9) 6

ETHICAL REVIEW COMMITTEE, ICDDR,B.

Date 29.9.83
6.10.83

cipal Investigator Dr Nigar S. Shahid
ication No. 83-036(P)
e of Study Investigation of Simulta-
eous outbreak of Classical Inaba
nd ElTor Ogawa

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)

le 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 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.

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

Nigar S. Shahid
Principal Investigator

Trainee

SECTION I - RESEARCH PROTOCOL

1. Title : Investigation of simultaneous outbreak of Classical Inaba and El Tor Ogawa Cholera.

2. Principal Investigator : Dr. Nigar S. Shahid

   Co-investigator : Drs. A.R. Samadi, M.I. Huq, S.C. Sanyal

   Consultant : Dr. W.B. Greenough III, Dr. K.A. Monsur

3. Starting Date : Depends on the occurrence of cholera epidemic

4. Completion Date : Six months from the date started

6. Total direct cost : US $ 3,058.00

7. Scientific Program Head :

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

Signature of Scientific Program Head : W.B. G

Date : 04.15.83

8. Abstract Summary

The El Tor variant of V. cholerae is nearly replaced by the classical variant in Bangladesh since the cholera epidemic of 1982 when both biotypes appeared simultaneously. Cases consisted of mainly the serotype Inaba in the classical group whereas both serotypes appeared among the El Tor cases. The main criticism of the family study conducted last year was that we were working with one serotype in classical against 2 serotypes in El Tor. At present strains are of classical Inaba and El Tor Ogawa. We wish to study the two strains, in the common environment and study important issues of severity of disease, spread, case to infection ratio and their ability to persist in a common environment. Fifty families of each group will be compared with each other for these important characteristics. This is in line with the protocol entitled "Investigation of outbreak of Cholera due to classical biotype" (82-050 P) by Dr. A.R. Samadi

8. Reviews :

a. Ethical Review Committee : _____

b. Research Review Committee : _____

c. Director : _____

d. BMRC : _____

SECTION II - RESEARCH PLAN

A. INTRODUCTION

1. Objective

a. To define the epidemiological patterns between the Classical Inaba and El Tor Ogawa V. cholerae. Secondary infection and case rates, presence in food and water, duration of excretion, clinical features and seroconversion will be studied.

To describe microbiological characteristics as regards to morphology, biochemical parameters phage specificity, sensitivity and genetic coding.

To describe the clinical spectrum as regards severity, fluid requirement and ORS utilization.

2. Background

In 1973, the classical biotype of V. cholerae was replaced entirely by the El Tor biotype in Bangladesh. Since then El Tor was the main strain responsible for endemic and epidemic cholera, however, a few classical isolates were detected in 1979, 1980 and 1981. In the cholera outbreak in 1982 the El Tor biotype has been entirely replaced by the new classical strain. During the epidemic we had an unique opportunity to study the epidemiology of both biotypes simultaneously. The results of our findings showed that hospitalization rate of family contacts of classical where higher than those of El Tor. Higher infection rates were observed amongst women and children in the classical group. However, here, we were dealing only with Inaba classical strains as against both serotype of El Tor (Inaba and Ogawa).

Although the classical cholera epidemic died down in February-March 1983, cases continued to occur. Classical Inaba and El Tor Ogawa are simultaneously present now both in Dhaka and in Matlab. Now in Matlab although cholera cases are few findings of the incidence of both biotypes are equal. One of the criticisms of the previous Cholera Outbreak Study was that we did not look for the serotype difference, but at the biotypes only. This study will rule out any differences in the epidemiological characteristics in the two serotypes.

This protocol is prepared so that in case there is another cholera epidemic in Dhaka where the above mentioned strains (classical Inaba and El Tor Ogawa) presents simultaneously we may compare them directly epidemiologically, microbiologically and clinically.

3. Rationale

The difference between clinical, epidemiological and microbiological features between El Tor and classical cholera has been well established in studies conducted both recently and in the past. Changes in biotype and serotype have been said to be due to mutation of the strains and during mutation characteristics of these strains tend to change. We now propose to study the characteristic of these Classical Inaba and El Tor Ogawa in case we have an epidemic where these two strains are simultaneously present.

B. SPECIFIC AIMS

To define characteristics of Inaba Classical and Ogawa El Tor cholera.

C. METHODS OF PROCEDURE

1. Population : Fifty cases as index cases of V. cholerae biotype classical serotype Inaba cases (Group A) and 50 cases of V. cholerae El Tor Ogawa controls (Group B) and their families will be studied. The groups will be selected from accessible areas of the Dhaka Metropolitan area.

2. Selection of cases and controls : All cases of watery diarrhoea coming to the Dhaka treatment centre, ICDDR,B and suspected for cholera will be enrolled sequentially for the study and kept for 24 hours to record the amount of stool input and output. Rectal swabs will be taken from all enrolled patients and cultured for V. cholerae. The first bacteriological confirmed case of classical Inaba cholera each day will be taken as an index case and will be matched for age, with the next El Tor Ogawa in sequence from the patients treated on the same day as control.

   The age group willbe as follows : < 1 year, 1-4 years, 5-9 years, 10-14 years, 15-19 years, 20-39 years, 40+ years.

Study of Index Case and Control: Medical history including history of visit within 7 days prior to development of diarrhoea to another area will be taken. The clinical features, volume of stool and vomitus, level of of education of mother/patient and type of amount of fluid ORS/IVF will be recorded. One hundred lambda finger prick blood will be taken on admission and will be repeated on tenth day for antitoxin titre either in the hospital or in the field depending on disposition of patient.

Study of the Family Contacts : The families of the index cases and controls will be visited by a team of health workers (1 male + 1 female). There will be three teams of health workers. A census of the family with identification of the family members will be made. Socio-economical information will be obtained. Diarrhoeal cases will be identified and sent to the hospital for appropriate treatment. Rectal swab/stool will be taken from all members of the family on daily basis upto the end of the study. Water sample will be collected from storage water, river/pond/tap for five consecutive days (340 ml triple strength of peptone water + 660 ml of water). Food samples will be taken for five days (one table spoon of each food will be kept in a sterilized container). Hands of the contacts will be washed with 100 ml of bile peptone 1%, pH 8.5 in a sterilized bowl for isolation of V. cholerae. The first team will take 2 families for the study on the 1st day and the number of families will be increased to a total of 6 families by the third day. On the 4th, 5th and 6th day the second team will take 2 families per day for the study. The third team will start their work on 7th, 8th, and 9th day. Each team will have a total of 6 families for study. The teams will visit the families daily until the last positive case in the family becomes negative for V. cholerae for 3 successive days. Daily visits will not be less than 7 days. When the team completes a family study then they will take a new family in order to have six families everyday.

Definitions :

Family : For the purpose of this study the family is defined as the number of people living in one court yard.

Secondary Case : A secondary case is defined as a case of diarrhoea which occurred after the first case (index case) and to comply with the biotype, serotype of the index case.

Secondary Infection: Secondary infection is defined as a family member excreting V. cholerae with or without diarrhoea and to comply with biotype and serotype of the index case.

Carrier : Carrier is defined as a family member excreting V. cholerae without diarrhoea and to comply with the biotype and serotype of the index case.

Analysis of Data :

1. Ratio of primary cases/secondary case for both Inaba classical and Ogawa El Tor cholera.
2. Secondary infection rate for both Inaba Classical and Ogawa El Tor.
3. Proportion of Classical Inaba to El Tor Ogawa cholera.
4. Carrier rates for Classical Inaba and El Tor Ogawa cholera.
5. Duration of excretion of each group in cases, carriers.
6. Incidence and severity by age.
7. Isolation rate of each group environmental samples.

D. SIGNIFICANCE

This study will give us a clear understanding about the two serotypes and biotype differences of Vibrio cholerae. In the past investigation we had many guidelines unresolved probably due to the fact that we were working with only one serotype in classical cholera as against 2 serotypes in El Tor cholera.

E. FACILITIES REQUIRED

No additional facilities will be required.

SECTION III

A. DETAILED BUDGET

1. PERSONNEL SERVICES

Name	% Time	Duration	Project Requirements Taka	US $
Dr. Nigar S. Shahid	20%	6 months		497.00
Dr. A.R. Samadi	5%	"		2654.00
Dr. S.C. Sanyal	5%	"		1535.00
Dr. M.I. Huq	5%	"		1838.00
Physician (to be named)	20%	"		432.00
Consultant(Dr. W.B. Greenough) (Dr. K.A. Monsur)				
Field Supervisor	50%	"		950.00
Health Assistant(3 male+ 3 female)	100%	"		5610.00
Laboratory Technician	100%	"		1200.00
Research Technician	50%	"		600.00
Overtime for Lab.Technician and Health Asstt.				500.00
		Sub total		$ 15,816.00

2. SUPPLIES AND MATERIALS

Media and chemicals			$ 1,200/-
ORS packets 500 x 2 taka		Tk. 1,000.00	
Miscellaneous items for field, medicine, balloons, candy etc.			100.00
	Sub total	Tk. 1,000.00	$1,300.00

3. EQUIPMENT

None

4. PATIENT HOSPITALIZATION

None

	Taka	US Dollar
5. OUTPATIENT CARE		
None		
6. TRANSPORT		
3 vehicles miling daily 40x3x60x4.50 taka	Tk. 32,400	
7. TRAVEL AND TRANSPORTATION OF PERSONS		
None		
8. TRANSPORTATION OF THINGS		
None		
9. RENT, COMMUNICATION AND UTILITIES		
None		
10. PRINTING AND REPRODUCTION		$ 100.00
11. OTHER CONTRACTUAL SERVICES		
Daily wager, boat, rickshaw	Tk. 1,000	
12. CONSTRUCTION, RENOVATION AND ALTERATION		
None		
13. COMPUTER ANALYSIS		
Tk. 800/hour (8 hours)	6,400	

B. BUDGET SUMMARY

	Category	Taka	Dollar
1.	Personnel Service	-	-
2.	Supplies and Materials	-	1300.00
3.	Equipment	-	-
4.	Patient Hospitalization	-	-
5.	Out patient care	-	-
6.	Transport	32,400.00	-
7.	Travel and Transportation of persons	-	-
8.	Transportation of things	-	-
9.	Rent,Communication and Utilities	-	-
10.	Printing and reproduction	-	100.00
11.	Other contractual services	1,000.00	-
12.	Construction, renovation and alteration	-	-
13.	Computer analysis	6,400.00	-
	Total	Tk. 39,800.00	$ 1,400.00

= $ 1,658.33 + $ 1,400.00

Grand total $ 3,058.00

Conversion rate 1 US $ = Tk. 24.00

Abstract Summary

1. The population in this study will be of all age groups as we shall be looking for information as severity of disease/infection, infectivity pattern, etc. in various age groups. Selection will depend on the availability of the first infectious case. In case of minors consent will be obtained from their guardians.

2. There is no potential risk to the subject and blood samples will be drawn under a septic conditions.

3. There are no risks in obtaining rectal swabs and 100 ul of blood by finger prick.

4. Confidentiality will be maintained by using patient numbers instead of names and addresses of patients. The results will be kept in locked cabinets and expressed as numbers when published.

5. A signed consent form will be obtained from patients or their guardians. No information will be withheld from the subjects. No risks are involved, however, treatment will be provided for any risk.

6. The initial interview lasting for 20 minutes will be performed in the hospital. The subsequent interview lasting for 15 minutes will be taken at the residence of the patients.

7. The patients and their family members will treated free of charge at home or at the hospital. This will outweigh any potential risk to the subject.

8. Hospital records will be made use of, blood, stool and R/S specimen will have to be examined.

OUTBREAK INVESTIGATION OF CHOLERA

WATER/FOOD SAMPLE

Source of Water	Day - 1	
	Sample obtain	Culture
Food Sample		

HAND-WASH/CULTURE RESULT

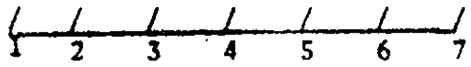
Sl. No.	Day : Date:	
	Hand-wash	Culture
1.		
2.		
3.		
4.		
5.		
6.		
7.		
8.		
9.		
10.		
11.		
12.		
13.		

OUTBREAK INVESTIGATION OF CHOLERA

INDIVIDUAL FORM

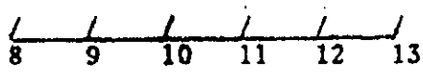
Used for cases who have diarrhoea

Identification no.

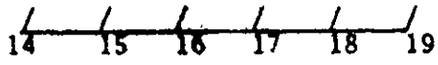


Household = 1-3
Family = 4-5
Individual = 6-7

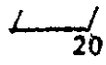
Date



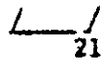
Age



Sex Male = 1, Female = 2

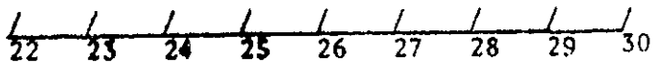


Diarrhoea

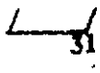


None = 0
Yes = 1
Yes

Date of onset of diarrhoea

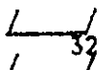


Stool **character**

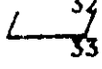


Watery = 1
Mucoid = 2
Mucoid blood = 3
Other = 4

Pregnancy **last 24 hours**

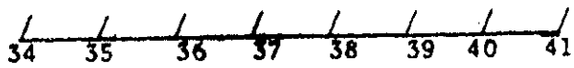


Vomiting

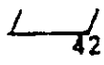


No = 0
Yes = 1

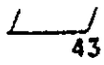
Date of onset of vomiting (hours)



Feeding of children
Exclusive BF = 1
BF+ FF and/or CM = 2
FF and/or CM = 3
BF + Suppl. food = 4
BF + FF and/or CM+ Suppl food
FF and/or CM + Suppl.
Family food

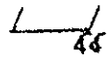


D/F



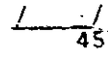
Vibrio negative = 0
Vibrio positive = 1

Handwash performed



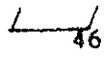
No = 0
Yes = 1

Assessment of dehydration



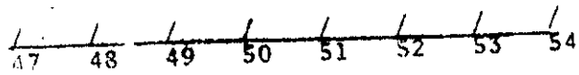
1 = No dehyd.
2 = Mild
3 = Moderate
4 = Severe

Treatment



ORS = 1
Ampicillin = 2
Oxy-tetracycline = 3
Furaxon = 4
Septrin = 5
Other(specify) = 6
Admitted in hospital = 7

Date of diarrhoea cured



Blood pressure : - / / / / (31 32 33)

Mucous membranes : 1=normal (moist), 2=dry, 3=very dry / / (34)

Urine flow: 1=normal, 2=reduced amount and dark 3=none passed for 12 hours / / (35)

Clinical assessment of dehydration : 1=none, 2=mild, 3=moderate, 4=severe / / (36)

Hospital stay

Output of stool in 24 hours (ml) / / / / / / (37 38 39 40 41)

Admission weight (kg) / / / / (42 43 44)

Discharge weight (kg) / / / / (45 46 47)

Height (cm) / / / / (48 49 50)

Duration of stay in hospital (hours) / / / / (51 52 53)

RS : (result). 1=INCCO, 2=OGCCO, 3=INCC+, 4=OGCC+ / / (54)

Treatment :

Initial rehydration : 1=ORS, 2= I.V. / / (55)

Amount of fluid (ORS+I.V.) in 24 hours (ml) / / / / / / (56 57 58 59 60)

Antibiotic :

1=Tetracycline, 2=Ampicillin, 4=Furoxone,
8=Chloramphenicol, 16=Septrin,
32=Metronidazole, 64=Gentamycin, 128=Kanamycin / / / / (61 62 63)

Blood taken :

Day 1 Yes=1, No=0 / / (64)

Day 10 Yes=1 No=0 / / (65)

OUTBREAK INVESTIGATION OF CHOLERA DUE TO CLASSICAL BIOTYPE

HOSPITAL FORM 1

Identification No. / / / / / / / / (1 2 3 4 5 6 7)

Age : (years/months) / / / / / (8 9 10 11)

Sex : Male=1, Female=2 / / (12)

Years of education of mother (< 12 patients) / / / (13 14)

Medical History :

Duration of diarrhoea : (days/hours) / / / / / (15 16 17 18)

Character of stool : 1=watery, 2=non-watery / / (19)

Content of stool : 0=none, 1=mucus, 2=blood, 3=mucus+blood / / (20)

Number of stool in past 24 hours : / / / (21 22)

Vomiting : 0=none, 1=yes, Precoding diarrhoea
2=yes, after diarrhoea / / (23)

Physical Examination :

Assessment of dehydration (guide for physician)*

Thirst : 1=normal, 2=mild thirsty, 3=very thirsty / / (24)

General Appearance : 1=normal, 2=restless,
3=lethargic but irrilable when touched
4=drowsy/cold & sweaty extremeties/coma / / (25)

Radial pulse : 1=normal rate + volume, 2=rapid and weak
3=rapid feeble/sometimes impalpable / / (26)

Respiration : 1=normal, 2=faster than normal, 3=deep and rapid / / (27)

Anterior Fontanclle : 1=normal, 2=sunken, 3=very sunken / / (28)

Skin Elasticity : 1=normal (pinch retracts immediately)
2=Pinch retracts slowly, 3=Pinch retracts
3=Pinch retracts very slowly / / (29)

Eyes : 1=normal, 2=sunken, 3=very sunken / / (30)

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*Physician guides

Without dehydration codes	: from 24-35 subcodes		(normal)
Mild dehydration codes	: from "	"	(1)
Moderate "	" : from "	"	(2 or more)
Severe "	" : from "	"	(3 or more)

OUTBREAK INVESTIGATION OF CHOLERA

FAMILY CARD

House-hold No. 1-3	Family No. 4-5	Indiv. Serial No. 6-7	Name and Relationship 8-9	Age 10	Diarr-hoea 11	Date of onset			Sex 18	Education 19	Religion 20	Source of water 21-22	Defecation practice 23	Type of housing 24	Ownership of house 25	Occupation Head of Family 26
						Month 12-13	Day 14-15	Hour 16-17								
Household is defined as the number of people living in one court yard	Family is defined as those eating from one cooking pot		Head=1 1st wife=2 2nd wife=3 3rd wife=4 Son=5 Daughter=6 Father-in-law=7 Mother-in-law=8 Father=9 Mother=10 Brother=11 Sister=12	<1yr=1 1-4yr=2 5-9yr=3 10-14 yr=4 15+=5	No=0 Yes=1				M=1 F=2	Non/ Maktab=0 Incomp.P.E.=1 Comp.P.E.=2 Incomp.S.E.=3 Comp.S.E.=4 S.E.=5	Muslim=1 Hindu=2 Chris-tian=3 Other=4	Tap-water=1 Unpro-tected T.Well=2 Protected T.Well=4 Pond= 8 River=16 Canal=32	Sanitary latrine=1 Service=2 Water-Seal=3 Dug-hole=4 No fixed place=5	Pucca=1 (Pucca brick built) Semi-Pucca=2 (brick + tin) Thatched shed=3 Slum	Owned=1 Rental=2 Other=3	None=0 Labour=1 Agr.=2 Land-holders=3 Business-man=4 Hawker=5 Civil-Servant=6

OUTBREAK INVESTIGATION OF CHOLERA

DAILY R.S. COLLECTION, RESULT, AND ILLNESS

Family No..... Hospital No.....

Sl. No.	Day 1			Day 2			Day 3			Day 4			Day 5			Day 6			Day 7			Day 8			Day 9			Day 10		
	Cnd	RS	CR	Cnd	RS	CR	Cnd	RS	CR	Cnd	RS	CR	Cnd	RS	CR	Cnd	RS	CR	Cnd	RS	CR	Cnd	RS	CR	Cnd	RS	CR	Cnd	RS	CR
1																														
2																														
3																														
4																														
5																														
6																														
7																														
8																														
9																														
10																														
11																														
12																														

Cnd = Condition of individual
V = R.S. obtained
A = Absent
R = refused
CR = culture result

0 = no diarrhoea
1 = mild diarrhoea
2 = moderate diarrhoea
3 = severe diarrhoea
4 = hospitalised

সম্মতিপত্র

আপনার কলেরা হয়েছে। চিকিৎসা ও গবেষনার জন্য আপনাকে আমরা প্রায় ২৪ ঘন্টা হাসপাতালে রাখবো। আপনার পায়খানা ও বমিতে দেওয়া স্যালাইন (ORS/IV) পরিমাপ করা হবে। আপনার শরীর থেকে এখন এবং ২০ দিন পরে পরীক্ষার জন্য কয়েক ফোঁটা রক্ত নেওয়া হবে। এই রোগ আপনার পরিবারের অন্যান্য সদস্য, প্রতিবেশী অথবা আপনার আত্মীয়ের মধ্যে সংক্রামিত হতে পারে। আপনার পরিবারের সদস্যরা এই রোগ থেকে মুক্ত কিনা তা দেখার জন্য আমরা ২০ দিন পর্যন্ত প্রতিদিন আপনার পরিবারের সকল সদস্যে পায়খানা বা ফোটাঁদ্বারা মলদ্বার থেকে পায়খানার নমুনা পরীক্ষা করবো। আপনার পরিবারের যে কোন অংশিয়া রোগীকে বাড়ীতে অথবা হাসপাতালে চিকিৎসা করবো কিন্তু আপনি ছাড়া আর কারো রক্ত নেওয়া হবে না।

আপনার রোগের বিবরন, পায়খানা ও রক্ত পরীক্ষার ফলাফল কারো কাছে প্রকাশ করা হবে না। আপনি আমাদের গবেষনায় অংশগ্রহন না করলেও আপনার চিকিৎসা করা হবে।

আপনি আমাদের প্রস্তাবে রাজী হলে নীচে স্বাক্ষর বা টিপ সই দিন।

স্বাক্ষর/টিপ সই _____

নাম _____

রোগীর নাম্বার _____

তারিখ _____