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Date June 30, 1981

ETHICAL REVIEW COMMITTEE, ICDDR,B.

49

Principal Investigator Barbara Stoll

Application No. 81-028 (P)

Title of Study Pilot project to follow-up surveillance patients with Shigella and other dysentery disease

Trainee Investigator (if any) _____

Supporting Agency (if Non-ICDDR,B) _____

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

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

1. Source of Population:
   (a) Ill subjects (Yes) No
   (b) Non-ill subjects Yes (No)
   (c) Minors or persons under guardianship (Yes) No
2. 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)
3. 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
4. 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 NA
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.

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

Barbara J Stoll
Principal Investigator

Trainee

81-028(B)
rec'd 2/7/81

SECTION I - RESEARCH PROTOCOL

1) Title: Pilot project to follow-up Surveillance patients with shigella and other dysentery diseases.

2) Principal Investigator: Dr. Barbara Stoll

Co-investigators: Dr. Imdadul Huq

Dr. Gerald Keusch

3) Starting Date: As soon as approved.

4) Completion Date: Four months after starting.

5) Total Direct Cost: $ 2,316.00

6) Scientific Program Head:

This protocol has been approved by the Disease Transmission Working Group

Signature of Scientific Program Head : [signature]

Date : 26-6-81

7) Abstract Summary:

Dysentery symptoms and shigella infections are important problems in Bangladesh. This pilot project will begin to study two groups of surveillance outpatient children in depth - those who come to the clinic complaining of dysentery and those whose stool cultures are positive for shigella - to begin to understand the course of initially uncomplicated outpatient shigella and dysentery, the subsequent complications and the changes in nutritional status over time.

SECTION II - RESEARCH PLAN

A. Introduction

1. Objective

The objective of this project is to study two groups of surveillance outpatient children in greater depth - (1) those who come to the clinic complaining of dysentery and (2) those whose cultures are positive for shigella (both dysentery and non-dysentery presentations) - to begin to understand the course of initially uncomplicated shigella and dysentery (i.e., disease not requiring hospitalization), the subsequent complications, and the changes in nutritional status over time.

Background

Shigella is a common and severe diarrheal disease in Bangladesh. We have reviewed Dacca Hospital Surveillance data for 1980 and have found shigella to be the second most common isolate in patients over 2 years of age - isolated from approximately 12 percent of all patients. Surveillance patients with shigella were more likely to present with stool blood, stool mucus, abdominal pain and fever than non-shigella patients. Fewer children with shigella were breast fed and there was a trend for patients with shigella to be more malnourished. Approximately one-third of Dacca Hospital Surveillance patients complained of dysentery. Of these, almost one-half had shigella. Two-thirds had shigella, salmonella campylobacter or ameba, but one-third had no etiologic agent found.

There is no routine follow-up of surveillance patients. The clinical course and outcome of outpatients who come to ICDDR,B complaining of dysentery and of those who are later found to have shigella is not well defined. This pilot project will begin to study these patients in depth.

B. Specific Aims

1. To follow out patient children who come to ICDDR,B complaining of dysentery and/or are found to have shigella to better define what happens to these mild-moderately ill patients after they leave the clinic.

2. To look for specific known complications of shigella and any intercurrent illnesses in these children.

3. To look at nutritional status at onset of disease and weekly thereafter for one month.

4. To look for shigella toxin in the stools of these children.

5. To look at the serologic response to shigella in these children.

6. To determine if some "non-shigella" dysentery cases are really missed shigella (i.e., toxin and/or sero positive, but culture negative).

C. Methods

All surveillance children between 2 and 10 years of age who come to ICDDR,B complaining of acute dysentery (acute defined as 3 days or less; dysentery defined as stool with blood+ /or mucus) will be enterred into the study at the time of initial visit. Patients whose stool cultures are positive for shigella will be enterred into the study after their initial visit, as soon as results of stool culture are known. New patients will be enterred into the study until 50 patients with shigella have been found (i.e., about 3-4 months). Routine surveillance data and specimens will be collected. In addition, an aliquot of stool will be obtained and processed for shigella toxin as described below and a fingerstick blood sample will be obtained for shigella antibodies. A field worker will visit the home of a shigella patients as soon as the culture result is known, to explain the nature of the study, to obtain stool and blood samples and to question the patient about the course of disease. If the patient is still ill, he or she will be brought back to ICDDR,B, will be examined by the principal investigator, and appropriate therapy will be given. All study patients will be visited in their homes by a field worker weekly for one month. At each visit information will be collected on course of disease, complications, intercurrent illness, subsequent care and medication usage, food intake and nutritional status (height, weight, arm circumference). At 3-4 weeks following the initial hospital visit a second fingerstick blood sample will be obtained (convalescent sera).

If a patient is still ill at the time of any home visit, a repeat R/S for stool culture will be done and the patient will be brought back to the principal investigator at ICDDR,B for care.

Procedures

Stool samples will be processed as follows: A 10% stool suspension in normal saline will be prepared. The sample will be centrifuged and the supernatant will be passed through a Millipore filter. The filtered supernatant will then be lyophylized. The lyophilized specimen will be sent to Dr. Gerald Keusch for shigella toxin determination.

A fingerstick blood sample will be obtained. 100 µl of blood will be mixed in 1 cc normal saline. Shigella type- specific antibody determinations will be performed by Dr. Gerald Keusch.

D. Significance

Dysentery symptoms (shigella and non-shigella) and shigella infections (dysentery or watery diarrhea) are important problems in Bangladesh. The clinical course and outcome of Bangladeshi children with these diseases is not well defined. This study will begin to learn more about the course of disease, complications, and changes in nutritional status over time in these children.

E. Facilities Required

1. No new office or lab space is required.
2. Personnel - 4 field workers 100% x 4 months
   1 lab technician 30% x 4 months
3. Hospital support - none.
4. Logistical support - transport to and from patients' homes for 4 follow-up visits will be needed.
5. Equipment - none new.

F. Collaborative Arrangements

Dr. Gerald Keusch, Professor of Medicine, Tufts Medical School, Boston, Massachusetts, will perform stool shigella toxin and serum antibody determinations and will be a full collaborator in this project.

Abstract Summary

1. Patients studied will be outpatient surveillance study patients between 2 and 10 years of age with dysentery and/or shigella. Dysentery and shigella are common problems in this age group, but the course of disease in these Bangladeshi children is not well known.

2. There are no risks to patients only mild discomfort from fingerstick blood drawing.

3. NA.

4. The confidentiality and anonymity of patients will be safeguarded. All records will be kept by the principal investigator. Patients will be referred to by number only, rather than name.

5. After the nature of the study is explained to parents or guardians, a consent form, in Bengali, will be obtained.

6. An approximately 5-10 minute interview will take place at the initial hospital visit and at 4 subsequent home visits.

7. The potential benefits to be gained by patients are a) more accurate diagnosis b) good follow-up c) improved care. Society in general will gain by a better understanding of these medical problems.

8. One stool smaple and 2 fingerstick blood samples will be obtained from each study patient.

SECTION III - BUDGET

A. Detailed Budget

1. Personnel Services

Name	Position	% time	Incremental Salary Taka	Dollar
Dr. B. Stoll	Scientist	20% x 4 mo	-	-
Dr. I. Huq	"	5% x 4 mo	-	-
Dr. G. Keusch	"	-	-	-
4 field assistants		100% x 4 mo	20,000	
1 lab technician		30% 4 mo	1,410	
		Subtotal	21,410	

2. Supplies and materials

Item	Unit cost	Taka	Dollar
Stool lyophylization	10 Tk. X 100	1,000	
Miscellaneous forms		500	

3. Equipment: None.

4. Patient hospitalization: None.

5. Outpatient care - non extra.

6. ICDDR,B transport

120 days x 30 miles x 3 = 10800 taka
120 days x 8 hours x 3.5 = 3360 taka
14160 taka

7. Travel and Transportation: none.

8. Transportation of things: none.

9. Rent, communication, utilities: none.

10. Printing, publication: none.

11. Other contractual services: none.

12. Construction, renovation, alterations: none.

B. Budget Summary

Category	Taka	Dollar
1. Personnel	21,410	
2. Supplies and Materials	1,500	
3. Equipment		
4. Patient hospitalization		
5. Outpatient care		
6. ICDDR,B Transport	14,160	
7. Travel and Transportation		
8. Transportation of things.		
9. Rent, Communication, utilities		
10. Printing publication		
11. Other contractual services		
12. Construction, renovation, alterations		
Sub total	Tk. 37,070	
	$ 2,316	

Consent Form

The type of illness your child has is a common problem in Bangladesh. Your child is not very very sick with his/her illness at this time. Some children improve quickly, while others continue to have diarrhea/dysentery, don't eat well and develop other complications. The course of your child's illness in Bangladeshi children is not well known. This project will study children with your child's illness in depth.

Today, we will ask you some special questions about your child's illness and will take a stool sample and fingerstick blood sample from your child. These samples are to help us diagnose exactly what kind of illness your child has. In addition, a fieldworker will visit you in your home every week for one month to find out if your child is still ill or if he/she is well and to weigh and measure your child. At 3-4 weeks we will repeat the fingerstick blood sample.

If your child is still ill at the time of any home visit, he/she will be brought back to ICDDR,B, will be examined by a physician and therapy will be given.

If you do not wish to participate in this study or if you choose to withdraw at anytime, your child will still receive the same good care at ICDDR,B.

If you understand the nature of the study and are willing to participate, please sign below.

_____

Patient or Guardian

_____

Investigator

আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র, বাংলাদেশ

সম্মতি পত্র

বর্তমানে এই গবেষণা কেন্দ্র কলেরা ও বিভিন্ন প্রকার উদরাময় রোগের উন্নততর চিকিৎসা উদ্ভাবনের জন্য গবেষণা চালিয়ে যাচ্ছে। এই রোগ বাংলাদেশের বিশেষ করে বাচ্চাদের এক সমস্যা হিসাবে দেখা দিচ্ছে। অনেক বাচ্চা অতি তাড়াতাড়ি ভাল হয়ে উঠে আবার অনেক জটিল রোগে আক্রান্ত হয়ে পড়ে। আপনার বাচ্চাও যদি এই রোগে আক্রান্ত হয়ে থাকে তাহলে এই গবেষণা আপনার বাচ্চার রোগ নির্ণয় গভীরতার সংগে লক্ষ্য রাখবে।

এই গবেষণার ব্যাপারে আপনার কাছে কতগুলি প্রশ্ন জিজ্ঞাসা করা দরকার এবং নিম্নলিখিত পরীক্ষার ব্যাপারে আপনার সহযোগীতার একান্ত প্রয়োজন হবে।

১। আপনার বাচ্চার পায়ুখানা ও আংগুল থেকে কয়েক ফোটা রক্ত পরীক্ষার জন্য নেওয়া হবে যাতেকরে আপনার বাচ্চার রোগ নির্ণয় সহজতর হয়।

২। আমাদের একজন স্বাস্থ্য কর্মী প্রতি সপ্তাহে একবার করে একমাস পর্যন্ত আপনার সংগে আপনার বাড়ীতে যাবে ও বাচ্চার ওজন ও মাপ নেবে এবং প্রতি সপ্তাহে আংগুল থেকে কয়েক ফোটা রক্ত নিয়ে পরীক্ষা করবে।

এরপরও যদি বাচ্চা ভাল হয়ে না উঠে তাহলে স্বাস্থ্য কর্মী বাচ্চাকে আমাদের হাসপাতালে নিয়ে আসবে এবং চিকিৎসক তার প্রয়োজনীয় চিকিৎসা করবে।

যদি আপনি এই গবেষণায় অংশগ্রহণ করতে না চান বা আপনি এই গবেষণায় অংশগ্রহণ করলেও আপনি ইচ্ছা করলে যে কোন সময় গবেষণা পরিত্যাগ করতে পারেন। তাতে স্বাভাবিক চিকিৎসার কোন ত্রুটি হবে না।

আপনি এই গবেষণায় অংশগ্রহণ করতে চাইলে দয়া করে নিম্নে স্বাক্ষর করুন।

গবেষকের স্বাক্ষর

রোগী বা অভিভাবকের স্বাক্ষর

তারিখ----------

SHIGELLA QUESTIONNAIRE - INITIAL VISIT

Study Number — — — (1-3)

Card Number — (4)

Name _____

Patient Number — — — — — — (5-10)

ILLNESS: 0 = No, 1 = Yes, 2 = Not known

Before this present illness :

Have you had dysentery before in the past month? — (11)

Have you had watery diarrhoea before in the past month? — (12)

Have you had measles in the past month? — (13)

Have you had any other illness in the past month? — (14)

If yes, to any of the above questions, have you received any medications for these illnesses? — (15)

Any antibiotic? — (16)

Name of antibiotic _____

Present illness :

Is this your first visit to ICDDR,B for this illness? — (17)

Have you been to any other medical facility for this illness? — (18)

If yes where _____

Have you taken an antibiotic for this illness? — (19)

If yes, name of antibiotic _____

If yes, for how many days? — — (20-21)

With your present illness have you suffered any of the following :

Rectal prolapse — (22)

Convulsion — (23)

Cough — (24)

Nasal discharge — (25)

Joint pain-arthritis — (26)

Conjunctivitis — (27)

Headache — (28)

DIET:

Is your appetite, 0 = normal, 1 = decreased
2 = increased, 3 = not known — (29)

What does your usual diet include?

Breast milk — (30)

Cow's milk — (31)

Powdered milk — (32)

Tea — (33)

Barley — (34)

Flour water gruel — (35)

Rice powder and milk — (36)

Bread	—	(37)
Rice	—	(38)
Dhal	—	(39)
Vegetable	—	(40)
Fruit	—	(41)
Fish	—	(42)
Meat	—	(43)
Other _____	—	(44)

Household :

How many people live in your house?	— —	(45-46)
How many children live in your house?	— —	(47-48)
How many rooms are these in your house?	— —	(49-50)

If anyone else in home is ill, who_____

How old are children who live in your house_____

SHIGELLA QUESTIONNAIRE - HOME VISIT

Study Number — — — (1-3)

Card Number — (4)

Name _____

Patient Number — — — — — — (5-10)

Date — — — — — — (11-16)

ILLNESS 0 = No, 1 = Yes, 2 = Not known

Are you completely well now? — (17)

If no, do you still have the same illness (diarrhoea/dysentery) for which you went to ICDDR,B — (18)

If no, did your first illness improve, but do you now have another episode of diarrhoea/dysentery? — (19)

If still ill, do you have :

watery diarrhoea — (20)

Stool blood — (21)

Stool mucus — (22)

Abdominal cramps — (23)

Tenesmus — (24)

Fever — (25)

Vomiting — (26)

Since you were last seen at ICDDR,B or by a field worker, have you had any of the following :

Rectal prolapse — (27)

Convulsion — (28)

Cough — (29)

Nasal discharge — (30)

Joint pain arthritis — (31)

Conjunctivitis — (32)

Nightblindness — (33)

Headache — (34)

Other _____ — (35)

Since you were last seen at ICDDR,B or by a field worker, have you :

Returned to ICDDR,B for care? — (36)

Received any medications at ICDDR,B — (36)

Name of medications _____

Gone to another facility for medical care? — (38)

If yes, where _____

If yes, have you received any medications? — (39)

Names of medications _____

Would you return to ICDDR,B for care with your next diarrhoeal illness? — (40)

If no, why not? _____

If you are still sick and have not returned to ICDDR,B why not? _____

DIET

Is your appetite, 0 = normal, 1 = decreased
2 = increased 3 = not known — (41)

What have you been eating since last visit?

Breast milk	— (42)
Cow's milk	— (43)
Powdered milk	— (44)
Tea	— (45)
Barley	— (46)
Flour water gruel	— (47)
Rice powder and milk	— (48)
Bread	— (49)
Rice	— (50)
Dhal	— (51)
Vegetable	— (52)
Fruit	— (53)
Fish	— (54)
Meat	— (55)
Other _____	— (56)

Nutritional Status

Height	— — — (57-59)
Weight	— — — (60-62)
Arm circumference	— — — (63-65)

Laboratory

R/S done _____

Blood drawn _____