Attachment 1.

EHICAL REVIEW CONMPITION, ICDDR,B.

Date 10/2/81

99

Principal Investigator Stan Becker, Roger Glass, Mukhlan   Trainee Investigator (if any) Nil

Application No. 81-007(P)   Supporting Agency (If Non-ICDDR,B) Nil

Title of Study Cholera Seasonality and Geographical Patterns in Matlab 1966-1979

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

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 ⎬ NA
   (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 ⎬ NA
   (e) Invasion of privacy   Yes No ⎪
   (f) Disclosure of informa-
       tion damaging to sub-
       ject or others   Yes No ⎭
3. Does the study involve:
   (a) Use of records, (hosp-
       ital, 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 ⎬ NA
   (d) Sensitive questions   Yes No ⎪
   (e) Benefits to be derived   Yes No ⎪
   (f) Right to refuse to
       participate or to with-
       draw from study   Yes No ⎭
   (g) Confidential handling
       of data   (Yes) No
   (h) Compensation &/or treat-
       ment 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 NA
7. Check documents being submitted herewith
   Committee:
   ___ 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 of
       nature of study, risks, types of ques-
       ions 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 confidential-
       ity
   ___ 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 question-
      naire will be presented to the Committee
      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.

Stan Becker, Roger Glass, Mukhlan

.... and Investigator

SECTION I - RESEARCH PROTOCOL

1. **Title:** Cholera Seasonality and Geographical
   Patterns in Matlab 1966-1979

2. **Principal Investigators:** Stan Becker, Roger Glass, M U Khan

3. **Starting date:**

4. **Completion date:** March 1981

5. **Total direct cost:** US $ 2,255.00

6. **Scientific Programme Head:**

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

   Signature of Scientific Programme Head: _____

   Date: ___16/2/1981___

7. **Abstract Summary:**

   The seasonal and geographic patterns of cholera are still largely
   unknown. With the existing data some of the questions may be answered.

   Our objectives are to document and try to explain as best as possible
   with macro-level data, the seasonal and geographic patterns of reported
   cholera incidence in Matlab over the past decade.

   The data of the Matlab hospitalized culture   positive cholera cases
   have been already punched from the surveillance villages with known
   population for the years 1966-1978 by Dr. Merson et al.

   These data will now be further analysed to answer the questions by a
   programmer using a computer. This will not involve any population
   and will not identify any one specifically. The works can be
   completed in a short time without appointing any new personnel.

8. Reviews:

    (a)   Ethical Review Committee: _____

    (b)   Research Review Committee: _____

    (c)   Director: _____

    (d)   BMRC: _____

ABSTRACT SUMMARY - PARTICULAR ITEMS

The purposes of this study are to document and try to explain as best as possible with macro-level data, the seasonal and geographic patterns of reported cholera incidence in Matlab over the past decade.

The out-patient and in-patient records have been kept at Matlab hospital since 1966. These data were coded and punched for the years 1966-1978. The data has been transferred to tape. Programs will be made and the data will be analysed by a programmer using computer.

1. The data is already in tape and no new population is required.

2. As the data does not mention any one's name and as no new population is needed there is no risk of any kind to any individual.

3. There is no risk for any one.

4. The data does not contain any name or any individual's identity. The data is thus already in a confidential state.

5. a) No consent of any kind is needed.

    b) Does not arise

    c) Does not arise

6. Not required.

7. Does not arise.

8. Requires hospital records only (already punched)

A. INTRODUCTION

Objective

The objectives of this study are to document and try to explain as best as possible with macro-level data, the seasonal and geographic patterns of reported cholera incidence in Matlab over the past decade.

Background

Seasonality: The causes of the seasonal patterns of cholera infection and the geographic spread of the disease are not well known. Cholera has different seasonal patterns in different parts of the world. In India the peak is during the premonsoon season, in the Philippines, the peak comes during the rainy season (3). In Bangladesh in the 1960's, a bimodal pattern was described (7,11) with a minor peak in the late spring and a major peak in early winter (Nov. - Jan.). With the introduction of the El Tor bio-type the second peak has shifted to Sept.-Nov. (10). During the same period, the time of the Eid holidays has progressed backward (10 days each year). Since these holidays involve visiting and eating at the houses of many friends and relatives and above-average numbers of diarrhoea cases have been seen clinically immediately after Eid, it has been hypothesized that the shift in cholera in Bangladesh may be due to the shift of Eid. On the other hand, since cholera is known to be predominantly a water-borne infection and the water level and temperature vary substantially with the seasons

in Bangladesh, these variables may be important in determining the
annual pattern of cholera incidence. The biotype of cholera seen in
Matlab changed from classical to El Tor in 1973. The El Tor type
reportedly survives better in the environment and has a higher carrier
to case ratio than classical cholera (5). Both of these factors
might lead us to expect a different relationship between the seasonal
patterns of meteorological/hydrological conditions and hospital
cholera cases.

Geographic patterns: Within cholera endemic areas, the geographic
spread of the disease with each new cholera season is also of interest.
Analysis of earlier data in Matlab showed "little indication of
village to village spread" suggesting multiple simultaneous introduction
of the infection (7). The seasonal migration pattern of adult males
who become infected has been offered as a possible explanation. Lending
support to this, it has been shown that first cases are significantly
older than secondary cases. Boatmen have also been implicated in
the spread of cholera (4).

Matlab Data

Since 1966 in and out-patient records have been kept at the Matlab
hospital. These data were coded and punched for the years 1966-1978
(under the direction of Drs. M.U. Khan and Michael Merson).

Rationale

The seasonal pattern of cholera remains to be explained. The mechanisms of geographic spread are also still largely unknown. With existing data it is possible to answer some hypotheses in these two areas.

B. SPECIFIC AIMS

1. To describe the seasonal pattern of cholera cases in Matlab -

   a) Can an equation be developed to predict the peaks, the shape of the curve, etc.

   b) Can the seasonal pattern be predicted better by incorporating knowledge of the shifting time of Eid over the past decade;

   c) Has the pattern changed significantly with the change from classical to El Tor biotype.

2. To determine the hydrological/meteorological variables which correlate best with the seasonal series of cholera incidence:

   a) water level

   b) water temperature

   c) rainfall

3. To determine the geographic pattern of cholera cases which have presented at the Matlab hospital in the past decade. The following questions will be answered with space-time plots of these data:

   a) how does distance from the hospital affect the data ?

   b) are there concentric circles of disease spread in space as well as time or is the distance between cases in the initial weeks a random variable ?

c)   is the disease spread by village independent of the location
     of the village vis-a-vis the river ?

d)   are the first cases in the same locality each year? Are they
     in river villages ?

e)   do villages experience cholera throughout the season or are
     some hit early and have no cholera later while other villages
     have epidemics, i.e. to what extent does a village pattern
     follow that of the whole area ?

f)   are the space-time plots for the spring peak the same as those
     for the fall peak ?

4.   To determine the extent to which certain age-sex groups get cholera
     proportionately more at the beginning of the cholera season.

C.   METHODS OF PROCEDURE

Cholera Data:

1.   Sort file by day of hospitalization. Retain village, age and biotype
     information.

2.   Plot cases by month and biotype.

3   Plot number of cases by village for the winter and spring peaks for
     each year.

4.   Define criteria for "hot" villages and determine "hot" villages in
     these data.

5.   Determine the age-sex distribution of the first cases in villages in
     several years as compared to later cases in those same villages.

6. Define geographical features of hypothesized importance (waterways, ambulance stations) and determine statistical tests to ascertain clustering of cholera cases with respect to these features. Also determine overall departures from randomness and whether these departures are the same from year to year.

Meteorological/hydrological Data:

7. Plot the levels of these monthly data for Matlab, for the last 12 years.

8. Determine to what extent each of these series is related to the cholera series.

    a) simple calculation of number and differences in time between peaks;

    b) cross-correlation time series analysis (1).

D. FACILITIES REQUIRED

Most of the work for items 1,2,4 and 6 is done. .

Some computer time is needed to complete item 5. Items 3 and 7 will require a few days of work by a data processing assistant.

E. COLLABORATION ARRANGEMENTS

None

REFERENCES

1.   Bloomfield, P.K.   1976.   Fourier Analysis of Time Series: An
     Introduction.

2.   Hyagett, P. et al.   1977.   Locational Methods, Vol.II, Halsted Press.

3.   Kafiluddin, A.K.   1973.   Modern Epidemiology.

4.   Khan, M. and Mosley, W.H.   1967.   "The role of Boatmen in the
     Transmission of Cholera," E.Pak. Med. J. 11:61-65.

5.   Khan, M.U. et al.   1970.   "The Changing Pattern of Cholera in East
     Pakistan; The Appearance of El Tor Vibrio cholerae," J. of Pak.
     Med. Assoc.

6.   Martin, A.R. et al.   1969.   "Epidemiological Analysis of Endemic
     Cholera in Urban East Pakistan 1964-66," Am.J. Epi. 89(5):572-582.

7.   McCormack, W.M. et al.   1969.   Endemic Cholera in Rural East Pakistan.
     Am. J. Epi. 89(4):393-404.

8.   Merson, M.H. et al.   1978.   Epidemiology of cholera and Enterotoxigenic
     Escherichia Coli Diarrhoea, Nobel Symposium paper.

9.   Mosley, W.H.   1970.   "Epidemiology of Cholera", in WHO Public
     Health Paper No. 40.

10. Oberle, M.W. et al. 1978.   "Diarrhoeal Disease in Rural Bangladesh:
     Epidemiology and the Cost and Mortality Averted by Rehydration
     Therapy, Manuscript copy.

11. Phillips, R.A.   1968.   "Asiatic Cholera," Annual Review of Medicine
     19:69-80.

12. Pollitzer. 1959.   Cholera.

SECTION III

A. DETAILED BUDGET*

1. PERSONNEL SERVICES

Name		Monthly Salary	Project requirements Taka	Dollars
Stan Becker[a]	(4 days)	$ 1,300	-	260
Roger Glass	(4 days)	$ 2,600	-	473
M.U. Khan	(4 days)	$ 2,000	-	364
Programmer	(2 weeks)	Tk.3,000	-	119
Data Processing Assistant	(3 weeks)	Tk.2,000	-	119
			Sub-total	1,335

2. SUPPLIES AND MATERIALS

   None

3. EQUIPMENT

   None

4. PATIENT HOSPITALISATION

   None

5. OUTPATIENT CARE

   None

6. ICDDR,B TRANSPORT

   3 Trips to Matlab @ Taka 400.00   -   75

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*The earlier costs of this work came from Disease Transmission
Working Group

[a]Stan Becker will finish this work in Paris with salary from another source.

| | Project requirements | |
| | Taka | Dollars |

7. TRAVEL AND TRANSPORTATION OF PERSONS

   None

8. TRANSPORTATION OF THINGS

   None

9. RENT, COMMUNICATION AND UTILITIES

   None

10. PRINTING AND REPRODUCTION

Publication charge	—	250
Typing charge and paper	—	25
Sub-total		275

11. OTHER CONTRACTUAL SERVICES

Computer time 1 hour	—	50

12. CONSTRUCTION, RENOVATION AND ALTERATION

    None

13. MISCELLANEOUS

    None

B. BUDGET SUMMARY

CATEGORY	TAKAS	DOLLARS
1. Personnel Services	-	1,335
2-5 Nil items	-	-
6. ICDDR,B Transport	-	75
7-9 Nil Items	-	-
10. Printing/Reproduction	-	275
11. Other contractual services	-	50
12-13 Nil Items	-	-

Total	1,735
Overhead @ 30%	520
Grand Total:	2,255