test. The the treats the treats the treats the treats of provide orces per stanta antitor all percer lesions we wan to be of work develop	Associate invession wave: Hendre wave: Acker Chemotherapy derivative transfer free prevalence an ablic health of reservoirs e diseases. antibodies of ary succoutar e series incle ent antimonia hent of cutan d with this d cried as a me cellular amas a tool to ma formel. Cons i to local me lies to drug ntage reverte vas shown for of no value i ch permitted of. However	(In the expect, not	s, Larry (U) 1) Sero (U) 1) Sero (U) 1) Sero solution of in 3 1 of in 3 1 otes.	J., MA Leptos logy (U the comment tion of f actua rs; and with p se was nts tre th amph can lei ocal me vitro d The Hem veillan ervices litics. was obs egativi monito t infec t on in	J piro piro piro par l or rima stud ated oter shma dica dica eter for ervec ty, l f Am ted tra-	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis l facilit mination ic Lepto- or diagnosi d in most but some erican cells to cellular
TELEPHONY 62- "FOREIGN IN (U) Parabit (U) Parabit (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil The efficat was studied A tissue cu of anti-lei spiral (HL) leptospiral of unusual 25. (U) A d cases of le predictive Metranidato leishmanias test compou amastigues	TELLIGENCE CO Extension of the second second tic Disease (L tic Disease (L	J) Jeishman of deta co a; recogni rease of k and contro hemotherapy asis and wi contibody o afferent iazole for o of patien reening sy wity again cablished t tong U.S. F fections was onse of ser Only a sm purrence of sively sho culture so o 10 days w	when the property of the second secon	Associate investica waw: Hendr waw: Hendr waw: Acker Chemotherapy corevalence an ablic health of reservoirs e diseases. antibodies of ary mucocutar e series incl ent antimonia dent of cutan d with this d cried as a me cellular amas a tool to ma connel. Cons i to local me lies to drug ntage reverter as shown for of no value i ch permitted cd. However	(I man) (I prob and di prob and di prob and di prob and di prob and di prob and and and and and and and and and and	s, Larry (U) 1) Sero (U) 1) Sero (U) 1) Sero attents of anti- and with a Americ of in 3 lo of in 3 lo of in sur- attive s attive	J., MA Leptos logy (U the comment f actua rs; and with p se was nts tre th amph can lei ocal me vitro d The Hem veillan ervices litics. was obs egativi monito f infec t on in . Lept	J piro: piro: par: par: l or rima: stud: ated oter: shma: dica: eter: olyt: ce for f Am. ted tra- ospi:	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis l facilit mination ic Lepto- or diagnosi d in most but some erican cells to cellular ra]
"FOREIGN 62- "FOREIGN IN (U) Parabit (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil The efficac was studied A tissue cu of anti-lei spiral (HL) leptospiral of unusual 25. (U) A d cases of le predictive Metranidazo leishmanias test compou amastigotes infections	TELLIGENCE CO TELLIGENCE CO TAGANASSION COMMUNICATION tic Disease (L Net 24 APPROACH 24 e acquisition h Latin America aportance; inc is, treatment e effect of ch can leichmanias et Fluorescent l pamoate, two by of metranication i by follow-up ulture drug so ishmanial action parasitic inf listinct respondent bishmaniasis. value for recommon sis. A tissue ands for up to s could ke dem for a common	J) Jeishman Prost Schement of deta co a; recogni rease of k and contro nemotherapy asis and wi c Antibody o afferent iazole for o of patien recenting sy vity again cablished t cong U.S. F Sections was onse of ser Only a sm currence of sively sho c culture s o 10 Crys w custo ated source of	ncerning p tion of pu- nowhedge of nowhedge of nowhedge of the treat the seconds test. The pentryale the treat the treat the treat star was t ist intra-of orces per star was t ist intra-of orces per star us t is provide orces per all percer lesion w to be of ystum which ar develop with a cla	Associate investica waw: Hendr waw: Hendr waw: Acker Chemotherapy Grevalence an ablic health of reservoirs e diseases. antibodies of ary mucocutar e series incle ent antimonia anti of cutan d with this d tried as a me cellular amass a tool to ma ionnel. Cons i to local me lies to drug ntage reverte vas shown for of no value i ch permitted ved. However	(I man prote and of prote and of and of an	s, Larry (U) 1) Sero (U) 1) Sero (U) 1) Sero (U) 1) Sero atients of an end of an end of in 3 lo of in 3 lo of in 3 lo of in sur- ative statistics attent to be seron cologic the treation of free of free of a end of a free of a free	J., MA Leptos logy (U the comment f actua rs; and with p se was nts tre th amph can lei ocal me veillan ervices lities. was obs egativi monito tment o f infec t on in . Lept n from	J piro:) Li par l or imp: rims: stud: ated oter shma: dica eter olyt: ce for ervecty, tra- ospi one	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis l facilit mination ic Lepto- or diagnosi d in most but some erican cells to cellular ra] company
"FOREIGN 62- "FOREIGN IN (U) Parabit (U) Parabit 23. (U) The diseases in military in of diagnosi 24. (U) The eous Americ the Indirec cycloguanil The efficac was studied A tissue cu of anti-lei spiral (HL) leptospiral of unusual 25. (U) A d cases of le predictive Metranidazo leishmanias test compou amastigotes infections	TELLIGENCE CO Extension of the second second tic Disease (L tic Disease (L	J) Jeishman Prost Schement of deta co a; recogni rease of k and contro nemotherapy asis and wi c Antibody o afferent iazole for o of patien recenting sy vity again cablished t cong U.S. F Sections was onse of ser Only a sm currence of sively sho c culture s o 10 Crys w custo ated source of	ncerning p tion of pu- nowhedge of nowhedge of nowhedge of the treat the seconds test. The pentryale the treat the treat the treat star was t ist intra-of orces per star was t ist intra-of orces per star us t is provide orces per all percer lesion w to be of ystum which ar develop with a cla	Associate investica waw: Hendr waw: Hendr waw: Acker Chemotherapy Grevalence an ablic health of reservoirs e diseases. antibodies of ary mucocutar e series incle ent antimonia anti of cutan d with this d tried as a me cellular amass a tool to ma ionnel. Cons i to local me lies to drug ntage reverte vas shown for of no value i ch permitted ved. However	(I man prote and of prote and of and of an	s, Larry (U) 1) Sero (U) 1) Sero (U) 1) Sero (U) 1) Sero atients of an end of an end of in 3 lo of in 3 lo of in 3 lo of in sur- ative statistics attent to be seron cologic the treation of free of free of a end of a free of a free	J., MA Leptos logy (U the comment f actua rs; and with p se was nts tre th amph can lei ocal me veillan ervices lities. was obs egativi monito tment o f infec t on in . Lept n from	J piro:) Li par l or imp: rims: stud: ated oter shma: dica eter olyt: ce for ervecty, tra- ospi one	ver fluke asitic potentia rovement ry cutan- ied with with icin B. niasis l facilit mination ic Lepto- or diagnosi d in most but some erican cells to cellular ra] company

.

. . . .

was diagnosed as an incidental finding.

This project has been transferred to Special Foreign Activities of Welter Reed Army Institute of Research and further progress will be reported in the Annual Technical report of WRATE.

BODY OF REPORT

PROJECT NO.	3A061102B71Q :	Communicable Diseases and Immunology
TASK NO.	00 :	Ecology and Control of Disease Vectors and Reservoirs
WORK UNIT	421 :	Studies of Parasitic Infections in Latin America

DESCRIPTION:

The objectives of this project are to determine, describe, and delimit the parasitic diseases of actual or porential military importance, and to develop improved methods for their diagnosis, treatment and prevention. The major proportion of the research effort was devoted to American leishmaniasis, a disease which continues to afflict US Forces personnel. A study of the effect of chemotherapy on serum antibody was made to determine if serologic testing would be of value in judging treatment efficacy. Although few patients reverted to seronegativity, there was a demonstrable effect in most cases, and lack of diminution of antibody level was shown to have some predictive value for treatment failure. Follow up of patients treated with metranidazole in Canal Zone and Republic of Panama medical facilities demonstrated unequivocally that this drug is of no value. In efforts to develop a tissue culture system for screening for antileishmanial activity, a Vero cell system was developed which allowed for drug exposure of infected cells for up to 10 days, but no effect on the intracellular parasites could be demonstrated in this system with a pentavalent antimonial compound which is clinically effective. In other diseases, the Hemolytic leptospirosis (HL) test was established to permit surveillance for this infection. An incidental finding of a human liver fluke (Amphimerus sp.) infection was of academic interest as the first such case in Panama, and only the third known locality in the Western Hemisphere.

PROGRESS:

In the past, effectiveness of chemotherapy of American leishmaniasis has been judged solely by the healing response of the lesion. However, it is well known that in some cases complete elimination of the parasite is not achieved in spite of clinical healing of the lesion, and recurrence or development of new lesions can occur. The new lesions may involve mucous membranes and can appear many years after the primary infection and cause severe facial mutilation, so the detection of residual viable parasites can be of extreme importance. It was considered that the effect of treatment on serum antibodies could add another

1.

parameter to judging the effectiveness of drug treatment and a study was instituted to measure indirect fluorescent antibody (IFA) titers during and after treatment. Retrospective studies were done on some of patients treated with Camolar⁽²⁾ and Fuadin⁽²⁾ and of patients treated more recently with Pentostam⁽³⁾ and Glucantime⁽³⁾.

There were detectable changes in serum antibodies following treatment in many cases. These data are presented in Figure 1. Increases in titer occurred only in cases of treatment failure demonstrated by the presence of parasites in culture or biopsy. Cases which showed no reduction in titer had a high rate of drug failures (9 of 16) while in those showing a titer reduction of even two-fold, the proportion was greatly reduced (8 of 27). With fourfold or greater reduction, there was only one failure in 23 cases. Nowever, in the majority of cases antibodies persisted over long periods in spite of a prompt healing response and some reduction in titer. One of our patients has had positive IFA tests for 6 years, and we recently tested an individual who was treated with antimonials 34 years ago and still has antibody.

The reversion to negativity after treatment exhibited by some patients, Table 1, suggests the possibility that the persistence of antibody in the others might be due to the continued presence of viable parasites. Since the great majority of treated cases have persistent titers, this is a rather disturbing hypothesis because of the known propensity of L. braziliencis to remain latent for many years and then produce the mucosal lesions of espundia. In a few cases it has been possible to demonstrate the presence of viable parasites in clinically cured patients with persistent titers. One such patient was previously reported in the Annual Report for 1969. He had received three injections of Camolar which produced healing of his multiple lesions, but no reduction in titer. Three months later, he had reactivation of the lesions and parasites were seen in a biopsy. After a course of treatment with Fuadin, his lesions again disappeared, his antibody level diminished, and then fell below detectable levels. Another patient treated with Glucantime had prompt healing of a small primary ulcer on a finger, and a 4-fold reduction in antibody titer. In spite of this, 4 months after treatment he developed a new fungoid lesion on his elbow from which parasites were cultured. After excision of the lesion and retreatment, his antibody dropped below 1:8, but 1 1/2 months later it had returned to 1:16 (Figure 2). Although these examples are few in number, and most of the persistent-antibody patients have never shown any indication that they would relapse, they are neverthe-less suggestive that drug treatment has not been completely effective for the majority of leishmaniasis cases in the Canal Zone and that the patients might retain latent infection which could result in mucosal lesions in the future.

The effect of treatment of advanced mucocutaneous leishmaniasis was studied in a Bolivian Army officer who presented with rapidly progressing lesions after a history of unsuccessful treatment with sodium antimony tartrate, repeated courses of stibophen and 3 courses of cycloguanil pamoate over the preceding 2 1/2 years. The antibody perponse to pentovalent antimony and amphotericin B is demonstrated in Figure 3. The rapid diminution of antibody following Pentostam treatment paralled impressive clinical improvement. After amphotericin B therapy was terminated because of signs of renal toxicity, the patient experienced a sudden explosive recrudescence, and a serum sample demonstrated a rise in antibody titer.

A recent article in a leading journal reported success in the treatment of one case of American leishmaniasis with metranidazole (Flagyl®) and cited another article reporting some success with this drug against leishmaniasis in Mexico. In contrast to these reports, metranidazole failed in 4 out of 5 cases reported from Brazil. USAMRU-P recently had the opportunity of monitor treatment of 6 cases of primary cutaneous leishmaniasis acquired in Panama which were treated with this drug.

Six male patients with laboratory-confirmed leishmanial ulcers of 8-10 weeks evolution were treated; 4 in Gorgas Hospital, one at Gamboa Medical Clinic and one under the supervision of the Sanidad Militaf of the Guardia Nacional in Panama City. Before treatment all patients had a general physical examination, chest roentgengram and base-line laboratory examinations consisting of urinalysis, complete blood count, platelet count, henoglobin, hematocrit and SMA-12 battery. These laboratory tests were repeated 4 times at 10-day intervals, i.e., after the first treatment period, at the end of the rest period, and after 10 and 20 days of the second treatment period. Cultures were made from the margins of the lesions on the same schedule, and at 2- and 4-weeks after treatment was terminated.

Five-patients between the ages of 19 and 52 years were found to be otherwise healthy and laboratory values were within normal limits. Patient #1, 14 years of age, had a neutropenia with a WBC count of 1,100/cu mm, polymorphonuclear neutrophils 15%, lymphocytes 79%, eosinophils 4%, and basophils 2%, a condition occasionally seen in children in Panama. This patient was hospitalized for diagnostic studies but no other abnormalities were encountered and the cause of these blood findings had not yet been determined.

Initial improvement of the appearance of the lesion was seen in all patients during the first treatment period. However, in patients no. 3 and 4 the improvement was temporary and by the end of the 10 day rest period (day 20) they had regressed to their original state. During the second treatment period improvement was much slower, even for those which did re-epithelialize.

Results of the cultures for leishmanial organisms are shown in Table 2. Only patient no. 2 showed consistently negative post-treatment cultures. Patient no. 6 at the conclusion of treatment appeared to have been successfully treated, but later developed a slight discoloration at the margin of the scar, and cultures inoculated at the 4-week follow-up grew promastigotes.

Some drug-attributable adverse effects were observed. Patient no. 1 exhibited a steady diminution of WBC count from 4,100/cu mm to 3,500/cu mm during the first period of treatment, rebounded slightly to 4,000/cu mm in the rest period, but again declined to 3,000/cu mm at day 30, whereupon treatment was terminated. Patient no. 2 likewise exhibited a steady diminution in the WBC from a baseline of 6,000/cu mm to 5,500/cu mm in the first treatment period, and to abnormally low values of 4,700/cu mm at day 30, and 4,300/cu mm at day 40, respectively. A weight loss of 8, 7, and 9 pounds was experienced by patients 2, 3 and 4 respectively.

The adult patients, nos. 2-6, were given 500 mg metranidazole 3 times daily for 10 days, a 10 day rest period was then followed by the same dose daily for 20 days. The additional 10 days beyond the standard regimen for amebiasis and trichomoniasis was decided upon because of steady improvement in the appearance, but incomplete healing of all lesions at the 20th treatment day, and the lack of any serious side affects due to the drug.

Patient no. 1, with a body weight of 41 kg, received 250 mg 3 times daily for 10 days, a 10 day rest period followed by another 10 days at 250 mg 3 times daily. The second treatment period was not extended as it was for the adult patients because of depression of his leucocyte count.

Successful treatment was achieved with only one patient. At the conclusion of the second treatment period two patients, nos. 2 and 6, had completely re-epithelialized the lesion and had no residual of the raised, erythymatous margin, but no. 6 subsequently was shown by culture to have residual viable leishmaniae.

The 5 treatment failures were subsequently treated with methyl glucamine antimoniate and complete healing with negative follow-up cultures was achieved with one course of 20 daily injections of 5 ml.

Although this series is small, these data demonstrate conclusively that metranidazole cannot be regarded as adequate chemotherapy for primary American leishmaniasis.

Lack of suitable experimental animal models for the screening of drugs for antileishmanial activity, and prior success in cultivating intra-cellular amastigotes of Panamanian strains of <u>Leishmania</u> in Vero

cells suggested the use of a tissue culture system for drug screening. A standardized inoculum of low-passage level promastigotes from blood agar media was found to give reproducible infections which could be maintained without overgrowth of the monolayer sufficient to interfere with accurate parasite counts through 10 days. A clinically effective drug, methyl glucamine antimoniate, was used for attempts to demonstrate drug effect, but no selective effect on parasites could be seen with this system, even when the exposure to the drug was extended to 10 days. At this juncture it was learned that a dog sarcoma-cell system developed by the Liverpool School of Tropical Medicine has been used for testing a small series of drugs, and althouch the system demonstrated the activity of other classes of compounds, no effect was seen on <u>Leishmania mexicana</u> by either tri- or penta-valent antimonial compounds. The Vero cell system is currently being evaluated with a series of non-antimonial drugs with known antiprotozoan properties.

In March 1971 a stool examination done by a UEARSO laboratory on a local foodhandler revealed small operculated trematode eggs which were identified as <u>Clonorchis sinensis</u> and referred to USAARU-P for confirmation. Repeated positive examinations over a period of several days established that this was not a spurious infection. Because <u>C</u>. <u>sinensis</u> is not known to occur in the Western Hemisphere, the foodhandler was again contacted for further investigation.

The patient was a 25 year old male Cuna Indian who had lived his entire life in the village of Mansukun, Comarca de San Blas in Panama. Two years after the original finding he was still passing the eggs. They were consistent in size and morphology with <u>Amphimerus guayaquilensis</u> previously reported from humans in one area in Ecuador and another in Colombia, and known to infect oppossums and domestic cats in Panama.

Although he had no current complaints, he was admitted to Gorgas Hospital for physical and laboratory examinations. All findings were within normal limits except for a diffuse abnormal pattern on a liver scan.

Six clinically-suspect cases of leptospirosis among U.S. Forces personnel, including 3 from a common-source exposure among members of one company of an Infantry battalion, were confirmed by the HL test.

Publications

7

Walton, B.C., Brooks, W.H., & Arjona, I. 1972. The Indirect Fluorescent Antibody Test for Serodiagnosis of American Leishmaniasis. <u>Am. J. Trop. Med. Hyg. 21</u> (3): 296-290.

Walton, B.C. & Yokogawa, M. 1972. Terrestrial Turbellarians as Pseudoparasites of Man. J. Parasit. 58 (3): 444-446.

Walton, B.C., Valverde, L. & Eguia, O. Onset of Espundia after Years of Occult Infection with <u>Leishmania braziliensis</u>. <u>Am. J. Trop. Med.</u> <u>Hyg.</u> In Press.

Table	2
-------	---

8

÷

2

Results of Culture for <u>Leishmania</u> Organisms with Metranidazole Treatment

Patient	Day of Treatment					1
No.	Pre Rx	10	20	30	40	Follow-up
1	+	+	+	. –	ND	+ (2 wks post)
2	+	+	+	-	-	- (thru 4 wks)
3	+	+	+	+	+	none-retreated
4	+	+	+	+	+	none-retreated
5	+	+	+	+	+	none-retreated
6	+	+	+	+	-	+ (4 wks post)

(This page intentionally left blank)

Ś

(This page intentionally left blank)

•

(This page intentionally left blank)

ANNUAL PROGRESS REPORT

PROJECT NO.	3A061102B71Q	:	Communicable Diseases and Immunology
TASK NO.	03	:	Entomology
WORK UNIT	110	:	Studies on Arthropods of Medical Importance in Latin America
REPORTING INSTALLAT	noir	:	U.S. Army Medical Research Unit, Panama Box 1809 APO New York 09826
PERIOD COVERED BY H	REPORT	:	1 July 1972 - 30 June 1973
PRINCIPAL INVESTIG	ATOR	:	Louis C. Rutledge, MAJ, MSC

REPORTS CONTROL SYMBOL: RCS-MEDDH-288 (R1) SECURITY CLASSIFICATION: UNCLASSIFIED

١.

TZ 05 30 18. tos	an a	UVKARY			73-06		DATA	NE (AR)63 TEEDECTOR
Name and the second sec		-		· ••• 666		I ONTRACTO	08 4(A WORK U
HE NO. COLLA PROGRAM	and the second state of th	<u> </u>	<u>NA</u>		<u>NL</u>	12 785		
	··· · · · · · · · · · · · · · · · · ·		TASK AREA				IT NUMBER	
A PHILARY : 611023	and a second sec		<u>+ 00</u>			110		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
6. CONTRIBUTINE 61102		11	03	{				
e. CONTRACTORS 10203 1								
(U) Studies on Art	threpods of Medic	al Imports	<u>nce in L</u>	atin A	merica			
CO5900 Environment	tal Biology 0101	00 Microbi	<u>ology</u> C	03500	<u>Clincel</u>	Medic	ine	
13. STANT CATC	14. ESTIMATEL COM	PLETION DATE	TA FUNDING A	GENCY		1		
69 07 01	73 06	30	DA		L	<u>"C"</u>	<u>in hous</u> i	
W. CONTRACT. G ANT NOT AT	pplicable			S ESTIMATE	A PROFESS	IONAL MAN	RS & FUND	s (In thousar
& DATES/EFFECTIVE:	EXPIRATION:		PARC		1	-		~
D. NUMBER:"			FISCAL	72	<u> </u>	1		
C TYFE.	& AMOUNT:		YEAR CURR		ł	•	1	~
C KIND OF ANARU	f. CUM. AMT.			73	1	1		21
13. RESECUSIBLE DID CAGANIZATION	N		20. PERFURMI	IG OPGANIZA	TION	Ŀ		
MANE:* US Army Medic	cal Research Unit	, Panama	HANE!" US	Army 1	Medical	Resear	rch Unit	t, Pan
, i i i i i i i i i i i i i i i i i i i		•		-				
ALORESS:* BOX 1009 APC	D New York 09826		ADDRESS:*	Box 180	09 APO	New Yo	ork 0982	26
			PRINCIPAL IN					
RESPONSIBLE INDIVIDUAL					e, Loui	5 C. M	Aul	
NAME Walton, Bryce	e C., COL		TELEPHONE	- •	•			
YELEFHONE: 62-3017			SOCIAL SECU	RITY ACCOU	NT NUMBER:			
21. GENERAL USC			ASSOCIATE IN					
			NAME: H	llenwo	od, Den	nis A.		
"FOREIGN INTELLIGE		(ED"	NAME:					
IL RETAURUS (PLACE & LALLS WIN SPC			(>					
U) Phlebotomine								
23. (U) Evaluatio								
for selected arth		-				COLLET	JI 1055.	TOTTT
24. (4) Studies	-	-				utanoo	ng loich	h moni
The methods and co								
on breeding habits in terms of human					and to	Incerp	ret the	Gara
							ing (Dia	
- 27. IUI K 2 7881	r study of breedi			-			-	
	-		-		-	-		
Psychodidae) in th								
Psychodidae) in the 6 major species, c	elshmanlasis. Th		species		ITZOMV1			ıcn
Psychodidae) in th 6 major species, c transmission of le								
Psychodidae) in th 6 major species, o transmission of le occupies 855 of th	ne area of the fo		at an a		popula			of 8.3
Psychodidae) in th 6 major species, o transmission of le occupies 85% of th per m ² of soil. I	ne area of the fo In all species, a	populatio	• at an a on maximu	m occu	popula s in e	arly ra	ainy sea	of 8.3 ason,
Psychodidae) in th 6 major species, o transmission of le occupies 85% of th per m ² of soil. I and in all except	ne area of the fo In all species, a 2 spp. a second	populatic peak occur	e at an a on maximu os in let	m occu e dry s	popula rs in e season.	arly ra Dista	ainy sea ribution	of 8.3 ason, n of
Psychodidae) in th 6 major species, o transmission of le occupies 855 of th per m ² of soil. I and in all except forest litter regu	ne area of the fo In all species, a 2 spp. a second ulated species dj	populatic peak occur stribution	e at an a en maximu es in let a, <u>L. tra</u>	m occu e dry s riáci v	popula rs in e season. vas gre	arly ra Dista ater on	ainy sea ribution n steep	of 8.3 ason, n of hill-
Psychodidae) in th 6 major species, of transmission of le occupies 85% of th per m ² of soil. I and in all except forest litter regu- sides with light 1	he area of the fo In all species, a 2 spp. a second ulated species di litter deposits,	population peak occur stribution while <u>L</u> . <u>p</u>	e at an a on maximu os in lat <u>, L. tra</u> anamensi	m occu e dry s <u>riáci</u> v <u>s, L</u> . s	popula rs in e season. vas gre <u>somezi</u> ,	arly ra Dista ater on <u>L. pes</u>	ainy sea ribution n steep ssoana a	of 8.3 ason, n of hill- and <u>L</u> .
Psychodidae) in th 6 major species, o transmission of le occupies 85% of th per m ² of soil. I and in all except forest litter regu sides with light 1 <u>insolita</u> were more	ne area of the fo In all species, a 2 spp. a second ulated species di litter deposits, e common on hillt	population peak occur stribution while <u>L. p</u> ops and pr	e at an a on maximu os in let <u>, L. tra</u> cominence	m occur e dry s <u>ridoi</u> v <u>s, L. (</u> s with	popula rs in e season. vas gre <u>somezi</u> , heavy,	arly re Distr ater or <u>L. pes</u> stable	ainy sea ribution n steep ssoana a e depos:	of 8.3 ason, n of hill- and <u>L</u> . its.
Psychodidae) in th 6 major species, of transmission of le occupies 85% of th per m ² of soil. If and in all except forest litter regu- sides with light 1 <u>insolita</u> were more Similarly, certain	ne area of the fo In all species, a 2 spp. a second ulated species di litter deposits, e common on hillt n large trees and	population peak occur stribution while <u>L. p</u> ops and pr vines pro	at an a on maximu s in lat <u>, L. tra</u> <u>canamensi</u> cominence duce lit	m occur e dry s <u>pidoi</u> y <u>s, L. (</u> s with ter whi	popula rs in e season. vas gre <u>somezi</u> , heavy, ich fav	arly re Distr ater or <u>L. pes</u> stable ors cer	ainy sea ribution n steep ssoana a e depos rtain sp	of 8.3 ason, n of hill- and <u>L</u> . its. pecies
Psychodidae) in th 6 major species, o transmission of le occupies 855 of th per m ² of soil. I and in all except forest litter regu sides with light 1 <u>insolita</u> were more	ne area of the fo In all species, a 2 spp. a second ulated species di litter deposits, e common on hillt n large trees and	population peak occur stribution while <u>L. p</u> ops and pr vines pro	at an a on maximu s in lat <u>, L. tra</u> <u>canamensi</u> cominence duce lit	m occur e dry s <u>pidoi</u> y <u>s, L. (</u> s with ter whi	popula rs in e season. vas gre <u>somezi</u> , heavy, ich fav	arly re Distr ater or <u>L. pes</u> stable ors cer	ainy sea ribution n steep ssoana a e depos rtain sp	of 8.3 ason, n of hill- and <u>L</u> . its. pecies
Psychodidae) in th 6 major species, of transmission of le occupies 85% of th per m ² of soil. If and in all except forest litter regu- sides with light I <u>insolita</u> were more Similarly, certain	he area of the fo In all species, a 2 spp. a second alated species di litter deposits, a common on hillt h large trees and on indicates Amer	populatic peak occur stribution while <u>L. p</u> ops and pr vines pro can leish	e at an a on maximu is in lat <u>anamensi</u> cominence duce lit maniasis	m occur e dry s <u>pidoi v</u> s <u>L</u> . f s with ter whi occurs	popula rs in e season. vas gre <u>somezi</u> , heavy, ich fav s in re	arly re Distr ater or <u>L. pes</u> stable ors cer stricte	ainy sea ribution n steep ssoana a e depos: rtain sp ed micro	of 8.3 ason, n of hill- and <u>L</u> . its. pecies ofoci,
Psychodidae) in th 6 major species, of transmission of le occupies 35% of th per m ² of soil. If and in all except forest litter regu- sides with light I <u>insolita</u> were more Similarly, certain Present information	he area of the fo In all species, a 2 spp. a second ulated species di litter deposits, e common on hillt n large trees and on indicates Amer ows vectors are d	population peak occur stribution while <u>L. p</u> ops and pr vines pro- rican leish istributed	e at an a on maximu os in lat <u>anamensi</u> cominence duce lit maniasis through	m occu e dry s <u>piáci</u> v <u>s</u> , <u>L</u> . g s with ter whi occurs out the	popula rs in e season. vas gre <u>comezi</u> , heavy, ich fav s in re s fores	arly re Disti ater on <u>L. pes</u> stable ors cen stricte t area	ainy sea ribution steep ssoana a e depos: rtain sp ed micro , indica	of 8.3 ason, n of hill- and <u>L</u> . its. pecies ofoci, ating
Psychodidae) in th 6 major species, of transmission of le occupies 85% of th per m ² of soil. If and in all except forest litter regu- sides with light I <u>insolita</u> were more Similarly, certain Present information but this study sho	he area of the fo In all species, a 2 spp. a second ulated species di litter deposits, a common on hillt n large trees and on indicates Amer ows vectors are d leishmaniasis ic	population peak occur stribution while <u>L</u> . <u>p</u> ops and pr vines pro- ican leish istributed limited b	at an a maximu s in let <u>. L. tra</u> <u>cominence</u> duce lit maniasis through y some f	m occu e dry s <u>pidoi</u> v <u>s</u> , <u>L</u> . i s with ter whi occurs out the actor of	popula rs in e season. was gre <u>comezi</u> , heavy, ich fav s in re e fores other t	arly re Distr ater or <u>L. pes</u> stable ors cer stricte t area han vec	ainy sea ribution steep ssoana e depos rtain sp ed micro , indica ctors, a	of 8.3 ason, n of hill- and <u>L</u> . its. pecies ofoci, ating and
Psychodidae) in th 6 major species, of transmission of le occupies 85% of th per m ² of soil. If and in all except forest litter regu sides with light 1 <u>insolita</u> were more Similarly, certain Present information but this study sho that incidence of	he area of the fo In all species, a 2 spp. a second ulated species di litter deposits, e common on hillt h large trees and on indicates Amer ows vectors are d leishmaniasis ic lant upon suitabl	population peak occur stribution while <u>L. p</u> ops and pr vines pro- can leish istributed limited b e vertebra	at an a n maximu s in lat <u>, L. tra</u> <u>anamensi</u> cominence duce lit maniasis through y some f te reser	m occur e dry s <u>pidoi</u> v <u>s</u> , <u>L</u> . g s with ter whi occurs out the actor o voir ho	popula rs in e season. was gre <u>comezi</u> , heavy, ich fav s in re fores other t	arly re Distr ater or <u>L. pes</u> stable ors cer stricte t area han vec	ainy sea ribution steep ssoana e depos rtain s ed micro , indica ctors, a earing c	of 8.3 ason, n of hill- and <u>L</u> . its. pecies ofoci, ating and of
Psychodidae) in th 6 major species, of transmission of le occupies 85% of th per m ² of soil. If and in all except forest litter regu- sides with light I <u>insolita</u> were more Similarly, certain Present information but this study sho that incidence of probably is depend sandflies in the I	he area of the fo In all species, a 2 spp. a second alated species di litter deposits, a common on hillt h large trees and on indicates Amer ows vectors are d leishmaniasis ic lant upon suitabl laboratory in pet	population peak occur stribution while <u>L</u> . <u>p</u> ops and pr vines pro- cican leish istributed limited b e vertebra ri dishes	at an a on maximu is in lat <u>anamensi</u> cominence duce lit maniasis through y some f te reser utilizin	m occurs e dry s <u>ridoi</u> v <u>s</u> , <u>L</u> , <u>f</u> s with ter whi occurs out the actor of voir ho g spil	popula rs in e season. vas gre <u>somezi</u> , heavy, ich fav s in re ofores other t substr	arly re Distr ater or <u>L. pes</u> stable ors cer stricte t area han vec Mass re ates ar	ainy sea ribution steep sooana deposi rtain sp ed micro , indica ctors, a earing on hd leaf	of 8.3 ason, n of hill- and <u>L</u> . its. pecies ofoci, ating and of litte
Psychodidae) in th 6 major species, of transmission of le occupies 85% of th per m ² of soil. If and in all except forest litter regu- sides with light I <u>insolita</u> were more Similarly, certain Present informatic but this study sho that incidence of probably is depend sandflies in the I for food of larvae	he area of the fo In all species, a 2 spp. a second ulated species di litter deposits, e common on hillt n large trees and on indicates Amer ows vectors are d leishmaniasis ic lant upon suitabl laboratory in pet e hatched from er	population peak occur stribution while <u>L</u> . <u>p</u> ops and pr vines pro- rican leish istributed limited b e vertebra ri dishes us of wild	e at an a on maximu es in lat <u>anamensi</u> cominence duce lit maniasis through y some f te reser utilizin -caucht	m occurs e dry s <u>ridoi</u> v <u>s</u> , <u>L</u> . g s with ter whit occurs out the actor of voir ho g spil sandli	popula rs in e season. was gre <u>comezi</u> , heavy, ich favy s in re fores other t osts. substr	arly re Distr ater or <u>L. pes</u> stable ors cer stricte t area han vec Mass re ates ar explor	ainy sea ribution steep ssoana a deposi rtain sp ed micro , indica ctors, a earing o nd leaf Zed. Y:	of 8.3 ason, n of hill- and <u>L</u> . its. pecies ofoci, ating and of litte ields
Psychodidae) in th 6 major species, of transmission of le occupies 85% of th per m ² of soil. If and in all except forest litter regu- sides with light I <u>insolita</u> were more Similarly, certain Present information but this study sho that incidence of probably is depend sandflies in the I	he area of the fo In all species, a 2 spp. a second ulated species di litter deposits, a common on hillt n large trees and on indicates Amer ows vectors are d leishmaniasis ic lant upon suitabl laboratory in pet a hatched from er ater than with tr	population peak occur stribution while <u>L</u> . <u>p</u> ops and pr vines pro- rican leish istributed limited b e vertebra ri dishes us of wild	e at an a on maximu es in lat <u>anamensi</u> cominence duce lit maniasis through y some f te reser utilizin -caucht	m occurs e dry s <u>ridoi</u> v <u>s</u> , <u>L</u> . g s with ter whit occurs out the actor of voir ho g spil sandli	popula rs in e season. was gre <u>comezi</u> , heavy, ich favy s in re fores other t osts. substr	arly re Distr ater or <u>L. pes</u> stable ors cer stricte t area han vec Mass re ates ar explor	ainy sea ribution steep ssoana a deposi rtain sp ed micro , indica ctors, a earing o nd leaf Zed. Y:	of 8.3 ason, n of hill- and <u>L</u> . its. pecies ofoci, ating and of litte ields

man-hours of effort, although the results were variable. Even with shortcoming, the method offer promise of providing sufficient numbers of adult sandflies for colonization trials and disease transmission studies.

This project has been transferred to Special Foreign Activities of Walter Reed Army Institute of Research and further progress will be reported in the Annual Technical report of WRAIR.

BODY OF REPORT

PROJECT NO.

TASK NO.

3A051102B71P : Communicable Diseases and Immunology 03 : Ecology and Control of Disease

WORK UNIT

110 : Studies on Arthropods of Medical

Vectors and Reservoirs

Importance in Latin America

DESCRIPTION:

The objective of this study is to evaluate the disease vector potential of and vector control possibilities for selected arthropods of medical importance in Central America. Current studies focus on the philobotomine sandflies as vectors of American leishmaniasis.

APPROACH.

The basic biology and field ecology of species of medical interest are investigated through an integrated program of laboratory and field studies. The results are interpreted in terms of the epidemiology of human disease and disease vector control.

PROGRESS:

Sandfly breeding sites. This study was initiated in FY 1971 and completed in FY 1973. Breeding populations of phlebotomine sandflies in the soil of the open forest floor were studied in a rain forest near Gamboa, Canal Zone. Sandfly collections were made with soil emergence traps from 43 selected sites within the study area. Supporting studies of local environmental effects on breeding populations were made concurrently with the sandfly collections. The general results of these studies are summarized in the following paragraphs.

The species complement of the forest floor breeding habitat includes 6 major species, of which 4 are anthropophilic and 2 are zoophilic (Table 1). The species <u>Lutzomyia gomezi</u> and <u>L. rorotaensis</u> had not been previously recovered from natural breeding sites. The species <u>L. insolita</u> had not been previously recovered from the forest floor habitat. All 4 of the anthropophilic species collected have been implicated in the transmission of American leishmaniasis in other studies. The species <u>L. pessoana</u> is the major day-biting anthropophilic species of the study area. This study represents the first application of the methods of population ecology to immature populations of New World sandflies. Erecaing populations were found to be thinly dispersed throughout the entire forest floor habitat (Table 1). The dominant species was <u>L</u>. <u>travidoi</u>, which occupies some 855 of the area of the forest floor at an average population density of 8.3 per m² of forest soil.

In all species a population maximum occurs in the early rainy season, and in all except <u>L</u>. <u>rorotaensis</u> and <u>L</u>. <u>insolita</u> a second population maximum occurs in the early dry season. Similarly, in all species a population minimum occurs in the late rainy season, and in all except <u>L</u>. <u>rorotaensis</u> and <u>L</u>. <u>insolita</u> a second population minimum occurs in the late dry season. In brief, population maxima tend to occur when soil moisture conditions are medarate, and population minimum atend to occur when soil moisture conditions are extreme, either wet or dry.

Supporting studies demonstrated that the forest litter tends to be removed by erosion from steep slopes and lower elevations and to cumulate on gentle slopes and higher elevations. This pattern of distribution of the forest litter was reflected in the spatial pattern of immature sandfly populations. Populations of <u>L. travidoi</u> were greater in streamside and hillside regions of the study area, while populations of <u>L. panamensis</u>, <u>L. gomezi</u>, <u>L. pessoana</u> and <u>L. insolita</u> were greater in hilltop regions of the study area. However, only <u>L. panamensis</u> and <u>L. pessoana</u> were collected from alluvial litter at the edge of the stream.

Similarly, certain large trees and lianas were found to produce exceptionally deep and extensive deposits of litter. Populations of immature sandflies were generally greater in this situation than elsewhere within the general forest area. Only <u>L. trapidoi</u> and <u>L. panamensis were collected from palm litter.</u>

The practical implications of the foregoing results seem clear. Since several vector species breed continuously throughout the forest, they are not amenable to control through selective treatment of restricted areas or at particular seasons. Effective control will depend on development of methods for treating large areas of the forest efficiently and cheaply. In the meantime, the use of personal protective measures should be emphasized.

Present information indicates that American leishmaniasis occurs in restricted microfoci within the general forest area. On the other hand, our study of sandfly breeding sites indicate that several vector species breed continuously throughout the forest area. This discrepancy in the patterns of distribution of the parasite and its vectors suggests that the incidence of leishmaniasis is limited by some factor other than the availability of suitable vectors. The limiting factor may be, instead, the availability of suitable vertebrate reservoir hosts.

Canal Zone Sandfly Associations.

An analytical study of available records of adult sandfly lighttrap collections from the Canal Zone was initiated and completed during FY 1973. These collections, representing 24 locations within the Zone, were made by elements of the U.S. Army, Southern Command, and the Middle America Research Unit over the period 1968 to 1972. A total of 551 collections records, representing 10,070 sandflies of 37 species, were analyzed.

It was concluded that the collections analyzed represented 2 basic sandfly consociations dominated, in one case, by the zoophilic species <u>L. carpenteri, L. triramula</u> and <u>L. composi</u> and, in the other, by the anthropophilic species <u>L. genezi</u> and <u>L. panamensis</u> and the zoophilic species <u>L. dysponeta</u>. Both consociations were highly variable, and a number of disparate and intergrading species compositions were present in the collections analyzed. Each consociation occurs in varying terrain and on both the Atlantic and Pacific slopes of the Isthmus. They occur successively in certain locations, but one or the other is prevalent throughout the year in other locations. The anthropophilic consociation was more prevalent than the zoophilic consociation.

It seems probable that those areas and seasons in which the anthropophilic species predominate are a greater hazard to human health than others. Our data suggest that the sandfly species compositions of differing areas and seasons are regulated primarily by patterns of rainfall and drainage and that the anthropophilic consociation is favored by relatively wet situations. More detailed study of sandfly associations in the field will be required for confirmation of this point.

Sandfly Ecology on the Pacific Slope

Previous studies of sandfly ecology and population dynamics in Panama have been made on the Atlantic slope of the Isthmus. However, ecological conditions are quite different on the Pacific slope, where the majority of infections with American leishmaniasis in U.S. personnel are acquired. A study of sandfly ecology at Empire Range (the area of most active transmission on the Pacific slope) was initiated in November, 1972.

Adult sandflies are collected with light-traps at 20-meter intervals along a 200-meter transect twice weekly. The transect samples 3 biotopes characteristic of the area: (1) A grassy, disturbed area intersected by a road and by rights-of-way for a power line and a pipeline. (2) An adjoining secondary forest of chiefly hardwoods, (3) A primary forest including numerous palm trees. The data obtained include population density data by species, biotope and season.

A total of 54 species have been collected in the study area (Table 2). The ubiquitous morphilic species <u>L. carrenteri</u> and the implement anthrophilic species <u>L. remanensis</u> together make up 75% of the species composition. Other anthropophilic species collected in the study area include <u>L. olmera</u>, <u>L. sanguinaria</u>, <u>L. trapidoi</u>, <u>L. poraris</u>, <u>L. poraria</u>, and <u>L. ylephiletorix</u>.

A summary of the collections by transect station is given in Table 3. The population trend is toward increasing densities deeper in the forest. Sundfly populations were least in the disturbed area (stations 1 to 4), intermediate in the secondary forest (stations 5 to 5) and greatest in the primary forest (stations 9 to 11). Population microfoci were conserved at station 3 in the disturbed area and at station 4 in the secondary forest. The region of station 9 in the primary forest evidently represents a "pocket" in the sandfly population distribution. Studies of environmental conditions prevailing at the several stations are being made in an effort to explain the occurrence of such microfoci and pockets.

Sandfly collections were continuous throughout the dry season (December through April) (Table 4) although the dry season of 1972-3 was one of the delest on record and the Pacific slope normally received only about 1/2 the amount of rainfall received by the Atlantic clope. The population maximum occurred in the early dry season (January 1973, 9.7 flies/trap/night) and the population minimum occurred in the late dry season (April 1973, 1.2 flies/trap/ night). The timing of there 2 events agrees fully with results obtained on the Atlantic clope in a prior study (see above). However, at Empire Range on intercalary population maximum was also observed (March 1973, 8.3 flies/trap/night). Since this resurgence occurred two months after that of January 1973, it may be due to population brock-effects. Data from laboratory rearing trials and from soil emergence trap collections indicate that the normal generation time is about 8 weeks for most species.

The species <u>L</u>. <u>carrenteri</u> was predominant throughout the dry season (Decerter 1972 to April 1973) in the Empire Range collections. The anthropopulitic species <u>L</u>. <u>panamensis</u> has been predominant in wet season months to date (November 1972, May-June 1973). Populations of <u>L</u>. <u>panamensis</u> declined steadily during the dry season, and this species was outnumbered by the common zoophilic species <u>L</u>. <u>trinidadensis</u> during the late dry season (February to April 1973).

The foregoing fluctuations in sandfly population densities and exchanges of dominance between zoophilic and anthropophilic species agree fully with the results obtained in our analysis of Canal Zone sandfly associations (see above). Their effects on the epidemiological pattern of sylvan leishmaniasis are uncertain, but they are undoubtedly important. We may expect to find, for example, that the pattern of incidence of leishmaniasis in animal populations is continually shifting and changing within the forest area.

Mass-Rearing of Sandflies

Experimental studies of the transmission of leishmaniasis are presently hampered by the lack of large numbers of sandflies for experimental use. In addition to problems connected with survival, mating, blood-feeding and oviposition in the adult stage, the laboratory production of sandflies presents unique problems in connection with rearing the immature stages. Several features of sandfly biology contribute to the difficulty of mass-rearing the immature stages: (1) The eggs are produced in relatively small numbers (about 30 per clutch in most species). (2) The immature stages (egg, larva and pupa) are exceptionally sensitive to extremes, of moisture and temperature. (3) The period of development is exceptionally long, usually 6 to 12 weeks. (4) The immature stages develop in a milieu of decomposing organic materials which is difficult to control and standardize.

Sandflies are traditionally reared in unglazed earthenware pots placed in trays of water. The method is cumbersome and requires constant attention to water level, larval food supply and fungal growth. Consequently, it is necessary to expend large amounts of manpower in the care of the colony to rear large numbers of sandflies by this method. The ideal culture would be self-regulating with regard to moisture content, food supply and fungal growth for the entire period of growth and development of the immature stages (6 to 12 weeks). Experiments toward this end were initiated during FY 1973.

In initial experiments 58 single-brood cultures (chiefly of <u>L</u>. <u>trapidoi</u>) were prepared as follows: Clay soil was homogenized with water to a pasty consistency in a Waring blendor. Standard disposable plastic Petri dishes (9 cm diam. x 1.2 cm deep) were filled with this substrate to a depth of \pm 6 mm. The clay substrate was then covered with a thin layer of leaf fragments prepared by comminuting dried leaves in a Waring blendor. A single blood-fed, wild-caught female sandfly was then introduced into each Petri dish and confined with the cover. These were allowed to oviposit and die within the dishes, and their progeny to develop without further care. The rationale for this kind of culture is as follows: (1) It simulates conditions in natural breeding sites in the forest (see above). (2) The moisturebinding properties of clay soils give long-term retention of moisture. (3) The decomposing leaf fragments provide food for the entire period of growth and development of the sandfly larvae.

Sandfly larvae failed to appear in 27 (47%) of the 58 cultures prepared. This loss is referable to shortcomings of survival, mating and oviposition in the adult stage and of hatching in the egg stage.

The efficacy of the method is best judged on the basis of the 32 cultures in which larvae appeared. A total of 240 adult sandflies were obtained from the latter cultures. This total represents an average yield of 7.5 sandflies per culture. The potential of this method, if refined and standardized, is indicated by the maximum yield obtained, 24 sandflies in culture no. 48. It was noted in these trials that the more moist cultures were more productive of sandflies and less affected by fungal overgrowth.

In a second series of trials, an attempt was made to improve on the foregoing results by increasing initial moisture content and replacing a part of the moisture loss. Due to the non-availability of <u>L. trapidoi</u>, <u>L. gomezi</u> was substituted in 15 of 148 cultures in this series. In addition, to greater amount of water initially, 1/2 of the moisture lost through evaporation in the first 5 weeks of culture was replaced with a pipette during the sixth week of culture.

The foregoing modification of technique was unsuccessful. A total of 117 (79%) of the cultures were larva-negative. The yield of adult sandflies from the 31 larva-positive cultures amounted to 86, for an average of 2.8 sandflies per culture. The maximum yield was 9 sandflies in culture no. 173 (\underline{L} . <u>trapidoi</u>).

The cause of the higher proportion of larva-negative cultures observed in this experiment is not definitely known. It is believed that the low yield obtained in larva-positive cultures was due to adverse temperature and humidity conditions in the laboratory environment. The cultures were kept in a non-mir-conditioned room at ambient temperature and humidity. The first experiment, yielding 7.5 sandflies per positive culture, was conducted during the wet season (August to November 1972). The second experiment, yielding 2.8 sandflies per positive culture, was conducted chiefly in the dry season (January to June 1973). Although no measurements were taken in the first experiment, the rate of evaporation from the cultures was noticeably less than in the second experiment. In the second experiment, moisture losses were determined on a weekly basis for 7 sample cultures (to which no water was added in the 6th week). The average weight of the cultures at the time of preparation (excluding the weight of the Petri dish) was 58.0 gm, of which 34.9 gm (60%) was water. After 6 weeks, an average of 15.7 gm of water (45% of the original content) had been lost, and after 12 weeks, an average of 27.9 gm of water (80% of the original content) had been lost. It seems clear from our results that this rate of evaporation is unsatisfactory and that it can not be remedied by a one-time replenishment.

A primary purpose of this investigation is to develop a culture method which does not depend on sophisticated, extraneous equipment (air conditioners, humidifiers, incubators, etc.) for success. If such a method can be developed, it will be effective under both controlled and uncontrolled conditions, as circumstances permit. Accordingly, current experiments continue to be directed toward development of a reliable, self-regulating culture system.

A total of 234 sandfly cultures of J2 types are currently in progress (Table 5). Evaporation has been reduced in cultures utilizing a dry substrate by reducing the surface area/volume ratio and the ventilation of the culture. The principle of the plaster substrate method is similar to that of the unglazed earthenware pot method, but evaporation is reduced by the plastic walls and cap of the container. The results of these and subsequent trials are expected to lead to a method of mass-rearing of the immature stages which will provide sufficient numbers of adult sandflies for colonization trials and/or disease transmission studies.

Publications

- Rutledge, L.D., R.A. Ward and D.E. Hayes. 1973. <u>Plasmodium eynomolgi</u>: The comparative infectiousness of individual rhesus nonkeys. Exper. Parasitol. 33; 120-126.
- Rutledge, L.D., R.A. Ward and R.M. Buckwalter. 1973. <u>Plasmodium</u> spp. Dispersion of malarial cocyst populations in anopheline and culicine mosquitoes. Exper. Parasitol. (In press).
- Christensen, H.A., and L.C. Rutledge. 1973. Two new synonyms in the genus Lutzomyia (Diptera, Psychodidae). J. Med Ent. 10:314.
- Ward, R.A., D.E. Hayes, S.C. Hembree, L.C. Rutledge, S.J. Anderson and A.J. Johnson. 1972. Infectivity of <u>Plasmodium falciparium</u> gametocytes from <u>Actus trivirgatus</u> to anopheline mosquitoes.

/

Table 1. Population data for sandfly species breeding on the open forest floor in Panama.

	Mean	
	Population	Areal
	Density	Prevalence
	$(per m^2)$	(%)
Lutzomyia trapidoi*	8.3	85
L. panamensis*	3.3	65
L. gomezi*	3.0	40
L. pessoana*	2.8	60 .
L. rorotaensis	2.7	70
L. <u>insolita</u>	2.3	70
Totals	22.4	100%

*Anthropophilic species.

.

Table 2. Sandfly collections at the Empire Range

study area by species as of 30 June 1973.

1513

99.99

		۱	Mean No. of
Station	No. Times Trapped	No. Flies caught	Flies/trap/night
l	27	6	0.22
2	20	10	0.50
3	25	24	0.96
4	. 26	9	0.35
5	29 .	150	5.17 -
6	27	219	8.11
7	18	120	6.67
8	25	146	5.84
9	16	42	2.63
10	24	289	12.04
11	20	498	24.90
		1513	

Table 3. Sandfly collections at the Empire Range study area by transect station as of 30 June 1973

Ч

• • •

27

.

Table 4. Sandfly collections at the Empire Range Study area by month and principal species as of 30 June 1973.

.

November 1972 152 flies 24 Trapping Nights 6.3 flies/trap/night 60 flies 39.47% L. panamensis 59 flies L. carpenteri 38.82% December 1972 206 flies 28 Trapping Nights 7.4 flies/trap/night 83 flies 40.29% L. carpenteri 64 flies 31.07% L. panamensis January 1973 339 flies 34 Trapping Nights 9.7 flies/trap/night L. <u>carpenteri</u> 175 flies 51.62% 58 flies 17.11% L. panamensis February 1973 149 flies 31 Trapping Nights 4.8 flies/trap/night 69.13% 6.71% **103** flies L. carpenteri103 fliesL. trinidodensis10 flies L. carpenteri 297 flies 36 Trapping Nights 8.3 flies/trap/night March 1973 L. <u>carpenteri</u> , 248 flies 83.50% L. <u>trinidadensis</u> 9 flies 3.03% April 1973 44 flies 36 Trapping Nights 1.2 flies/trap/night L. <u>carpenteri</u> 26 flies L. <u>trinidadensis</u> 4 flies 59.09% 9.09% May 197393 flies35 Trapping Nights2.7 flies/trap/night 48 flies 51.61% L. panamensis 17 flies . 18.28% L. carpenteri June 1973 233 flies 32 Trapping Nights 7.3 flies/trap/night 174 flies 74.68% L. panamensis 16 flies 6.87% L. carpenteri 1513 flies TOTALS 5.7 flies/trap/night

L. carpenteri48.05%L. panamensis26.77%L. trinidadensis2.71%

4	Sand	fly			Conta	iner	
No. of cultures	Species	No.	Stage	Material	Dimensionsl	Ventilation ²	Substrate ³
100	L. trapidoi	l	Adult	Plastic	2.3x8.4	-	Clay
15	L. gomezi	1	Adult	Plastic	2.3x8.4	-	Clay
70	L. trapidoi	l	Adult	Glass	5.4x2.8	1 Perforation	Clay
30	L. gomezi	l	Adult	Glass	5.4x2.8	1 Perforation	Clay
5	L. trapidoi	l	Adult	Plastic	6.5x5.0	5 Perforations	Clay
٦	L. sanguinaria	5	Adult	Plastic	7.0x4.3	1 Perforation	Clay
l	L. trapidoi	96	Adult	Plastic	8.5x10.5	1.5 cm screen	Plaster
5	L. trapidoi	500	Egg	Plastic	8.5x10.5	1.5 cm screen	Plaster
2	L. gomezi	500	Egg	Plastic	8.5x10.5	1.5 cm screen	Plaster
2	L. gomezi	200	Egg	Plastic	8.5x10.5	1.5 cm screen	Plaster
4	L. trapidoi	200	Egg	Plastic	6.0x6.0	1.5 cm screen	Plaster
2	L. gomezi	200	Egg	Plastic	6.0x6.0	1.5 cm screen	Plaster

Table 5. Sandfly cultures in progress on 30 June 1973.

234

1. Dimensions are given as depth x diameter in cm.

2. The provision for ventilation of the culture is either a 1.5 cm diam. nylon screen in the cap or 1 or more perforations in the cap.

3. The plaster substrate is 9 parts plaster of Paris: 1 part activated charcoal (V/V). The container is perforated on the bottom and kept in a tray of water.

ANNUAL PROGRESS PEPORT

PROJECT NO. 3A061102B71Q : Communicable Diseases and Immunology TASK NO. 00 : Ecology and Control of Disease Vectors and Reservoirs WORK UNIT 419 : Pathology and Pathogenesis of Naturally Occurring Infections in Latin America REPORTING INSTALLATION : U.S. Army Medical Research Unit, Panama Box 1809 APO New York 09826 PERIOD COVERED BY REPORT : 1 July 1972 - 30 June 1973 PRINICIPAL INVESTIGATOR : Larry J. Ackerman, MAJ, VC ASSISTANTS : John A. Williams Emilia P. Hoyos Michael E. Hajduk, SFC, AMEDS

REPORTS CONTROL SYMBOL: RCS-SGRD-288 (R1)

SECURITY CLASSIFICATION: UNCLASSIFIED

12 State 28 C State Astar Bandara Bandara Carata Santa S	and a substantial state production of the substant state of the substate of the substant state of the substant state of the substant	L. AUL	CY ALCESSIC	DN# 2 U+76 OF 50	11/14 A T Y	P POPT CONTROL SHE DOLL
COLOR ADD ADD ADD ADD ADD ADD ADD ADD ADD AD	Y NORK DRIT SUE PARY	1		1 73 06	30	Ind A Carpon
S. C. M. S. MARY	S SUMARY SCTY A BOUN LECURE	TY IL PE SA	AUING	IN CITE'N DISTRIA	TAL SERVICE	ALA- D. LLVEL CF LUM
H. Terminat	cn U U		\	777.		NO A VOAK UNIT
NU NE NULL PRESIMAN ELEMENT	FINJECT NUMPLER	TASK	APEA NUMB	ER	#DAK UNIT	NUNDER
Preserve 1 4 LOCA	340611021710		00	1	1.1.4	
C. CTHESE CTHESE 1.221.0A	3/062110A 006		00			
RESERVES 1 0108 124 ([·)					
IL TITLE SHEPTHE & WILL Security Classification Code		Patholo	mr and	Pathogene	sis or h	aturally
· commine Infectio	ons in Latin Americ					-
2 SUNTERCAND SECANFLOGICAL AREAS						
000600 Biology 010100 :	Microbiology 00350	0 Clini	cal Me	dicine		
TA LTANT LATE	14. LATINATED COMPLETION CATE	100.00	HI NG AGENCY	1	16. PE -OF OPMA	-
67.07	72 06	D		1	"c	" IN HOUSE
17. CLATKALT GRANT	· · ·	18. RES	OUNCES ESTI	MATE & PROFEL	SIGNAL MAN YRS	h FUNDS (In thousands)
Not applical	DLE Expiration:		PAECEDING			
N. NUMBER:		FISCAL	72		1	25
4 TYPU:	& AMOUNT:	YEAR	CURAENT			
E N ND OF AWARD	I. CUM. AMT.	ļ	73		1	25
19. RESPONSIBLE DOD CREANIZATION	1	26. PEP	TORMIN J ORC	GANIZATION		
NAME. II C Ammin Modical I	L	NAVE!	U.S.	Army Medic	al Resea	rch Unit, Param
"AME. U.S. Army Medical I	Research Unit, Pana	ma	0.01			
ADDRESS.* 170 New Yearly 00 904	<u>(</u>	ADDRES	si* APO	New York	09826	
APO New York 09826				non rorn		
l		PRINCIP	AL INVESTIG	ATOR (Fumish SSAN	It U.S. Acadamie	[nelituti en]
RESPONSILLE INDIVIDUAL		NAME	• Acke	rman, L.J.	, Major.	VC
MARE Walton, Bryce C.,			HONE: 82		,,	
TELEMONE 22-3017				ACCOUNT NUMBER:		•
21. GLALALUSE		ASSOCIA	TE INVESTIG	ATORS		
i		NAME	John .	A. William	S	
"FOREIGN INTELLIGENCE I	OT CONSIDERED"	•		el E. Hajd		AMEDS
22. OLTOWAS (PROCODE EACH WIN Security Closelli	and the second					
ł						
23. TLC-NICAL OBJECTIVE," 24 APPROACH, 25	PROGRESS (Furnish Individuel persing	a Identified b	number Pret	ode leas of each with	Sucurity Classific	silan Code.j
23. (U) 1. To gather	r information conce	rning t	he res	ervoir sta	tus, mod	es of transmis-
sion and pathogenesis of						
and amphixenotic agents						
of the MARU staff. 3.						
medical facilities for						
24. (U) Necropsies of	<u> </u>				lemented	with standard
and special histopathol			-			
Searches are made of po				-	-	_
invertebrate hosts. Th						
experimental animals.			•P			
25. (U) 727-73-06-	The pathology serv	ice cor	tinued	to suppor	t the st	udies of
Venezuelan equine encer	-					
and other natural and o						
support continued to be					•	~
Canal Zone zoos, as well			•			-
the area. Concentrated						—
changes in Sigmodon his	. =				-	
maniasis and (3) incide						-
Anticotrongylus costari	-	-	-			
<u>reoffryi</u> .	COLLIGITS CHILL THE UNE	ion-nui:	orr hr.r.			THUS MIN WIELES
1						
linis project has been t	transferred to Spec	ial Fer	bign A	ctivities	of Walte	r Reed Army
Institute of Lesearch (and further progres	s will	te rer	orted in t	he Annua	1 Technical
resort of WRAIR.	10/4-		- F			
transferrer and the second second second second and						
DD. W. 1498 ANTANA	LT TONTOF THIS DON ART	КН 6. 10 - 5 - 5	STELES	DRMS 1498A, 1 N	40 V 65	
	· · · · · · · · · · · · · · · · · · ·	· ·				

• • • • •

BODY OF REPORT

PROJECT No.	3A061102B71Q : Communicable Diseases and Immunology
TASK NO.	00 : Ecology and Control of Disease Vectors and Reservoirs
WORK UNIT	419 : Pathology and Pathogenesis of Naturally Occurring Infections in Latin America

DESCRIPTION:

The objective of this study is to gain information on the reservoir status, modes of transmission and pathogenesis of diseases of animals occurring in the area. Necropsies of subhuman animals supplemented by routine and special histopathologic examinations were performed in monitoring and characterizing a variety of disease changes in wild, domesticated and laboratory animals. Experimental infections and clinical pathology techniques are utilized whenever necessary for complete characterization of a disease process.

PROGRESS:

During FY 73 347 animals were examined and 181 accessions made. Part of the case material resulted from the support and pathology services rendered to other investigators of USAMRU-P and MARU and to the Air Force and Army Veterinarians servicing the Canal Zone and Republic of Panama. The remainder of case material resulted from independent research conducted by the Pathology section.

Diagnostic consultation support service included: 22 <u>Calomys</u> <u>callosus</u> for the Bolivian hemorrhagic fever studies, 10 horses for the Venezuelan equine encephalomyelitis studies, 4 <u>Actus trivirgatus</u> monkeys in support of Yellow fever studies, numerous mice for tests for human <u>Coxsacki</u> virus infection, and over 200 additional animals for disease surveillance.

Angiostrongylus costaricensis

During this fiscal year, a laboratory cycle of <u>Angiostrongylus</u> <u>costaricensis</u> was established and maintained using the natural rodent host, <u>Sigmodon hispidus</u> and a slug <u>Vaginulus sp</u>. as the molluscan intermediate host. Important segments of the life cycle were clucidated. Fourteen days after the feces of infected <u>Sigmodon</u> were fed to slugs, a molt of second stage larvae into third stage larvae occured. At 21 days, the third stage larvae were extracted by pepsin-Hcl acid digestion of the infected slugs. Laboratory reared <u>Sigmodon</u> were fed these infectious larvae by gavage. Larvae penetrated the mucous of the small intestine and/or cocur, migrated to the submucosa of the same organ and molted within these tissues. Inmature adult worms migrated to a regional artery and 6 days following infection, the young adults penetrated the artery and continued to mature within the lumen. Between 14 and 21 days oviposition occurred and by 28 days first stage larvae were passed in the foces of the infected rodents.

In order to gain information regarding the natural reservoir hosts, several species of wild caught and laboratory raised rodents and 2 species of nonhuman primates were tested to determine their susceptibility to infection with <u>A. costaricensis</u>. The results of these studies are summarized in Table 1.

These studies demonstrated several interesting facts. (1) When exposed to 3rd stage larvae Sigmodon hispidus has yielded as high as 70% recovery of adult worms in branches of the cranial mesenteric artery, aorta and even in the left ventricle of the heart. (2) Rattus norvegicus can serve as a laboratory model for this infection. (3) The wild rodents Zygodontorys microtinus, Proechings semispinosus, Nyctorys sumichrasti, and Marmosa sp. do not pass 1st stage larvae and thus do not perpetuate the lifecycle of this parasite. (4) The hamster and guinea pig react similarly and do not perpetuate the lifecycle. (4) A massive single dose of 3rd stage of A. costaricensis in a susceptible host can result in mechanical blockage of branches of the cranial mesenteric artery with subsequent infarction of the lower intestinal tract and/or cecum resulting in peritonitis and/or death. (6) Two species of non-human primates, Cebus convernue and Ateles reoffroyi are able to perpetuate the cycle of A. coctoricensis following experimental infection. The route of migration of the worms and the time sequence for maturation and oviposition closely paralleled that of Sigmodon hispidus. Both species developed granulomatous inflammatory reactions similar to those reported in human infections; and 4 of the infected monkeys subsequently died of this disease. (7) Some monkeys (but not all) of both species passed 1st stage larvae in the feces 28 days after infection; a finding which has not yet been demonstrated in human infections.

Exo-antigen was obtained from adult worms maintained up to 14 days in medium 199 containing 25 penicillin-streptomycin and 0.5% amphotericin B. Crude antigen from adult <u>A. costaricensis</u> and the exo-antigen were utilized for serological testing of non-human primates. Thus far, ouchterlony, complement-fixation, and hemagglutination tests have not yielded a reliable test system. Skin tests administered to infected <u>Cetus capucinus</u> and <u>Ateles geoffroyi</u> monkeys have negative results regardless of whether or not the monkey was passing first stage <u>A</u>. <u>costaricensis</u> larvae in its feces.

Hematology of Sigmodon hispidus

Prior to initiation of studies of infection with Leishmania and agents of other tropical diasess in Sigmodon it was deemed necessary to establish average or standard hematologic values for the animals of our colony in order to interpret disease-induced changes.

Hemograms were obtained on 36 <u>Sigmodon</u> (21 males and 15 females) once a month for 6 months. Additional hemograms were determined on 19 of these animals (13 males and 6 females) for an additional period of 1-7 months. Each hemogram consisted of hematocrit, hemoglobin concentration, total erythrocyte, reticulocyte and leukocytes counts and leukocyte differential. Absolute leukocyte values and erythrocyte indices were calculated utilizing standard formulas.

Blood samples (0.5 ml) were collected during light ether anesthesia from the ophthalmic venous plexus using sterilized nonheparinized Pasteur-type pipettes. Thin blood films were prepared and the remaining blood transferred to a tube containing EDTA anticoagulant (1.5 mg EDTA/ml of whole blood).

Hematocrit was estimated using the microhematocrit method and hemoglobin concentration was determined by the cyanmethemoglobin method.

Total erythrocyte and leukocyte counts were done by the standard methods with a model A Coulter Counter, using dilutions of 1:500,000 and 1:500 respectively. The diluent was isotonic saline and the stromalysing agent was LYSES (Coulter). The machine was calibrated for <u>Sigmodon hispidus</u> blood utilizing the following settings: aperture, 6; erythrocyte threshold, 10; and leukocyte threshold, 20. Each count was made in triplicate and an average recorded for the sample.

Thin blood films were air dried and stained with Wrights'-Giemsa stain (buffered pH 6.8). Two hundred leukocytes were differentiated utilizing the cellular morphology criteria of Hepworth⁺ including the distinction between large and small lymphocytes.

Reticulocytes were enumerated per 1000 erythrocytes according to the method of Johns² on smears of blood vitally stained with brilliant cresyl blue and counter stained with Wrights' stain.

The erythrocytic parameters are presented in Tables 2-3. During the entire 13 months of sequential sampling, there were no significant differences between male and female S. <u>hispidus</u> for any given age group. The erythrocyte numbers and hematocrit values did not change significantly over the 13 month period. There was however, a significant regression (F test: P<.001) of the hemoglobin concentration with age in both male and female <u>Sigmodon</u>. During the first two months of life both male and female <u>Sigmodon</u> had a sharp reduction in the number of reticulocytes. After 2 months of age, these values progressed in a linear fashion throughout the next 11 months of life.

The erythrocyte parameters in our study are in close agreement with the erythrocyte and hematocrit values reported by Dunaway and Lewis³ and with the hematocrit and hemoglobin values reported by Forman⁴. Our values, however, are higher than the values reported by Hepworth¹ for both "conditioned" and "stressed" wild caught <u>Sigmodon</u>; including reticulocyte values above 1%.

The leukocyte values are presented in Tables 4-5. During the 13 month period of investigation there was no significant difference between the leukocytes of males versus females or among age groups.

All the <u>Sigmodon</u> had a significantly higher number of lymphocytes than of neutrophils with the small lymphocytes outnumbering the large type. These findings are in agreement with Hepworth and others in classifying <u>Sigmodon</u> as one of the "lymphocytic-type" rodents (5). Other points of agreement with Hepworth's <u>Sigmodon</u> population are similar eosinophil and basophil counts and lower number of neutrophils in female versus males. Points of difference are lower monocyte counts and higher total leukocyte counts of our animals when compared to the "conditioned" wild-caught animals of Hepworth.

Even though previous results are based on single or double samples, the differences between individual results stress the importance of evaluating blood parameters of study groups thus avoiding differences which can arise due to geographic location or environmental conditions.

LITERATURE CITED

- 1. Hepworth, J.L.: Hematology of Sigmodon hispidus: Average parameters compared with those under induced stresses. FhD Thesis, Oklahoma State University, May 1966.
- Jones, F.M.: An inexpensive ocular ruler to facilitate reticulocyte counting. Am. J. Clin. Path. <u>2</u> (4): 351-352, 1932.
- 3. Dunaway, P.B. and Lewis, L.L.: Taxonomic relation of Erythrocyte count, Mean Corpuscular Volume, and Body-weight in Mammals. Nature 205: 481-484, 1965.
- 4. Forman, C.W.: Notes and blood data on some mammals of Durham County, North Carolina. J. Mamm. <u>37</u>: 427-428, 1956.
- 5. Lieb, J.R. and Wilber, C.G.: Some hematological studies on the Alaskan ground squirrel. Trans. Am. Microsc. Soc. <u>73</u> (4): 412-415. 1954.

FUBLICATIONS AND REPORTS

- Tesh, R.B., Ackerman, L.J., Dietz, W.H. and Williams, J.A.: <u>Angiostroncylus costaricensis</u> in Panama. Prevalence and Pathologic Findings in Wild Rodents. Am. J. Trop. Med Hyg. <u>27</u> (3): 348-356, 1973.
- 2. Ackerman, L.J. & Walton, B.C.: <u>Angiostrongylus costaricensis</u> in Panama. Presented at the Medical Service Conference Gorgas Hospital, Canal Zone, October 1972.
- 3. Ackerman, L.J., Tesh, R.B., Dietz, W.H. and Williams, J.A.: Prevalence of <u>Angiostrongylus costaricensis</u> in Panamanian Rodents. Presented at the annual meeting of the Amer. Soc. Trop. Med. Hyg., Miami Beach, Fla. November 1972.

	SUMMARY OF FRONGYLUS COSTARICENSIS N SEVERAL SPECIES OF A					
GENUS SPECIES	(COMMON NAME)	POSITIVE	NEULLE FECALS	NEGATIVE FECALS	MULTINE ADULTS	THAT HATE
ATELES GEOFFROYI	(SPIDER MONKEY	11	10	1	0	2
CAVIA PORCELLUS	(GUINEA PIG)	3	0	3	3	0
CEBUS CAPUCINUS	(WHITE FACE MONKEY)	7_	6	1	0	2
LIOMYS ADSPERSUS	(SPINY POCKET MOUSE)	1	11	0	0	1
MARMOSA SP.	(MOUSE OPOSSUM)	2	0	2	2	0
MESOCRITETUS AURATUS	(HAMSTER)	2	0	2	0	2
MUS MUSCULUS	(MOUSE)	10	10	0	0	2
NYCTOMYS SUMICHRASTI	(VESPFR RAT)	2	0	2	0	2
PROECHIMYS SEMISPINOSUS	(SPINY RAT)	2	0	2	2	1
RATTUS NORVEGICUS	(NORWAY RAT)	4	4	0	0	0
SIGMODON HISPIDUS	(COTTON RAT)	18	18	0	0	5
ZYGODONTOMYS MICROTINUS	(CANE MOUSE)	16	0	16	8	с
	TOTAL	78	49	29	15	16

TABLE 1

38

۰.

/

2	
TABLE	

١

·· .

.

ERYTHROCYTE CONSTITUENTS OF SIGNODON HISPIDUS

							• •		
	9	5.97± 0.6 ¹ (4.40-7.25)	45.65± 4.34 - (34.00-56.00)	12.88± 1.36 (7.80-15.50)	77.09± 9.85 (55.86-109.09)	21.68± 2.29 (16.46-26.22)	28.39± 3.31 (16.25-35.23)	3.66± 1.92 (1.20-12.82)	36
	ŝ	5.88± 0.53 (4.80-7.14)	44.05± 3.78 (37.00-51.50)	13.51± 1.51 (10.80-16.50)	75.42± 8.78 (53.23-100.00)	23.09± 2.78 (17.93-27.08)	30.66± 2.03 (27.08-34.38)	4.27± 1.18 (1.80-8.70)	36
	শ	6.23± 0.66 (4.86-7.87)	46.75± 2.86 (40.50-55.00)	14.15± 1.51 (10.00-16.80)	75.63± 6.75 (63.53-90.73)	22.91± 3.06 (14.84-29.42)	30.34± 3.38 (21.28-35.11)	3.33± 1.28 (1.40-6.50)	36
AGE IN MONTHS	£	6.16± 0.52 (5.32-7.59)	46.75± 2.66 (39.00-52.00)	13.69± 1.54 (11.50-17.50)	76.31± 5.71 (64.56-86.67)	22.26± 2.35 (18.42-26.66)	29.30± 3.48 (23.96-35.56)	3.20± 1.50 (0.70-6.90)	36
A	ດ	6.11± 0.48 (4.94-7.23)	47.81± 2.97 (40.00-55.00)	14.18± 1.31 (11.80-17.20)	78.70± 7.29 (64.52-99.19)	23.36± 2.87 (18.07-31.98)	29.70± 2.63 (24.08-36.60)	3.87± 1.44 (1.20-6.30)	36
·	г	5.67± 0.82 * (3.70-8.90)	42.47± 4.56 (31.00-52.00)	14.69± 2.00 (10.00-18.50)	75.92± 10.02 (46.07-102.70)	26.28± 4.20 (15.17-36.49)	34.64± 3.47 (27.78-43.78)	10.58± 6.97 (2.10-25.60)	36
PARMETER		ERYTHROCYTES (X10 ⁶ /mm ³)	HEMATOCRIT (ズ)	HEWOGLOBIN	с жсv (л)	ЖСН (µид)	MCHC (%)	RETICULOCYTES (#/100 RBC)	No. of Animals

* Mean± S.D. (Range) TABLE 3

•

ERYTHROCYTE CONSTITUENTS OF SIGNDON HISPIDUS

PARAMETERS			AGE IN P	MONTHS			
	7	• ©	6	ТО	11	12	13
ERYTHROCYTES	5.56± 0.67*	5.73± 0.75	6.09± 0.75	5.90± 0.59	6.06± 0.48	6.04± 0.41	5.33± 0.74
(x10 ⁶ /mm ³)	(4.26-7.06)	(3.82-6.54)	(5.14-8.22)	(4.54-6.88)	(5.13-6.82)	(5.43-6.97)	(4.20-6.21)
HEMATOCRIT	44.00± 2.96	45.50± 2.49	45.90± 3.29	43.30± 2.71	44.13± 4.26	43.83± 3.41	41.83± 4.69
(%)	(38.50-49.00)	(41.00-50.00)	(42.50-55.50)	(38.00-48.50)	(38.00-51.00)	(39.00-50.00)	(31.00-48.00)
(Twol/2)	13.47± 0.65	13.05± 1.63	12.83± 1.19	11.21± 1.85	12.00± 0.98	12.84± 1.21	11.87± 1.49
NIGCTOPIN	(12.50-14.50)	(7.50-14.80)	(9.80-14.50)	(8.50-14.30)	(10.30-13.30)	(10.00-14.30)	(9.30-14.30)
Cactor (n)	80.02± 9.77	80.68± 11.28	75.90± Å.97	73.81± 6.3¼	72.89± 5.99	72.71± 5.70	79.41± 11.35
	(62.00-105.63)	(71.21-117.80)	(67.52-83.66)	(63.23-85.90)	(62.09-81.77)	(63.93-85.64)	(63.92-103.57)
.XCH	24.54± 3.15	23.14± 4.07	21.32± 3.09	18.96± 2.12	19.86± 1.82	21.31± 2.71	22.69± 4.148
	(20.13-34.04)	(13.00-33.51)	(14.71-25.38)	(14.97-22.31)	(17.16-22.78)	(17.04-24.86)	(15.37-32.14)
MCHC	30.70± 1.67	28.77± 3.75	28.05± 3.00	25.86± 3.66	27.35± 2.68	29.32± 2.18	26.48± 3.03
(%)	(27.14-33.75)	(15.46-32.44)	(20.21-31.76)	(21.25-31.43)	(22.55-32.82)	(25.00-33.33)	(22.41-33.33)
RETICULOCYTE	3.79± 0.67	4.91± **	4.33± **	4.98± 4.59	2.92± 2.27	3.20± 0.93	3.60± 1.17
	(2.80-5.10)	(1.50-22.80)	(1.20-19.70)	(1.60-20.00)	(0.60-8.60)	(1.80-4.40)	(2.20-6.30)
No. of animals	19	17	15	15	12	12	12
*Nean±5.D. (Range)	**Skewed Distribu Rendered Calcul for Population.	**Skewed Distribution of Values Rendered Calculated S.D. Invalid for Population.	es Valid				

		ן דווגרערעיד.	STATESTU MOGONOLS GO SUMMITURE	STATASTU MOGOV		
PARANETER		11 12012		CONT SETU NOCOS		
	,	ċν	m	4	ŗ	ુ
LEUKOCYTES	9.05± 2.30	7.58 2.66	7.75 [±] 1.68	7.8<u>9+</u> 2.13	7.75± 1.78	8.38-2.39
(x10 ^{3/mm³)}	(5.03-15.10)	(3.50-14.20)	(5.10-12.10)	(4.00-12.90)	(3.30-12.80)	(4.70-16.50)
NEUTROPRILS	9.91± 7.27	12.40± 8.95	17.33 15.00	17.16 [±] 10.41	23.88 [±] 8.59	20.05± 10.61
*(x10 ² /m ³)	(0.87-35.49)	(1.56-40.12)	(1.78-76.23)	(2.12-50.31)	(7.26–53.53)	(7.05-55.77)
EANDS	0.64± ***	0.64± ***	0.76± ***	0.62* ***	0.27 [±] ***	0.72 0.61
(x10 ² /m ²)	(0.00-4.96)	(0.00-4.52)	(0.00-2.70)	(0.00-3.13)	(0.00-1.92)	(0.00-2.18)
r LIMPH SIMLL (x10 ² /r ¹² 3)	72.70 <u>+</u> 21.19 (40.55-124.79)	57.67 <u>+</u> 27.28 (18.48-132.06)	53.02± 15.14 (23.40-95.76)	53.71± 18.84 (0.00-91.25)	49.924 13.72 (24.75-93.44)	56.96⁴ :16.59 (31.78-98.87)
LUNTH LARGE	1.71± ***	1.54± ***	1.97± 1.40	1.92 [±] 1.32	0.25± ***	1.37 [±] ***
(x10 ² /s=3)	(0.00-8.76)	(0.00-4.84)	(0.00-6.30)	(0.00-5.10)	(0.00-1.74)	(0.00-8.45)
(x10 ² /m3)	1.08± 0.98	0.93± 0.83	0.94± 0.57	1.16± 0.95	0.43± ***	0.68 [±] ***
	(0.00-3.65)	(0.00-3.08)	(0.00-2.13)	(0.00-3.87)	(0.00-1.76)	(0.00-5.5 ^g)
EDSINOPHTLS	4.41± 2.48	2.63± 1.53	3.11± 1.94	3.48± 2.05	2.77± 1.32	4.34± 2.80
(x10 ² /mm ³)	(0.00-9.31	(0.50-6.00)	(0.00-9.00)	(0.83-10.40)	(0.00-7.70)	(1.08-14.50)
E£SOPHILS	0.04± ***	0.04± ***	0.17± ***	0.05± ***	0.00	0.07± ***
(x10 ² /mm ³)	(0.00-0.52)	(0.00-0.57)	(0.00-1.19)	(0.00-0.65)		(0.00-0.5¼)
No. of Animals	36	36	36	36	36	36
*Absolute count	** Mean± S.D. (Range)	t S.D. Ce)	*** Skewed Distribution of Invalid for Population.	Skewed Distribution of Valucs Rendered Invalid for Population.	ered Calculated S.D.	D.

TABLE 4

-		LEUKOCY	AO SUERDELESIOS ALASES OF	CETERITY HIGHLING			•
PARAMETER			AGE IN MONTHS	SHLNOV			•
LEUKOCYTES	6.68± 1.06**	7.20± 2.04°	7.23± 2.00	8.47± 2.70	6.78± 2.87	7.45± 1.27	7.43± 1.27
(x10 ³ /m ³)	(5.00-9.40)	(3.70-10.80)	(4.50-10.70)	(4.30-13.40)	(3.10-11.60)	(5.70-9.80)	(5.20-9.83)
NEUTROPHILS	16.45± 7.15	13.14± 11.89	16.37± 10.33	17.83± 14.12	19.36± 15.78	17.51± 6.27	18.40± 5.85
*(x10 ² /mm ³)	(4.35-28.35)	(1.80-43.74)	(6.49-43.17)	(3.64-59.59)	(2.64-63.22)	(9.69-30.55)	(11.56-28.11)
BANDS	0.28± ***	0.52± ***	0.46± ***	0.50± 0.49	(61.0-00.0)	0.75± 0.55	0.60± ***
(x10 ² /mm ³)	(0.00-1.90)	(0.00-1.90)	(0.00-1.61)	(0.00-1.50)	(91.0-00.0)	(0.00-1.80)	(0.00-2.58)
LYWPH S.AALL	46.30± 7.94	53.80± 16.38	51.04± 12.24	59.60± 18.78	44.21± 18.93	51.90± 11.38	50.93± 12.02
(x10 ^{-/mm3})	(33.75-64.86)	(22.76-88.80)	(30.38-75.44)	(34.19-102.51)	(22.36-78.80)	(33.32-73.01)	(35.88-76.4±)
LYMPH LARGE	0.42± ***	0.89± 0.52	0.94± 0.45	1.40± 1.22	1.10± ***	0.73± 0.71	0.57± **
(X10 ² /mm ³)	(0.00-1.52)	(0.00-1.78)	(0.32-2.08)	(0.00-3.60)	(0.00-4.06)	(0.00-2.35)	(0.00-2.35)
(^{min/2} 01x)	* 0.52± 0.44	0.38± ***	0.4 <u>9±</u> 0.45	1.05± 0.95	0.33± ***	0.88± 0.47	0.48± ***
	(0.00-1.45)	(0.00-2.35)	(0.00-1.61)	(0.00-3.00)	(0.00-1.64)	(0.00-1.54)	(0.00-1.78)
EOSINOPATLS	2.79± 1.65	2.23± 1.16	3.06± 0.91	4.42± 3.02	2.77± 2.2 4 -	2.74± 1.49	3.35± 1.23
(x10 ² /= n ³)	(0.74 -7.60	(0.00-3.78)	(1.83-4.85)	(0.65-12.00)	(0.16-6.70)	(0.00-5.39)	(1.56-5.10)
BASOPIELS (x10 ² /m ³)	0.02± *** (0.00-0.38)	0.01± *** (0.00-0.19)	0.00	0.04± *** (0.00-0.54)	0.00	0.00	0.50
No. of Animals	ls 19	17	15	15	12	12	12
*Absolute count		** Mean± S.C. (Range)	*** Skewed For Pop	Skewed Distribution of Values For Population.		Rendered Calculated S.D.]	Invalid

•

DISTRIBUTION LIST

5 copies to:

U.S. Army Medical Research and Development Command Washington, D.C. 20314

43

1

12 copies to:

Defense Documentation Center Alexandria, Virginia 22314

l cc_jy to:

U.S. Army Combat Development Command Medical Department Agency, BAMC Fort Sam Houston, Texas 78234

Dội	CUMENT CONTROL DATA	R&D	
(Service stassification of title, Lody of and	teect and indexing enrolation mus	1 be eritered whon 1	he overall report is classified) SECURITY CLASSIFICATION
U.S. Army Medical Research Unit	Panama		LASSIFIED
Bux 1809		25. GROUP	
APO New York 09826			
REPORT TATLE		· · ·	
Annual Progress Report, 1 July	1972-30 June 1973		
4. DESCRIPTIVE NOTES (Type of report and inclusion)	va dales)		
			•
AUTHOR(5) (First name, middle initial, last name)			-
bryce C. Walton, COL, MSC	Louis C. Rut	·	
Larry J. Ackerman, MAJ, VC	Larry D. Hen	aricks, CPT	, MSU
REPORT DATE	74. TOTAL N	O. OF PAGES	76. NO. OF REFS
		46 + vi	5
. CONTRACT OR GRANT NO.		OR'S REPORT NU	
6.11.0].A			
PROJECT NO.		73-A	
34061102871Q			
•	9b. OTHER R this report	EPORT NO(\$) (Any	other numbers that may be seeligned
		MEDDH-288	(91)
. DISTRIBUTION STATEMENT			
	U.S. Ar Command		Research and Developmen
B. ABSTRACT		<u>*-</u>	· · · · · · · · · · · · · · · · · · ·
The research program of US military importance in Latin An concerned with American leishma	merica. The investig	ations repo	rted are primarily
personnel.			
A study of the effect of a	chemotherapy on serum	antibody w	as made to determine
• • • • • • • • • • • • • • • • • • • •	• • •		•
if serologic testing would be a	gativity, there was	a demonstra	
few patients reverted to serone			
few patients reverted to serone cases, and the rate of treatment		ely correla	ted with diminution
few patients reverted to serone cases, and the rate of treatmen of titers. In one espundia cas	e declining titers p	ely correla aralled cli	ted with diminution nical imp rovem ent
few patients reverted to serone cases, and the rate of treatmen of titers. In one espundia cas and an increase in titer accomp	se declining titers p panied an explosive r	ely correla aralled cli ecrudescenc	ted with diminution nical improvement e.
few patients reverted to serone cases, and the rate of treatmen of titers. In one espundia cas and an increase in titer accomp Follow-up of patients treat	se declining titers p panied an explosive r ated with metranidazo	ely correla aralled cli ecrudescenc le in the C	ted with diminution nical improvement e. anal Zone and Republic
few patients reverted to serone cases, and the rate of treatmen of titers. In one espundia cas and an increase in titer accomp Follow-up of patients treat of Panama medical facilities de	se declining titers p panied an explosive r ated with metranidazo emonstrated conclusiv	ely correla aralled cli ecrudescenc le in the C ely that th	ted with diminution nical improvement e. anal Zone and Republic is drug is of no value.
few patients reverted to serone cases, and the rate of treatmen of titers. In one espundia cas and an increase in titer accomp Follow-up of patients treat of Panama medical facilities de A vero cell experimental is	se declining titers p panied an explosive r ated with metranidazo emonstrated conclusiv infection model for a	ely correla aralled cli ecrudescenc le in the C ely that th ntileishman	ted with diminution nical improvement e. anal Zone and Republic is drug is of no value. ial drug screening was
few patients reverted to serone cases, and the rate of treatmen of titers. In one espundia cas and an increase in titer accomp Follow-up of patients treas of Panama medical facilities de A vero cell experimental is developed which permits exposur	e declining titers p panied an explosive r ated with metranidazo emonstrated conclusiv infection model for a re of intracellular a	ely correla aralled cli ecrudescenc le in the C ely that th ntileishman mastigotes	ted with diminution nical improvement e. anal Zone and Republic is drug is of no value. ial drug screening was to drug for up to 10
few patients reverted to serone cases, and the rate of treatmen of titers. In one espundia cas and an increase in titer accomp Follow-up of patients treas of Panama medical facilities de A vero cell experimental is developed which permits exposun days. However, no effect on the	se declining titers p panied an explosive r ated with metranidazo emonstrated conclusiv infection model for a re of intracellular a ne parasites could be	ely correla aralled cli ecrudescenc le in the C ely that th ntileishman mastigotes demonstrat	ted with diminution nical improvement e. anal Zone and Republic is drug is of no value. ial drug screening was to drug for up to 10 ed with this system
few patients reverted to serone cases, and the rate of treatmen of titers. In one espundia cas and an increase in titer accomp Follow-up of patients trees of Panama medical facilities de A vero cell experimental is developed which permits exposun days. However, no effect on th using a clinically effective day	se declining titers p banied an explosive r ated with metranidazo emonstrated conclusiv infection model for a se of intracellular a he parasites could be rug, methyl glucamine made of the first hu	ely correla aralled cli ecrudescenc le in the C ely that th ntileishman mastigotes demonstrat antimoniat man liver f	ted with diminution nical improvement e. anal Zone and Republic is drug is of no value. ial drug screening was to drug for up to 10 ed with this system e. luke (<u>Amphimerus sp</u> .)
few patients reverted to serone cases, and the rate of treatmen of titers. In one espundia cas and an increase in titer accomp Follow-up of patients treas of Panama medical facilities de A vero cell experimental is developed which permits exposun days. However, no effect on th using a clinically effective do An incidental finding was infection in Panama, which cons	se declining titers p banied an explosive r ated with metranidazo emonstrated conclusiv infection model for a se of intracellular a he parasites could be rug, methyl glucamine made of the first hu	ely correla aralled cli ecrudescenc le in the C ely that th ntileishman mastigotes demonstrat antimoniat man liver f	ted with diminution nical improvement e. anal Zone and Republic is drug is of no value. ial drug screening was to drug for up to 10 ed with this system e. luke (<u>Amphimerus sp</u> .)
few patients reverted to serone cases, and the rate of treatmen of titers. In one espundia cas and an increase in titer accomp Follow-up of patients treat of Panama medical facilities de A vero cell experimental if developed which permits exposun days. However, no effect on th using a clinically effective du An incidental finding was infection in Panama, which const Hemisphere.	se declining titers p panied an explosive r ated with metranidazo emonstrated conclusive infection model for a re of intracellular a he parasites could be rug, methyl glucamine made of the first hu stitutes only the thi	ely correla aralled cli ecrudescenc le in the C ely that th ntileishman mastigotes demonstrat antimoniat man liver f rd report f	ted with diminution nical improvement e. anal Zone and Republic is drug is of no value. ial drug screening was to drug for up to 10 ed with this system e. luke (<u>Amphimerus sp</u> .) rom the Western
few patients reverted to serone cases, and the rate of treatmen of titers. In one espundia cas and an increase in titer accomp Follow-up of patients trees of Panama medical facilities de A vero cell experimental is developed which permits exposun days. However, no effect on th using a clinically effective do An incidental finding was infection in Panama, which cons Hemisphere. Normal hematologic values	se declining titers p panied an explosive r ated with metranidazo emonstrated conclusiv infection model for a re of intracellular a he parasites could be rug, methyl glucamine made of the first hu stitutes only the thi	ely correla aralled cli ecrudescenc le in the C ely that th ntileishman mastigotes demonstrat antimoniat man liver f rd report f tton rats (ted with diminution nical improvement e. anal Zone and Republic is drug is of no value. ial drug screening was to drug for up to 10 ed with this system e. luke (<u>Amphimerus sp</u> .) rom the Western <u>Sigmodon hispidus</u>) used
few patients reverted to serone cases, and the rate of treatmen of titers. In one espundia cas and an increase in titer accomp Follow-up of patients treas of Panama medical facilities de A vero cell experimental is developed which permits exposun days. However, no effect on th using a clinically effective da An incidental finding was infection in Panama, which cons Hemisphere. Normal hematologic values for experimental infection stud	se declining titers p panied an explosive r ated with metranidazo emonstrated conclusiv infection model for a re of intracellular a he parasites could be rug, methyl glucamine made of the first hu stitutes only the thi	ely correla aralled cli ecrudescenc le in the C ely that th ntileishman mastigotes demonstrat antimoniat man liver f rd report f tton rats (ted with diminution nical improvement e. anal Zone and Republic is drug is of no value. ial drug screening was to drug for up to 10 ed with this system e. luke (<u>Amphimerus sp</u> .) rom the Western <u>Sigmodon hispidus</u>) used
few patients reverted to serone cases, and the rate of treatmen of titers. In one espundia cas and an increase in titer accomp Follow-up of patients treas of Panama medical facilities de A vero cell experimental i developed which permits exposun days. However, no effect on th using a clinically effective du An incidental finding was infection in Panama, which cons Hemisphere. Normal hematologic values for experimental infection stud	se declining titers p panied an explosive r ated with metranidazo emonstrated conclusiv infection model for a re of intracellular a he parasites could be rug, methyl glucamine made of the first hu stitutes only the thi	ely correla aralled cli ecrudescenc le in the C ely that th ntileishman mastigotes demonstrat antimoniat man liver f rd report f tton rats (ted with diminution nical improvement e. anal Zone and Republic is drug is of no value. ial drug screening was to drug for up to 10 ed with this system e. luke (<u>Amphimerus sp</u> .) rom the Western <u>Sigmodon hispidus</u>) used
few patients reverted to serone cases, and the rate of treatmen of titers. In one espundia cas and an increase in titer accomp Follow-up of patients treas of Panama medical facilities de A vero cell experimental is developed which permits exposun days. However, no effect on th using a clinically effective do An incidental finding was infection in Panama, which cons Hemisphere. Normal hematologic values for experimental infection stud- month period.	se declining titers p panied an explosive r ated with metranidazo emonstrated conclusiv infection model for a se of intracellular a he parasites could be rug, methyl glucamine made of the first hu stitutes only the thi for the colonized co lies were derived fro	ely correla aralled cli ecrudescenc le in the C rely that th ntileishman mastigotes demonstrat antimoniat man liver f rd report f tton rats (m monthly s	ted with diminution nical improvement e. anal Zone and Republic is drug is of no value. ial drug screening was to drug for up to 10 ed with this system e. luke (<u>Amphimerus sp</u> .) rom the Western <u>Sigmodon hispidus</u>) used amples over a 6-13
few patients reverted to serone cases, and the rate of treatmen of titers. In one espundia cas and an increase in titer accomp Follow-up of patients trees of Panama medical facilities de A vero cell experimental i developed which permits exposun days. However, no effect on th using a clinically effective du An incidental finding was infection in Panama, which cons Hemisphere. Normal hematologic values for experimental infection stud month period.	se declining titers p panied an explosive r ated with metranidazo emonstrated conclusiv infection model for a re of intracellular a he parasites could be rug, methyl glucamine made of the first hu stitutes only the thi	ely correla aralled cli ecrudescenc le in the C ely that th ntileishman mastigotes demonstrat antimoniat man liver f rd report f tton rats (m monthly s	ted with diminution nical improvement e. anal Zone and Republic is drug is of no value. ial drug screening was to drug for up to 10 ed with this system e. luke (<u>Amphimerus sp</u> .) rom the Western <u>Sigmodon hispidus</u>) used amples over a 6-13

The life cycle of <u>Angiostrongylus costuricensis</u> was established in the laboratory and experimental infections studied in several species of wild rodents and 2 species of sub-human primates, which showed monkeys develop a disease picture resembling that of humans.

A 2 year study of breeding populations of phlebotomine sandflies and local environmental effects on these populations was completed. The species complement is divided into 2 major consociations, one dominated by anthropophilic species and the other by zoophilic species. The species complement includes 6 major species of which 4 are anthropophilic and have been implicated in transmission of American leishmaniasis. The effect of clinatologic, hydrologic, phytologic, and edaphic factors on sandfly distribution was studied.

Mass fearing techniques using standard laboratory glassware were developed which produced improved yields over traditional methods, with greatly reduced expenditure of man hours. Wild caught females were placed in culture preparations in which eggs were laid, hatched and immature stage development progressed with essentially no attention or care, which constitutes an important first step to colonization.

Security Cirabilication		LIN	nandaniko serentza. K. A.	Citi	an an suiveann as F	می ند بیدهمی ۱۰ یا	nonaar Korg
NEY WORDS		POLE		ROL'			<u>م</u> ر
Leichmania, leichmaniasis, cutaneous, espu chemotherapy, serology, vector, <u>Lutzomyic</u> phlebotomine sandflies, <u>Angiostrongylus</u> <u>costarioensis</u> , pathogenesis, <u>Amphimerus</u> , fluke, Panama.	s.			,			
	:						
	•						
)			
	• •						
				•			
	••						
•	•						
			•				
		*					
12.2346		UNCL	ASSIFE	1 11D	1004 4- 1416 , 3, 3, 7 8 %, 5		
1	-6		Sermit	Classifi	cetion		