REVIEW BOARD ON THE USE OF HUMAN SUBJECTS. (CDDR,B.

4e

ipal Investigator Dr Barbara Stoll Trainee Investigator (if any) _____

cation No. 80-005 (Revised) Supporting Agency (if Non-(CDDR,B) _____

of Study Surveillance of Urban Cervical Patients Project status:
(✓) New Study
( ) Continuation with change
( ) No change (do not fill out rest of form)

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

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

oes 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)

es 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

re subjects clearly informed about:
a) Nature and purposes of study (Yes) No
b) Procedures to be followed including alternatives used Yes No NA
c) Physical risks Yes No NA
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 NA
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 Board:
___ Umbrella proposal - Initially submit overview (all other requirements will be submitted with individual studies)
✓ Protocol (Required)
✓ Abstract Summary (Required)
✓ Statement given or read to subjects re 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 complete 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 Board for review.

gree to obtain approval of the Review Board on the Use of Human Subjects for any change affecting the rights and welfare of subjects before making such change.

Barbara J Stoll
Principal Investigator Trainee

80-005 / Revised
Rec'd 4/3/80

SECTION I - RESEARCH PROGRAMME

1. Title: Surveillance of Urban Diarrheal Patients

2. Principal Investigator: Dr. B. Stoll

   Co Investigator: Dr. M.U. Khan

3. Starting Date: February 1, 1980

4. Completion Date: To be continued as long as the Institute requires.

5. Total Direct Cost:

6. Availability of funds:

   a. Scientific Director's Remarks:

   b. Controller's Remarks:

7. Abstract Summary: Because the number of patients being treated at the ICDDR,B treatment centre has increased over the past few years to approximately 350 to 500 patients per day, it has become impossible to study each patient in depth and the routine collection of clinical and microbiologic data on each of these patients has been abandoned. This data, however, is very important in helping to understand the patient population we see at ICDDR,B, in assessing the quality of care provided and in generating new ideas for research.

We have chosen to study a systematic sample of 2%-5% of all patients seen at the treatment centre each day, 24 hours per day. Treatment will be provided as usual, by the usual hospital staff, with emergency cases treated on a priority basis. In addition, a special questionnaire will be administered by an interviewer from the community studies branch, a physician or trained paramedical personnel will perform a detailed physical examination and anthropometry and laboratory examinations will be performed. Information on hospital course and outcome will be collected on hospitalized surveillance patients.

8. Review:

a. Research Involving Human Subjects: _____

b. Research Review Committee: _____

c. Director: _____

d. BMRC: _____

e. Controller/Administrator: _____

SECTION II - RESEARCH PLAN

A. INTRODUCTION

1. Objective:

Approximately 150,000 patients per year are treated at the ICDDR,B treatment center. It has become impossible to study each of these patients in depth. The objective of this activity is to set up a surveillance system based on a random sample of patients, which will collect demographic, clinical and microbiological data. Data will be analysed on an on-going basis to better characterize the diarrheal illnesses seen at ICDDR,B, to assess the quality of care provided and make recommendations for improvement of clinical care, and to help generate new research ideas.

2. Background:

The International Center for Diarrheal Diseases Research, Bangladesh (formerly the Cholera Research Laboratory) has been a pioneer in reserch on diarrheal diseases. The epidemiology, clinical characteristics, etiologic agents and treatment of diarrheal diseases seen at ICDDR,B has changed over the years. For example, between 1973 and 1974 there was a shift in the predominant biotype of vibrio cholerae from the virulent classical biotype to the less severe El Tor biotype.(1) There have been similar changes for other diarrheal agents. In the 1960's most shigella isolated were shigella sonnei; there were few shigella flexneri and no shigella shiga. In 1970 shigella shiga was isolated for the first time and by 1973 it had increased to about 2/3 of all shigella isolated. (2) Though the number of shigella shiga has since decreased, cases continue to be seen. Moreover, new agents and agents not previously thought to produce enteric disease have been identified and studied at ICDDR,B. A large number of diarrheas especially among infants and young children have been found to be caused by rotavirus and have been extensively investigated here. (3) In August 1979 campylobacter was first isolated at ICDDR,B - 8 cases were identified from 105 patients with bloody mucoid diarrhea. (4)

In an attempt to collect useful information about patients seen at the ICDDR,B treatment center, a pilot surveillance system was begun by Dr. R. Wilson in August 1979. A summary of his findings are reported below (for more detailed information, see Outpatient Treatment Center Surveillance Report - Wilson et al) (4). Two hundred and five patinets - a two percent random sample of all treatment center patients - were studied. Sixty one percent (125) of

patients were male and 39 percent (80) were female. Most patients were children - 19 percent were less than one year of age; 35 percent, 1-4 years; 14 percent, 5-9 years; 7 percent 10-14 years. Only 25% were 15 years of age or older. Ninety one patients (44%) had an illness they called dysentery which was accompanied by a history of blood and mucous in the stools of 64 patients (70%), mucous only in 23 patients (25%), blood only in 1 patient (1%) and neither symptom in 2 patients (2%). Watery diarrhea was the chief complaint of 81 (40%) patients. Duration of illness ranged from less than 1 day to 90 days. By further analysis, 3 patterns became apparent: (1) patients with an acute illness with a median duration of 3 days, (2) patients with an illness which had lasted 15-20 days prior to presentation, and (3) patients with chronic diarrhea of 30 days duration or greater. Forty seven patients (23%) gave a history of diarrhea in at least one other family member in the week preceding their own clinic visit. Physical examination on arrival revealed mild dehydration in the majority of patients (113/205); only 21% (44/205) had moderate or severe dehydration. Twenty one patients (10%) had signs of vitamin deficiency or protein calorie malnutrition as evidenced by edema, glossitis, angular stomatitis or xerosis. Seventy eight percent of patients (160/205) received antimicrobial therapy, primarily ampicillin. Forty eight patients (23%) were admitted to the treatment center or hospital ward. Of these, one died (4.88 deaths per 1000 patients). The bacterial pathogens isolated were: shigella (24), enterotoxigenic E.coli (14), ETEC and shigella (3), V. cholerae (8), salmonella (4) and NAG (1). In addition, 5 cases of acute amebiasis were identified by stool microscopic exam using the criteria of erythrophagocytosis of E. histolytica trophozites. Follow up visits were completed for 172 (84%) patients: 33 (19%) showed no improvement, 53 (31%) showed some improvement and 86(50%) had no diarrhea. Eleven patients (6%) sought other care after leaving ICDDR,B.

This pilot project established that a surveillance system is workable at ICDDR,B and reaffirmed the usefulness of such a system. The pilot project was extended in October 1979 and data has been collected from mid October to date. Data collected on a pre-coded questionnaire (see appendix) has been punched onto computer cards and card sorting and simple data analyses have been performed. Reports from October/November, December and January have been issued (see appendix).

3. Rationale:

Attendance at the ICDDR,B treatment center has increased about ten fold in the past ten years. As a result, the volume of diagnostic work and health care provided has increased tremendously and it has become impossible to study each individual case. However, surveillance is essential in helping to understand the patient population and spectrum of disease seen at ICDDR,B and in assessing the quality of care given. Therefore, a representative sample - i.e., a 2-5% random sample of patients will be studied in depth.

B. SPECIFIC AIMS:

1. To establish on-going surveillance of patients seen at ICDDR,B based on a sample of patients seen.

2. To describe the patient population cared for at ICDDR,B- demography, geographic distribution, seasonality, etc.

3. To study signs and symptoms of disease.

4. To outline the causative organisms of diarrheal illness seen at ICDDR,B.

5. To follow treatment and hospital course.

6. To study the use of oral rehydration and the effect of oral rehydration education at ICDDR,B.

7. To help generate new ideas for further research.

C. METHODS AND PROCEDURES:

Study patients will be a 2-5% systematic sample of all patients seen at the ICDDR,B treatment center. The outpatient charts of study patients will be stamped in advance. Whenever the OPD clerk finds a pre-stamped study chart he/she will hand it over to the surveillance team. All patients will receive routine care as provided by paramedics, nurses and physicians in the treatment centre. No attempt will be made to influence care. Only after the patient has been seen by the clinic personnel, and the initial decisions about treatment and disposition have been made (e.g., patient admitted to ward, or patient sent home immediately with medication and/or advice, etc.) will he be interviewed by the

surveillance team. The surveillance team will not discuss any individual patient with the personnel who are providing care.

Study assistants will be on duty from 6 A.M. to 2 P.M. and from 2 P.M. to 10 P.M. Study patients who arrive between 6 A.M. and 10 P.M. will be interviewed in the order they arrive. Study patients who arrive between 10 P.M. and 6 A.M. will be treated as usual, but will be retained in the treatment center until the next morning when they will be interviewed by a study assistant and examined by a physician or trained paramedic. The ward physician on duty at night will, however, record the state of hydration at the time of admission.

Each study patient will be interviewed by a field assistant who will administer a detailed questionniare (See Appendix) including questions on demographic factors, signs and symptoms of this illness, medical history and previous therapy. Stools or rectal swab (RS) will be obtained for culture and microscopic exam (ME). Because the clinical pathology section closes at 5 P.M., stools obtained after 5 P.M. will be collected in MIF solution for ME to be performed the following morning. All RS will be handled by the microbiology section immediately or kept in a prefixed incubator. Stools will be cultured for salmonella, shigella, cholera, NAG and E. coli.Selected patients (i.e., all patients less than 5 years plus 25% of all other patients) will have rotavirus identified by ELISA technique. Toxin assays will be performed on E. coli isolated (i.e. LT and ST). A detailed physical examination inlcuding vital signs, admission weight, state of hydration and signs of vitamin deficiency and malnutrition will be performed by a physician or specially trained paramedic. Information on therapy and hospital course will be collected by a field assistant. Anthropometry including height, weight and arm circumference will be done prior to discharge to accurately assess severity of dehydration (weight) and to assess the nutritional status of the patients we care for.

The data collected will be kept separate from the regular hospital records. Questionnaire forms will be precoded and data will be punched onto cards and/or entered onto the computer monthly. Because a large amount of data will be collected, a part-time programmer will be required. Monthly card sorting and/or computer print-outs will be made available and data analysis will become an on-going activity. Periodic reports will be issued to hospital staff and investigators (See Appendix). In the pilot study, data punching and card sorting proved to be easy and useful for simple data analysis.

D. SIGNIFICANCE:

This surveillance activity will collect a wide range of information on the patients seen at ICDDR,B which is essential for understanding the patient population we see here, for assessing the quality of care and outcome of treatment provided and for helping to generate new research ideas. After the surveillance system is established, other protocols may be linked with the basic data collection system. The findings of this surveillance activity will be of great interest to health personnal in Bangladesh as well as in other countries.

E. FACILITIES REQUIRED:

1. No new office space is needed.

2. Personnel -- 1 supervisor - part-time
   3 interviewers - full-time
   1 study physician - part-time
   1 programmer - part-time

3. No new laboratory space is needed.

4. Hospital support: Routine hospital care will be given. The study interview will be done at a separate desk in the triage area of the treatment centre.

5. For ST and LT determinations, mice will be needed regularly, approximately 100-200 mice per month.

6. Logistical support: None.

7. Major items of equipment: No major item of equipment is needed except the reagents for ELISA assay and mice for ST and LT determinations.

8. Other special requirements: Culture materials, medicines, computer cards and tapes and stationary will be needed.

F. COLLABORATIVE ARRANGEMENTS:

None at present.

References

1. Khan, M.U., Alam A.K.M.J., and Rahman, A.S.M.M., Ten Years Review of the Age and Sex of Cholera Patients. Scientific Report No. 14. Cholera Research Laboratory. May 1978.

2. Khan M.U. and Curlin, G. , Shegellae Dysentery: A New Health Hazard in Bangladesh. Bangladesh Med. J. 3 : 42 (1974).

3. Taylor, P.R., Merson, M.H., Black, R.E., Rahman, A.S.M.M., Yunus, Md., Alim, A.R.M.A., and Yolken. R.H., Oral rehydration therapy for treatment of rotavirus diarrhea in a rural treatment center in Bangladesh. Arch. Dis. Child. (in press).

4. Wilson. R.. Outpatient Treatment Center Surveillance Report, August 1979 (personal communication).

Statement to Patients

The International Centre For Diarrhoeal Disease Research, Bangladesh is studying every 50th patient who comes to the clinic to learn about the patients who come here for medical care. A special questionnaire will be administered to you (or your parent or guardian) after you have been examined by a nurse or doctor. If you are very ill and require intravenous fluid or other emergency care, care will be given first and you will be interviewed after your condition has improved. Stool will be obtained for culture and examination under the microscope. As a service to you, we will get you all medication prescribed by the nurses or physicians so that you don't have to wait on the pharmacy line. All records will be kept strictly confidential. There are no risks associated with this study; only potential benefits to you, such as more contact with health workers and more personal care.

Abstract Summary:

Because the number of patients being treated at the ICDDR,B treatment centre has increased over the past few years to approximately 350 to 500 patients per day, it has become impossible to study each patient in depth and the routine collection of clinical and microbiologic data on each of these patients has been abandoned. This data, however, is very important in helping to understand the patient population we see at ICDDR,B in assessing the quality of care provided and in generating new ideas for research.

We have chosen to study a random sample of 2% of all patients seen at the treatment centre each day, 24 hours per day. Treatment will be provided as usual, by the usual hospital staff, with emergency cases treated on a priority basis. In addition, a special questionnaire will be administered by an interviewer from the community studies branch, a physician or trained paramedical personnel will perform a detailed physical examination and anthropometry and laboratory examinations will be performed. Information on hospital course and outcome will also be collected on hsopitalized surveillance patients.

1. A random sample of all patients treated at ICDDR,B will be studied. No attempt will be made to influence care; only information will be collected. Verbal consent will be obtained from patients or guardians.

2. No risks are involved.

3. Not applicable.

4. Records will be strictly confidential and will be kept separate from the routine record. by the principal investigator. All patients will be given a study number. Individual patient names will only be used to find a patient for follow-up.

5. Because there are no risks to the patients-only information will be collected-only verbal consent will be obtained (see attached statement).

6. An approximately ten minute interview will be conducted by a trained field assistant, in a special area of the outpatient department. Interviews will be conducted after the patient has already been examined by a nurse and/or physician and decisions about immediate care have already been made.

7. The potential benefits to be gained by the patient include more personal contact with health workers who are less busy than the routine staff and have more time to answer questions, etc. Moreover, data collected will be useful in assessing the quality of care provided and in making recommendations for its improvement. As a scientific endeavor, the data will provide demographic, clinical, and micro-biologic information on the patient population we see at ICDDR,B and will help to generate new ideas for research.

8. Stool will be obtained for culture and microscopic examination.

Section III -- Budget

A. Detailed Budget

I. Personnel Services :

Name	Position	% time used	Salary (first year) Taka	Dollar
Dr. Barbara Stoll	Scientist	40%	-	7,000
Dr. M.U. Khan	Scientist	20%	18,400	-
Mr. Mridul Chowdhury	Br. Head	5%	2,000	-
Dr. W.B. Greenough	Director	-	-	-
Dr. R. Islam	Ch. Physician	-	-	-
Dr. to be named	Physician	20%	8,000	-
Supervisor	Supervisor	100%	43,620	-
3 Field Assistants	Field Asst.	100%	86,400	-
1 Microbiology tech.	Technician	50%	15,000	-
1 Clinical Path tech.	Technician	50%	9,300	-
1 programmer	Programmer	25%	9,000	-
	Sub-Total		191,720	7,000

2. Supplies and materials

Item	Unit cost	Taka	Dollar
Stool culture	360x10x15.5	55,800	
Rotavirus assay	360x7x.25		700
E. coli toxin(ST,LT)	360x10x3	10,800	
Stool microscopy	360x10x2.55	9,180	
Stationary, forms,etc.		20,000	
IBM cards and tape			200
MICE	360x5x3	5,400	
Medicine	360x10x10	36,000	
Miscellaneous		500	
	Sub-Total:	142,180	900

3. Equipment:

None

4. Patient hospitalization:

For this study no special patient hospitalization is n Patients may be hospitalized as usual at the discretion of staff.

5. Outpatient care:

360x10 - 3600 patients x Tk. 50 = 180,000 Taka.

6. ICDDR,B Transport:

None.

7. Travel and transportation of persons:

Local travel	Taka 1,000	
International travel (air transport, per diem, misc.)		$3,200
Sub-Total:	Tk. 1,000	$3,200

8. Transportation of things:

None.

9. Rent, communication, utilities:

Utilities	Taka 1,000	$ 20

10. Printing and publications:

Forms, xerox	Taka 1,000	$ --
Special reproduction	15,000	--
Publication	--	300
Sub-Total:	Tk. 16,000	$ 300

11. Other contractual services:

Computer time will be required every month.

12. Construction, renovation, alteration:

NIL

Budget Summary:

Category	Year 1 Taka	Year 1 Dollar	Year 2 Taka	Year 2 Dollar	Year 3 Taka	Year 3 Dollar
1. Personnel	191,720	7,000	210,892	7,700	231,981	8,470
2. Supplies	142,180	900	156,398	990	172,037	1,089
3. Equipment	-	-	-	-	-	-
4. Hospitalization	-	-	-	-	-	-
5. Outpatient care	180,000	-	198,000	-	217,800	-
6. ICDDR,B Transport	-	-	-	-	-	-
7. Travel, persons	1,000	3,200	1,100	3,520	1,210	3,872
8. Transport, things	-	-	-	-	-	-
9. Rent/communication	1,000	20	1,100	22	1,210	24
10. Printing/reprod.	16,000	300	17,600	330	19,360	363
11. Contractual service	?	?	?	?	?	?
12. Construction	-	-	-	-	-	-
Sub-Total:	531,900	11,420	585,090	12,562	643,598	13,818
30% overhead:	159,570	3,426				
Grant Total:	691,470	14,846				

= $ 60,944