

ETHICAL REVIEW COMMITTEE, ICDDR,B.

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Principal Investigator Barbara Stoll

Trainee Investigator (if any) _____

Application No. 80-036(P)

Supporting Agency (if Non-ICDDR,B) _____

Title of Study Pilot Study to Intensively Investigate Diarrhea in Children Under 1 year of Age

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 NA
- (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 Ctee. for review.

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

Barbara Stoll
Principal Investigator

Trainee

80-036 (P)
recd 17/9/80

SECTION I - RESEARCH PROTOCOL

- (1) Title: Pilot Study to Intensively Investigate Diarrhea in Children Under 1 year of Age
- (2) Investigator: Dr. B. Stoll
- (3) Starting Date: As soon as approved
- (4) Completion Date: 4 months after starting
- (5) Total Direct Cost: \$ 2745
- (6) Scientific Program Head:

This protocol has been approved by the Disease Transmission Unit,
 Signature of Scientific Program Head: W.B. Stoll
 Date: 3/9/80

(7) Abstract Summary:

Infantile diarrhea is a major cause of morbidity and mortality in Bangladesh. Recent advances in knowledge about diarrheal disease have resulted in improved diagnoses of acute diarrhea. In the last decade, the importance of viral agents has been increasingly recognized. Between 1/4 and 1/3 of Dacca surveillance patients are under 1 year of age. This pilot project will intensively investigate diarrhea in this select group to learn more about agents that we already identify and to begin to look for some of the newer viral agents associated with diarrhea.

(8) Review:

(a) Ethical Review Committee: _____

(b) Research Review Committee: _____

(c) Director: _____

(d) BMRC: _____

(e) Controller/Administrator: _____

SECTION II - RESEARCH PLAN

A. INTRODUCTION

1. Objective:

The objective of this study is to intensively investigate diarrhea in children under 1 year of age.

2. Background:

Infantile diarrhea is a major cause of morbidity and mortality in Bangladesh. Recent advances in knowledge about diarrheal disease have resulted in improved diagnoses of causes of diarrhea. In the last decade, the importance of viral agents as causes of diarrhea in infants and children has been recognized. Rotavirus, first detected in man in Australia in 1973,⁽¹⁾ has been studied in both developed and developing countries. Work on the virology, epidemiology and clinical characteristics of rotavirus diarrhea has been done at and continues to be an important research area of the ICDDR^{2,3,4,5}. Since 1972, the Norwalk agent^{6,7} has been recognized as a cause of diarrhea. This agent has been identified in several outbreaks of generally mild gastroenteritis⁸. Although it has been increasingly identified in developed countries, little work on Norwalk agent has been done in developing countries⁹. The paucity of work on Norwalk agent from developing countries probably results from technical difficulties in identifying the agent. The virus can only be identified in stool by immune electron

microscopy or by a radioimmunoassay technique. In addition, a serologic response to the agent can be measured.¹⁰ A number of other viral agents have been associated with diarrheal disease (e.g. adenovirus, astrovirus, calicivirus) but their etiologic role remains unclear.

Between 1/4 and 1/3 of patients seen in the Dacca surveillance system are under 1 year of age. In this 4 month pilot project, we will intensively investigate diarrhea in this select group.

B. SPECIFIC AIMS

1. To begin to look for other, newer viral agents which have been associated with diarrhea in other countries.
2. To learn more about diarrheal agents already studied at ICOPB in a select group under 1 year of age.

C. METHODS OF PROCEDURE

Study patients will be all children under 1 year of age who come to the Dacca Hospital and are studied in the surveillance system for a four month period. Routine surveillance data will be collected. In addition an aliquot of stool will be obtained and frozen for later virologic studies and acute & convalescent sera will be

obtained to look for a serologic response to some of the "newer" viral diarrheal agents. Lactating mothers will be asked to provide a sample of breast-milk for breast-milk antibody determinations (to rotavirus, cholera, ETEC). A nasopharyngeal swab will be performed on each child to look for possible respiratory carriage of rotavirus (identification by ELISA technique). In addition, exact stool pH will be measured in an attempt to find out if exact pH can aid in a rapid bedside diagnosis. Home visits will be required to obtain convalescent sera. If the child is still ill at the time of home visit, he will be referred back to ICDDRB for further care.

D. SIGNIFICANCE

Because diarrhea is such an important cause of morbidity and mortality in children in Bangladesh this study which attempts to learn more about diarrhea in young infants and children and to begin to look for newer viral agents is important.

E. FACILITIES REQUIRED

1. No new office space is needed.
2. Personnel - 2 field assistants x 4 months
1 lab technician 10% x 4 months.
3. No new lab space is needed.

4. Hospital support: No additional

5. Logistical support : None

6. Equipment : None

F. COLLABORATIVE ARRANGEMENTS

None at present.

References

1. Bishop RF, Davidson GP, Holmes IH and Ruck BJ: Virus particles in epithelial cells of duodenal mucosa from children with acute non-bacterial gastroenteritis. *Lancet* (1973) 2: 1281.
2. Taylor PR, Merson MH, Black RE, Rahman ASMM, Alim ARMA and Yolken RH: Rotavirus in Bangladesh: Diagnosis, Clinical Characteristics and Therapy in a Rural Treatment Center (Manuscript in preparation)
3. Ryder RW, Sack DA, Kapikian AZ, McLaughlen JC, Chakraborty J, Rahman ASMM, Merson MH, Wells JG: *Lancet*, (1976) 1: 659.
4. Sack DA, Chowdhury AMAK, Eusof A, Ali MA, Merson MH, Islam S, Black RE, Brown RH: *Lancet* (1978) 2: 280.
5. Mutanda LN : approved protocol:
6. Dolin R, Blacklow NR, Dupont H, Buscho RF, Wyatt RG, Kasel JA, Hornick R and Chanock RM: Biological Properties of Norwalk agent of acute infectious nonbacterial gastroenteritis. *Proc. Soc. Exptl. Biol. Med.*, (1972) 140: 578.
7. Wyatt RG and Kapikian AZ,: Viral agents associated with acute gastroenteritis in humans. *Amer. J. Clin Nutrition* (1977), 30: 1857.
8. Thornhill TS, Wyatt RG, Kalica AR, Dolin R, Chanock RM and Kapikian AZ: Detection by immune electron microscopy of 26-27 nm virus - like particles associated with two family outbreaks of gastroenteritis. *J. Inf. Dis.* (1977), 135: 20.
9. Black RE : personal communication.
10. WHO Report of a sub-group of the Scientific Working Group on Epidemiology and Etiology: Rotavirus and other Viral Diarrhoeas. 1979.

Abstract Summary

Infantile diarrhea is a major cause of morbidity and mortality in Bangladesh. Recent advances in knowledge about diarrheal disease have resulted in improved diagnoses of acute diarrhea. In the last decade, the importance of viral agents has been increasingly recognized. Between 1/4 and 1/3 of Dacca surveillance patients are under 1 year of age. This pilot project will intensively investigate diarrhea in this select group to learn more about agents that we already identify and to begin to look for some of the newer viral agents associated with diarrhea.

1. Subjects will be children with diarrhea under 1 year of age who come to the Dacca Hospital for treatment and are studied in the surveillance system. This group of children is chosen for study because they are particularly vulnerable to morbidity and mortality from diarrheal disease.
2. The only minor potential risk is pain from fingerstick blood drawing which be performed twice. The risk is outweighed by the potential for improved diagnosis.
3. Blood drawing will only be done by trained field workers.
4. All surveillance records are strictly confidential and kept separate from the regular medical record by the principal investigator. All patients are given a study number. Individual patient names will only be used to find a patient for follow-up.
5. A signed consent in Bengali will be obtained from a parent or guardian of the child (see attached consent form), as well as the routine verbal surveillance statement.
6. All surveillance patients are interviewed for approximately 10 minutes, after acute medical care has been given.
7. The potential benefits to the patient include more personal contact with health workers, improved diagnoses, and follow-up to see how the child is two weeks after his clinic visit. Potential scientific benefits include learning more about diarrhea in infants and about viral agents associated with diarrhea.
8. Stool, blood, nasal secretions and breast milk will be examined.

SECTION III - BUDGET

A. Detailed Budget

1. Personnel Services

<u>Name</u>	<u>Position</u>	<u>% time used</u>	<u>Salary</u>	
			<u>Taka</u>	<u>Dollar</u>
Dr. B. Stoll	Scientist	10% x 4 mths.	-	615
2 field assistants		100% x 4 mths.	9400	-
1 lab technician		10% x 4 mths.	470	-
1 programmer	100% already on original surveillance protocol and underutilized			
Sub total:			9870	615

2. Supplies and Materials

<u>Item</u>	<u>Unit Cost</u>	<u>Taka</u>	<u>Dollar</u>
NP and Throat swab for RV ELISA	400 x \$.25	-	100
Exact stool PH	400 x 3	1200	-

At present, other lab tests will be done outside of ICDDR,B at no cost to the lab. If they prove useful, techniques will be set up here

Stationery forms		500	-
Miscellaneous		500	-

3. Equipment: None

4. Patient hospitalization: None extra

5. Outpatient care: None extra

6. ICDDR,B transport: 120 days x 20 miles x 3 = 7200 taka
120 x 4 hours x 3.5 = 1680 taka

8880 taka

7. Travel and transportation: None

8. Transportation of things : None

9. Rent, Communication, utilities: None

10. Printing, publications: None

11. Other contractual service

12. Construction, renovation, alternation: None

B. Budget Summary

<u>Category</u>	<u>Taka</u>	<u>Dollar</u>
1. Personnel	9870	615
2. Supplies and Materilas	2200	100
3. Equipment	-	-
4. Hospitalization	-	-
5. Outpatient care	-	-
6. ICDDR,B Transport	8880	-
7. Travel	-	-
8. Transport, things	-	-
9. Rent/communication	-	-
10. Printing/publication	-	-
11. Contractual services	-	-
12. Construction	-	-
	<hr/>	
Sub Total:	20950	715
30% overhead:	6285	214
Total:	27235	929

\$ = 2745

Consent Form

Your baby has diarrhea. To make a proper diagnosis of your baby's illness we will question you, examine your baby and look at his or her stool under the microscope and culture it. However, some causes of diarrhea cannot be diagnosed by these tests alone. To improve our diagnosis, we will freeze a specimen of stool for special studies. Also, we will take a fingerstick specimen of blood from your baby now and in two weeks to see if his or her body has responded to infection. We will also take a specimen of your breast milk if your baby still takes breast milk to look for antibodies, substances which help fight disease. Finally we will do a swab of your baby's nose to check if he or she carries a special virus which causes diarrhea. A field worker will visit your home in two weeks to see how your baby is and to collect a second specimen of blood. If your baby is still ill, he/she will be referred back to ICDDR,B.

If you do not want to participate in this study, your baby will still be given the same care at ICDDR,B. Also, you may withdraw your baby from the study at any time.

Subject's guardian

Investigator

Date