ment 1.

Date February

REVIEW BOARD ON THE USE OF HUMAN SUBJECTS, ICDDR,B.

95

cipal Investigator M.I. Huq

Trainee Investigator (if any) _____

ication No. 80-011(P)

Supporting Agency (if Non-ICDDR,B) _____

e of Study Isolation and characterisa-
n of MARV in cases, contacts and
vironmental samples.

Project status:
( ) New Study Pilot
( ) 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:
(x) 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 Board:
   ___ 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 Board for review.

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

Principal Investigator

Trainee

80-011(P)
Rec'd 25/2/80

ABSTRACT SUMMARY

The pilot study proposal is a laboratory based study for the isolation and characterisation of the antibiotic resistant *Vibrio cholerae* isolated from patients coming to the hospitals at Dacca and Matlab, their family contacts and environment. There is no potential risk to the patients or any other subjects as only a stool sample or rectal swab will be taken for study. The purpose of the study will be communicated to the patient or his/her guardian (if minor) and a consent form will be signed by them.

The multiple antibiotic resistant *Vibrio cholerae* isolated from this study by using conventional and special technique will be studied in the laboratory in terms of a) Determination of resistance factor in the MARV isolates; b) study of the viability of the R-plasmid in the patients gut as well as in environment; c) transfer of R-plasmid from these MARV strains to recipient *E.coli* strains.

PILOT STUDY PROJECT

ISOLATION AND CHARACTERISATION OF MULTIPLE ANTIBIOTIC RESISTANT *V.CHOLERAE* IN CASES, CONTACT AND ENVIRONMENTAL SAMPLES

M.I. Huq, L.N. Mutanda, A.R.M. Alim

INTRODUCTION

It has been well documented that effective antibiotic therapy shortens the duration of diarrhoea caused by *V.cholerae*. Tetracycline has been confirmed to be highly effective *in vitro* and *vivo*, and has been the drug of choice for the treatment of cholerae (Greenough et al 1964). Other drugs which have been tried include Furazolidine (Karchmer et al 1970) and Septrin (Francis et al 1971). Ampicillin was not found to be very effective *in vivo* against cholera (Northrup 1969) and as such has not been much used.

Since the start of treating cholera with Tetracycline at the Cholera Research Laboratory in 1962, we have been watching the sensitivity pattern of the *V.cholerae* isolates against the commonly used antibiotics especially Tetracycline. Though Ampicillin resistance (equal to or greater than 25 µg/ml) showedup from 1974, and that of Streptomycine (equal to or greater than 25 µg/ml) as early as 1968-69, resistance to Tetracycline has never been encountered in our Laboratory until July 1979. However, multi-antibiotic resistant *V.cholerae* have been reported by Prescott et al (1968) in several countries and most recently by Mahln et al (1979) in Tanzania.

In December, 1979 while testing *V.cholerae* isolates for antibiotic sensitivity, we isolated five multiply resistant *V.cholerae* Inaba, El Tor biotype from Matlab. All these strains were resistant to Tetracycline, Ampicillin, Kanamycin, Streptomycin and Septrin. A retrospective search on the laboratory stock cultures revealed that the first case with multiple antibiotic resistant *V.cholerae* (MARVC) appeared in August 26, 1979. Since then the number has continued rising. This has thus prompted a pilot study aimed at isolation and characterisation of these MARVC.

OBJECTIVES

The objectives of this project are to -

(1) To isolate MARV from stool or rectal swab of the patients being seen at Matlab and Dacca Hospitals with choleraic diarrhoea and also from the environment using a suitable antibiotic incorporated isolation medium which will help in selecting out resistant vibrios within 18-24 hours. This medium is to be used in conjunction with the routine diagnostic medium for the isolation of *V.cholerae*.

(2) To test the vibrio isolates for antibiotic resistance and to compare those with the other gut flora of the patient and also from the environment .

(3) To test the ability of these MARV: to transfer resistance factor to recipient *E.coli* strain K_{12}.

(4) To study the viability of this resistant plasmid in the patients' gut, as well as in the environment.

EXECUTION OF THE PROJECT

Selection of patients:

In Dacca all the patients with watery diarrhoea above two years of age attending the ICDDR,B Treatment Centre will be included in the study. The selection criterion will be adopted in Matlab as well irrespective of whether they come from in or outside the VTS area.

Collection and examination of stool and environmental samples:

Stool or rectal swab will be collected from the patients on admission before any antibiotic therapy is started. Initial screening of *V.cholerae* will be done by using dark field microscopy followed by bacteriologic culture on routine diagnostic medium as well as antibiotic incorporated gelatin agar medium. Antibiotic therapy is to be withheld and the patient found harbouring resistant *Vibrio cholerae* or non-cholera vibrios will have their rectal swab taken everyday. Family contacts will also be cultured for the presence of MARV. Screening for resistance against selected antibiotics will be done by using disc susceptibility method as described by Kirby and Bauer, followed by the tube dilution method for the determination of minimum inhibitory concentration. Screening water samples for the presence of MARV will be done monthly from our 18 points in Dacca and 17 points in Matlab (Protocol No.) and *V.cholerae* and non-cholerae vibrios will be tested for antibiotic susceptibility.

Personnel and Supplies:

For this pilot study to be continued up to March 1980, no new personnel or laboratory space will be needed. However, funds will be needed for media, antibiotics and transportation of supplies and personnel. The budged has been worked out and is within a range of U.S.$ 2,000.00.

সম্মতি পত্র

বাংলাদেশ আন্তর্জাতিক উদরাময় সংক্রান্ত গবেষণাকেন্দ্র নানাবিধ উদরাময় রোগের চিকিৎসা ও গবেষণায় নিয়োজিত।

কলেরা ও টাইফয়েড জীবাণুর জন্য পায়খানা ও পাতলা পায়খানা হয়। আমাদের হাসপাতালে এই রোগের জীবাণু পরীক্ষার জন্য ভর্তির সময়ে, ভর্তির চব্বিশ ঘন্টা পরে ও হাসপাতাল থেকে ছুটির সময়ে আপনার পায়খানা নেয়া হবে। প্রয়োজনানুসারে আমাদের কর্মীগণ আপনার বাড়ী থেকে পঞ্চম, অষ্টম, একাদশ ও চতুর্দশ দিবসে ও আপনার রোগের ভালভাবে পরীক্ষার জন্য পায়খানা আনতে পারে। চিকিৎসাধীন থাকাকালে আপনার বিশেষ যত্ন নেয়া হবে।

আমাদের কাজে সহযোগিতা করতে আপনার আপত্তি থাকলে অথবা গবেষণা চলাকালে যে কোন সময়ে আপনি বন্ধ করতে চাইলে আপনি তা পারবেন। তবুও আপনার চিকিৎসা যথারীতি চলতে থাকবে।

CONSENT FORM

ICDDR, B is working on problems related to diarrhoeal diseases. Several bacteria causes watery diarrhoea. We would like to investigate enteric bacteria, such as Vibrio cholerae, E. coli etc.

To do this we would like to obtain your stool specimens at the time of hospitalization, after 24 hours and at the time of being discharged. The stool will also be collected from your residence on the 5th, 8th, 11th and 14th day after being discharged from the hospital. Appropriate treatment would be provided during this time.

You will receive proper treatment whether or not you would like to take part in our study. You can withdraw at any time.