acinment 1.

Date 27.04.1982

ETHICAL REVIEW COMMITTEE, ICDDR,B.

incipal Investigator Dr. M. Moshaddequr Hossain Trainee Investigator (if any) _____

plication No. 82-020(P) Supporting Agency (if Non-ICDDR,B) _____

le of Study Pilot study of amoebiasis in Matlab

Project status:
(✓) New Study (Pilot study)
( ) Continuation with change
( ) No change (do not fill out rest of form)

rcle the appropriate answer to each of the following (If Not Applicable write NA).

Source of Population:
(a) Ill subjects (Yes) No
(b) Non-ill subjects (Yes) No
(c) Minors or persons under guardianship (Yes) No

Does the study involve:
(a) Physical risks to the subjects Yes (No)
(b) Social Risks Yes (No)
(c) Psychological risks to subjects Yes (No)
(d) Discomfort to subjects (Yes) No
(e) Invasion of privacy Yes (No)
(f) Disclosure of information damaging to subject or others Yes (No)

Does the study involve:
(a) Use of records, (hospital, medical, death, birth or other) Yes (No)
(b) Use of fetal tissue or abortus Yes (No)
(c) Use of organs or body fluids Yes (No)

Are subjects clearly informed about:
(a) Nature and purposes of study (Yes) No
(b) Procedures to be followed including alternatives used (Yes) No
(c) Physical risks (Yes) No
(d) Sensitive questions (Yes) No
(e) Benefits to be derived (Yes) No
(f) Right to refuse to participate or to withdraw from study (Yes) No
(g) Confidential handling of data (Yes) No
(h) Compensation &/or treatment where there are risks or privacy is involved in any particular procedure (Yes) No

5. Will signed consent form be required:
   (a) From subjects Yes (No)
   (b) From parent or guardian (if subjects are minors) Yes (No)
6. Will precautions be taken to protect anonymity of subjects (Yes) No
7. Check documents being submitted herewith to Committee:
   ___ Umbrella proposal - Initially submit an overview (all other requirements will be submitted with individual studies).
   ✓ Protocol (Required)
   ✓ Abstract Summary (Required)
   ✓ Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw (Required)
   ✓ Informed consent form for subjects
   ✓ Informed consent form for parent or guardian
   ✓ Procedure for maintaining confidentiality
   ___ Questionnaire or interview schedule *

* If the final instrument is not completed prior to review, the following information should be included in the abstract summary:
1. A description of the areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy.
2. Examples of the type of specific questions to be asked in the sensitive areas.
3. An indication as to when the questionnaire will be presented to the Cttee. for review.

agree to obtain approval of the Ethical Review Committee for any changes olving the rights and welfare of subjects before making such change.

M. Moshaddequr Hossain
Principal Investigator

Trainee

[redacted] 15 JUN 1998

SECTION I - RESEARCH PROTOCOL

1. Title : Pilot study of amoebiasis in Matlab

2. Principal Investigator : Dr. M. Moshaddeque Hossian

   Co-Investigator : Dr. Roger I. Glass, Dr. P. Speelman, Dr. K. Zaman
   M.R. Khan

3. Starting Date : May 15, 1982

4. Completion Date : Sept. 14, 1982

5. Total Direct Cost : US $ 3,350 (Incremental Cost: US$2,526)

6. Availability of Funds :

7. Scientific Programme Head :

This protocol has been approved by the Disease Transmission Working Group.

Signature of Scientific Programme Head: M Zaman

Date: 27/4/1982

8. Abstract Summary:

Members of randomly selected families (50 approx.) in a Matlab village will be screened by stool microscopy to identify 25 individuals with asymptomatic amoebiasis (cases) and 25 age and socio-economic status matched non-infected controls. We will follow these 2 groups for 3 months to determine the rate of acquisition of asymptomatic intestinal amoebic infection among controls and of symptomatic amoebiasis among both cases and controls. The rate of spontaneous loss of infection in asymptomatic carriers will also be determined. To study changes in serum anti-amoeba antibody titres with the acquisition or loss of infection finger-prick blood samples (100 lambdas) will be collected from each subject on entry into and discharge from the study. Information obtained in this pilot study will be used as a background for designing the methods for a full-scale prospective longitudinal study of the incidence of symptomatic and asymptomatic intestinal amoebiasis in our population.

9. Review:

   a. Ethical Review Committee: _____

   b. Research Review Committee: _____

   c. Director: _____

   d. BMRC: _____

   e. Controller/Administrator: _____

SECTION II - RESEARCH PLAN

A. INTRODUCTION

1. Objective:

We intend to develop a protocol to study the incidence of intestinal amoebiasis in a rural Bangladeshi population. However, due to lack of essential background information, we are unable to estimate the optimal size of samples to be followed for arriving at statistically valid conclusions. We also can not determine how long and how frequently should we re-examine stools and sera from the study subjects to obtain the requisite data without wasting time and resources. In this pilot study, we will try to address these methodologic problems through obtaining preliminary information about the epidemiology of amoebiasis in a rural community. The experience gained would guide us to develop scientifically acceptable and operationally practicable methods for a full-scale study.

2. Background:

Amoebiasis is the condition of harbouring the protozoan parasite Entamoeba histolytica with or without symptoms (1). Although prevalent worldwide, amoebiasis occurs more frequently in the tropics and subtropics, where faecal-oral transmission of E. histolytica is facilitated by the low levels of personal and public hygiene (2). In Dacca city, 4% of 1- to 15-year-old

community children were found to pass E. histolytica in the stool (3), where as in villages around the city the corresponding rate was 41% (4). Among patients examined at the ICDDR,B Matlab hospital, the age-specific prevalence of stool-positivity for amoeba ranged from <1% to 11% (unpublished, 1977). Among ICDDR,B Dacca hospital surveillance patients, age-specific stool-positivity for E. histolytica was recorded to be <1% to 17% (unpublished, 1979-80). All these studies used direct-smear examination of single stool samples as the screening method. Cyst-concentration techniques were not used and no attempt was made to distinguish E. histolytica from E. hartmanni and E. coli by using micrometry. Despite these limitations, these figures probably reflect the extent of amoebic infection in our populations.

At any point in time, a large proportion of the individuals infected with E. histolytica may be asymptomatic (5) mainly because the parasite lives usually as a commensal in the lumen of the large bowel of the host (6). However, under circumstances that are still not well understood, amoebae invade intestinal and extra-intestinal tissues of the host causing disease and sometimes even death.

The prevalence of E. histolytica in different population groups in Bangladesh has been estimated by conducting stool surveys.

However, to the best of our knowledge, the association of this potentially pathogenic parasite with the occurrence of gastro-intestinal symptoms in infected persons has never been studied. We also do not know the rate of change in states of Bangladeshi individuals in terms of amoebic infection and disease.

Stool- or sero-prevalence surveys for amoebiasis, when properly conducted provide useful epidemiologic information through estimating the extent of occurrence of the infection in a population. But for more direct assessment of the intensity of transmission of the disease and for understanding the dynamics of the host-parasite interactions longitudinal studies are essential.

We are interested in developing a protocol to study the incidence of symptomatic and asymptomatic intestinal amoebiasis in the Matlab community. In that study we will prospectively monitor selected groups of people to determine : (a) the incidence of symptomatic disease among persons with asymptomatic intestinal amoebiasis (cases), (b) the incidence of symptomatic and asymptomatic intestinal amoebiasis among initially non-infected persons (controls) and (c) the influence of suspected risk factors on the acquisition of amoebic infection.

OUTLINE OF THE METHODS TO BE USED FOR STUDYING THE INCIDENCE OF AMOEBIASIS IN MATLAB

INITIAL STOOL MICROSCOPY

N=?

PERSONS WITH ASYMPTOMATIC AMOEBIASIS
N=?

NON-INFECTED PERSONS
N=?

FOLLOW-UP

? DURATION

? FREQUENCY OF STOOL ME

? FREQUENCY OF SERUM TESTS

Keeping these questions in mind, we have developed an outline of the methods to be used in our proposed study (see flow-chart). However, due to lack of basic information about the epidemiology of amoebiasis in our population, we could neither estimate the size of samples to be studied nor could we decide on the frequency of stool or serum examination to be performed. We also could not determine the length of follow-up period necessary.

3 Rationale:

A preliminary understanding of the dynamics of host-amoeba interaction in the study population will be acquired through this pilot study. This will help us to design the methods for a full-scale study of amoebiasis, so that we can get the desired data through optimal utilization of time and resources.

B. SPECIFIC AIMS:

The specific aims of this pilot study are to:

1. Determine the rate of development of symptoms in 25 persons with asymptomatic intestinal amoebiasis (cases) followed for 3 months.

2. Determine the rate of acquisition of symptomatic and asymptomatic intestinal amoebiasis in 25 non-infected persons (controls) followed for 3 months.

3. Determine the duration of excretion of the parasite in persons with asymptomatic infection.

C. METHODS OF PROCEDURE:

1. Field methods: Members of randomly selected families in a village near our Matlab hospital will be screened by microscopic examination (ME) of stool to identify 25 persons with asymptomatic amoebic infection (cases). An equal number of age and socio-economic status-matched non-infected individuals will be selected as controls. Based on our observation at the Matlab hospital we have estimated that approximately 250 individuals (50 familiies) will have to be tested to identify the requisite number of study subjects. Demographic and socio-economic characteristics of each family will be recorded and information will be obtained about individual and family practices of personal hygiene, water use and defacation practices. On selection and weekly thereafter the cases and controls will be interviewed to record their G.I. symptoms. Stool from each subject will be re-examined by microscopy at 2-weekly intervals for 3 months. Finger-prick blood samples (100 lambdas) will be collected from each on entry into and exclusion from the study. Study subjects with G.I. symptoms will be examined by stool ME and culture and treated with approved drugs when indicated.

2. Laboratory Methods: Each stool sample collected will be examined first by the direct smear technique. Samples negative for E. histolytica on direct smear examination will be re-tested following formol-ether concentration. Ocular micrometry will be used to measure and identify E. histolytica. For this study, any individual negative for E. histolytica on 3 consecutive stool examinations will be taken as a non-infected. To determine the titres of anti-amoeba antibodies we will examine serum samples using the indirect immunofluorescence (IF) technique in our laboratory.

3. Data Analysis: Data collected will be analysed to determine the acquisition rates of symptomatic and asymptomatic intestinal amoebiasis in the appropriate group of study subjects. We will try to correlate G.I. symptoms and stool ME findings with the results serological tests. The influence of individual and family demographic, socio-economic and hygienic characteristics on the occurrence of amoebiasis will be examined as well.

D. SIGNIFICANCE:

The results of this pilot study will provide us with essential background information for developing a full-scale protocol to determine the incidence of symptomatic and asymptomatic amoebiasis in a rural community.

E. FACILITIES REQUIRED:

1. Office Space: No additional space required.

2. Laboratory Space: No additional space required.

3. Hospital Resources: No additional resources required.

4. Animal Resources: None.

5. Logistic Support: Field and laboratory personnel and transportation will be required. These have been included in the budget.

6. Major Items of Equipments: None

7. Specialized Requirements: None

F. COLLABORATIVE ARRANGEMENTS:

The National Bacteriological Laboratory, Stockholm, Sweden, will collaborate in performing the serological tests for amoebiasis.

SECTION III - BUDGET

A. DETAILED BUDGET

1. PERSONNEL SERVICES

Name	Position	% of effort No.of days	Annual salary	Project Requirement Taka	Project Requirement Dollar
Dr. M.M. Hossain	P. Investigator	25% x 4m	34,500	2,875	-
Dr. K. Zaman	Co-Investigator	20% x 4m	40,000	2,667	-
Dr. R. Glass	CO-Investigator	5% x 2m	35,000	-	292
Dr. P. Speelman	Co-Investigator	5% x 1 wk	35,000	-	34
Mr. M.R. Khan	F.R.O.	10% x 4m	55,000	1,833	-
To be named	Tech. Cl.Path.	25% x 4m	28,000	2,333	-
To be named	2 Female Health Assistants	100% x 4m	22,000	14,667	-
			Sub total Tk.	24,375	326
			Incremental cost	14,667	-

2. SUPPLIES AND MATERIALS

Items	Unit cost	Amount Required		
Misc. drugs & ORS Packets	-	-	2,000	-
Candy, balloon, stool cups	-	-	500	-
Stool ME	Tk.5.00	1,000	5,000	-
Serological Tests	$ 0.5	100	-	50
Stool culture (Shigella, Salmonella, V. cholerae, ETEC, Campylobacter)	Tk.35.00	50	1,750	-
Office supplies	-	-	3,000	-
		Sub total	Tk. 12,250	$ 50

		Project Requirement	
		Taka	doller
3.	EQUIPMENT		
	None		
4.	PATIENT HOSPITALIZATION		
	None		
5.	OUTPATIENT CARE		
	None		
6.	ICDDR,B TRANSPORT		
	Matlab speed boat 100 h x Tk. 100	10,000	-
	Dacca-Matlab-Dacca Trips: 16 x Tk. 400	6,400	-
	Sub total Tk.	16,400	-
7.	TRAVEL AND TRANSPORTATION OF PERSONS		
	None		
8.	TRANSPORTATION OF THINGS		
	None		
9.	RENT, COMMUNICATION AND UTILITIES	1,000	-
	Sub total Tk.	1,000	-
10.	PRINTING AND REPRODUCTION		
	Questionnaires and forms	2,000	-
	Sub total Tk.	2,000	-

	Project Requirement	
	Taka	dollar
11. CONTRACTUAL SERVICES		
Matlab: country boats		
Tk. 22/day x 90 days	1,980	-
Sub total	Tk.1,980	-
12. CONSTRUCTION		
None		
Total	Tk. 58,005	376

Total US $ 3,350

Incremental cost US $ 2,526

(Conversion rate US $ 1.00= Tk. 19.50)

B. BUDGET SUMMARY

		Taka	Dollar
1.	Personnel Services : Total	24,375	326
	Incremental	(14,667)	-
2.	Supplies and Materials	12,250	50
3.	Equipment	-	-
4.	Patient hospitalization	-	-
5.	Outpatient care	-	-
6.	ICDDR,B Transport	16,400	-
7.	Travel and Transportation of Persons	-	-
8.	Transportation of Things	-	-
9.	Rent, Communication and Utilities	-	-
10.	Printing and Reproduction	2,000	-
11.	Contractual Services	1,980	-
12.	Construction	-	-
	Total Tk.	58,005	376

Total US $ 3,350

Incremental cost US $ 2,526

(Conversion rate US $ 1.00= Tk. 19.50)

REFERENCES

1. World Health Organization. Amoebiasis: Report of a WHO expert committee. Geneva, 1969. Tech. Rep. Ser No. 421.

2. DuPont HL, Pickering LK. Infection of the gastrointestinal tract. In Greenough III WB et al, eds. Current topics in infectious disease. New York: Plenum Medical Book Company, 1980.

3. Huq MN, Shaikh AA. Incidence of intestinal parasites in children of different socio-economic population of Dacca city. Bangladesh Med Res Council Bull 1976; 2:1-7.

4. Muttalib MA, Islam N, Islam S. Prevalence of intestinal parasites in rural children of Bangladesh. Bangladesh Med J. 1976; 9-27.

5. Anonymous: Parasite related diarrhoeas, Bull WHO 1980; 58:819-30.

6. Adams EB, Maclead IN. Invasive amebiasis: I. Amoebic dysentery and its complications. Medicine 1977; 56:315-23.

ABSTRACT SUMMARY

Members of randomly selected families (50 approx.) in a Matlab village will be screened by stool microscopy to identify 25 individuals with asymptomatic amoebiasis (cases) and 25 age and socio-economic status matched non-infected controls. We will follow these 2 groups for 3 months to determine the rate of acquisition of asymptomatic intestinal amoebic infection among controls and of symptomatic amoebiasis among both cases and controls. The rate of spontaneous loss of infection in asymptomatic carriers will also be determined. To study changes in serum anti-amoeba antibody titres with the acquisition or loss of infection finger-prick blood samples (100 lambdas) will be collected from each subject on entry into and discharge from the study. Information obtained in this pilot study will be used as a background for designing the methods for a full-scale prospective longitudinal study of the incidence of symptomatic and asymptomatic intestinal amoebiasis in our population.

1. Prevalence surveys in Bangladesh have shown that persons of all age groups are susceptible to infection with E. histolytica. In this study we will try to determine the rate of acquisition of symptomatic and asymptomatic amoebic infection in a rural community. As the rate may vary in different age groups, persons of all ages must be studied.

2. There are no potential risks to the study subjects. Only stool and finger-prick blood samples will be collected for examination. When indicated, patients will be treated with approved drugs.

3. There are no significant risks to the subjects of this study.

4. To maintain anonymity, the study subjects will not be identified by name in analysis on presentation of data.

5. Verbal consent will be obtained from each person (guardian in case of children) included in the study. The subject (or guardian) will be informed about the (a) nature and purpose of the study, (b) nature and purpose of each diagnostic procedure involved, (c) potential risks to the subjects, (d) the benefits derived, (e) the right to refuse to participate or withdraw from the study and (f) confidentiality of collected data.

6. Subjects will be interviewed at home to collect information about their illness, demographic and socio-economic characteristics and personal hygienic practices.

7. The potential benefit will be to the society in general through providing preliminary epidemiologic data on amoebiasis in Bangladesh population.

8. In this study stool and finger-prick blood will be obtained for diagnosing amoebiasis.