

Library (2)

Date 29.1.86

ETHICAL REVIEW COMMITTEE LIBRARY B.

DHAKA - 12

Principal Investigator /Caren Rosenmans
Thomas Wierzba

Trainee Investigator (if any)

Application No. 86-005

Supporting Agency (if Non-ICDDR,B)

Title of Study Developing an Algorithm

Project status:
(X) New Study
() Continuation with change
() No change (do not fill out rest of form)

for the Field Management of Diarrhea in an area with a High Prevelence of Dysentery

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

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 Committee:

NA 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)

NA Informed consent form for subjects

NA Informed consent form for parent or guardian

NA 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.

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

Handwritten signature

Principal Investigator

Trainee

86-025-
- 29.1.86

TITLE: DEVELOPING AN ALGORITHM FOR
THE FIELD MANAGEMENT OF DIARRHEA IN AN AREA WITH A
HIGH PREVELENCE OF DYSENTERY

PRINCIPAL INVESTIGATORS: KAREN ROSENMANS, MEDCINE SANS FRONTIERS
THOMAS WIERZBA, RANGPUR DINAJPUR RURAL SERVICES

CONSULTANT: MICHAEL BENNISH, ICDDR,B

STARTING DATE: AS SOON AS APPROVAL IS GRANTED

COMPLETION DATE: ONE YEAR AFTER BEGINNING THE STUDY

TOTAL INCREMENTAL COST: \$11,524

SCIENTIFIC PROGRAM: THIS PROTOCOL HAS BEEN APPROVED BY THE
DISEASE TRANSMISSION WORKING GROUP

SIGNATURE OF THE ASSOCIATE DIRECTOR, DTWG



DATE

28.1.86

RECEIVED 8 OCT 2001

ABSTRACT

Current algorithms for the field management of diarrheal illness have focused almost entirely on the use of ORT for the treatment and prevention of dehydration. Although such an algorithm is relatively simple to implement, it ignores for the most part issues related to the management of dysenteric illness, which in many areas of Bangladesh is thought to contribute more to diarrhea associated mortality than does watery diarrhea.

The major decision for a field health worker to make in the treatment of diarrhea is whether ORS is sufficient for the treatment of the diarrhoeal illness, or whether additional specific antibiotic therapy is required. In Bangladesh, antibiotic therapy would be most often required in patients with shigellosis. Thus a clinical algorithm, to be useful, must be able to distinguish, with some reasonable degree of probability, which patients have shigellosis. In addition, it would be of interest to know, based on clinical information, which patients are likely to be infected with *Entamoeba histolytica* or *Giardia lamblia*, as diarrhea due to these thought to be caused by these organisms is a frequent reason for medication, given either by doctors or minimally trained village doctors.

Current management schemes in use among the family health workers of the Rangpur Dinajpur Rural Services' Health Programme (RDRS) depend on the history of the type of diarrhea. These are classified for the most part into three groups - patla paikana (watery diarrhea), rokto amasha (blood dysentery) and shaddher amasha (white dysentery). Over a five month period we plan to identify 100 children less than five years of age in the RDRS working area who have one of the three types of diarrhea. Each child would have a simple history, physical examination and visual inspection of stool performed. Stool would be collected and transported to Dhaka for culture

and examined for the presence of ova and parasites. Based on the stool examination findings we would then attempt to construct a clinical algorithm that would let us reliably identify those patients requiring antibiotic therapy.

OBJECTIVE

To develop an effective algorithm for the field management of acute diarrheal illness in an area endemic for dysentery. This algorithm will be based on the local classification of diarrheal illness and will essentially attempt to divide patients with diarrhea into two groups - those requiring ORS alone for the therapy of their diarrhea, and those requiring in addition antimicrobial therapy for shigellosis.

BACKGROUND

The Health Programme of Rangpur Dinajpur Rural Services (RDRS) provides primary health care services to approximately 800,000 persons in five upazillas of Rangpur district. These services are provided mainly by 350 family health workers (FHW) who have received three months of training prior to starting their work, and who visit every household in their working area once in four to six weeks.

A major focus of the RDRS Medical Programme has been the diagnosis and treatment of diarrheal disease. Patients come to the FHW for therapy of a diarrheal illness, and during their regular village rounds the FHW carries out active surveillance for diarrheal illness that is either currently ongoing or has occurred in the seven days prior to their visit.

The active surveillance program has shown that dysentery (as defined by the passage of stools with mucous and blood) is endemic in Rangpur, and as a cause of death exceeds watery diarrhea. When classifying diarrheal illness the FHW's and RDRS have adapted a classification scheme that makes use of the local characterization of diarrheal illness into three types: patla paikana (watery diarrhea); rokto amasha (blood dysentery) and shaddher amasha (white dysentery). Using this classification scheme, active

surveillance for a four month period in 1985 (May through August) showed that the incidence of the three types of diarrhea was as follows: patla paikana: 3,747 cases with 10 deaths; rokto amasha 3842 cases and 62 deaths; shaddher amasha: 2787 cases and 4 deaths.

In determining management the FHW does not routinely have access to laboratory investigations. The current management schemes that the FHW's follow are based mainly on the local classification scheme, although the relative contribution of different pathogens to the three types of diarrhea is not known.

The treatment options available to the FHW at the current time are essentially two: to give ORT alone, or to also offer antibiotic therapy if the diarrhea is presumed to be due to Shigella infection. This treatment scheme is based upon the assumption that Shigella infections are associated with a high mortality rate, and that early and effective antibiotic therapy can reduce the mortality rate. (1,2) It is not felt that infections due to other pathogens besides cholera warrant specific therapy. This conclusion is based on the following assumptions: 1. In few other diarrheal infections is an effective specific therapy available 2. Many of these infections are associated with very low case fatality rates, making drug therapy cost ineffective even if therapy was effective in providing symptomatic relief. That the prevalence of some of the treatable infections is rare enough that accurate diagnosis, based on clinical information, is unlikely. Thus under the current scheme the FHW's need an algorithm based on clinical information that will allow them to predict with some accuracy which patients will have shigellosis.

Currently, it is assumed that most of the patients with rokto amasha have shigellosis, (2) and these patients are routinely offered antibiotic therapy.

It is thought unlikely that patients with patla paikana have shigellosis, and these patients are given only ORT. Patients with shaddher amasha do not fit neatly in the current treatment scheme: are they patients with mild, early or late shigellosis? Do they have giardia? What should their treatment consist of? What happens if they are untreated?

Most of the assumptions underlying the current diagnosis and treatment algorithm are based on very little in the way of "hard evidence". As mentioned above it is not known what the breakdown by infecting organism is of the three clinical types of diarrhea. The etiology specific patient outcome is also not known, and can only be inferred from sketchy information available in the literature. And once the prevalence of different types of pathogens in Rangpur is known, how well does the current clinical classification scheme distinguish between them? Is there additional clinical information that could reliably and routinely be obtained that would help predict which patients need specific antibiotic therapy, and for which patients ORS alone is sufficient?

Current algorithms for the management of persons with diarrhea in developing countries focus almost exclusively on the diagnosis of dehydration, and the use of ORT for the treatment and prevention of dehydration. (3-8) Although most of these manuals constantly refer to diarrhea - they in fact mean watery diarrhea. The problem of dysentery is either mentioned briefly or not at all. Certain manuals even state that ORT is effective treatment for diarrheal illness caused by Shigella. (3). Thus these manuals devote little attention to determining in which patients ORT is insufficient therapy, and additional therapy might be required. Certain manuals will mention that patients with dysenteric illness should be referred to secondary or tertiary level medical facilities, but this is not a realistic

option in the Rangpur field area.

There are a number of reasons that the currently available clinical management schemes largely ignore the problem of dysenteric illness. One might be that the schemes were developed in areas that have a low prevalence of dysenteric illness. That is clearly not the case in Rangpur, and it is clear that for an area such as Rangpur it is necessary to develop a scheme that takes dysenteric illness into account. Another reason is that there has been an understandable reluctance to incorporate drug therapy into the treatment part of such algorithms. Drug therapy, much of it useless, amounts to about 40 taka per capita in Bangladesh, which is about four times the amount of money that is spent by all government health programs. Similar situations exist in many other less developed countries. Thus the efforts to limit the use in drug therapy have been well intentioned. However it is clear that effective drug therapy for the treatment of shigellosis, a disease that has a high attendant morbidity and mortality.

RATIONALE

Shigellosis is a disease that is endemic in many parts of Bangladesh, as well as in other areas of the developing world. Current manuals and algorithms for the field management of diarrhea focus almost exclusively on the treatment of watery diarrhea, and either ignore the problem of dysentery or suggest that patients with this problem be referred to local facilities where physicians are available. The latter options are not practicable ones in most field village based programs, where even if there were access to a trained physician (which is usually not the case) the cost of such a visit would be prohibitive for most villagers. Thus there is a need for the

development of a diarrhea treatment algorithm which takes into account the treatment of shigellosis, and is based on information that could routinely and reliably be obtained by a village health worker.

SPECIFIC AIMS

The specific aims of this protocol are as follows:

1. To develop an algorithm for the field management of diarrhea that allows a village health worker to predict with some accuracy which patients have shigellosis and require treatment with antibiotics.
2. To determine if, given the resource constraints of the health program, there are ways to reliably identify patients with other types of diarrhea that are responsive to specific antibiotic therapy.
3. To follow the patients for a one year period of time to determine the impact that infections due to the different pathogens have on mortality and growth.

PATIENTS AND METHODS

During a five month period (February through June, 1986) 300 patients will have stool obtained for determination of infecting pathogen. These 300 patients will be divided into groups of 100 based on the type of diarrhea they have: patla paikana, rokto amasha, or shaddher amasha. The study is being spread out over a five month period in order to limit the effect that the seasonality of certain pathogens might have on the usefulness of the algorithm.

During one week of every month 60 patients (20 with each type of diarrhea) will be identified by a FHW who is the team leader for a union. All patients will be children, five years of age or less, who have had diarrhea for 72 hours or less, and who have not had allopathic medicine within the week prior to the FHW visit. The FHW will attempt to obtain a standardized set of information from each of the patients. (See attached form). This information will include simple historical and physical examination information, along with visual inspection of the stool. Treatment given will be noted.

Two rectal swab and stool sample will be obtained from all patients. The rectal swab will be placed in buffered glycerol saline transport media, one in Cary-Blair transport media, and swabbed onto MacConkey and Salmonella-Shigella agar. The stool specimen will be divided: some will be placed in PBS for rotavirus ELISA, and the rest of the specimen will be placed in formalin for subsequent examination for ova and parasites.

All specimens will be collected in the field, and brought to Lalmonirhat by early afternoon. In Lalmonirhat they will be logged in and prepared for shipment to ICDDR,B by overnight courier. All specimens should arrive at the ICDDR,B microbiology laboratories within 24 hours of the time that they were obtained.

After arrival at the ICODR,B laboratories the specimens will be processed as follows:

1. Cary-Blair: Cultured onto TTGA for isolation of vibrionacie, and Campy plate.
2. BGS: Cultured onto SS and MacConkey agar for isolation of Salmonella and Shigella.
3. SS and MacConkey direct plates: For isolation of Salmonella and Shigella, and for E. coli picks for LT and ST toxin testing.
4. PBS: For rotavirus ELISA
5. Formalin: Trichrome stain for O and P.

Each patient will be followed up at two weeks, four weeks and then monthly for a one year period of time from when initially cultured. During the followup visits weight, height, and interval history of diarrhea will be obtained.

Information from all forms will be entered onto a data base and statistical program on a IBM compatible computer. Based on the clinical information that is obtained, and the culture results, we will attempt to develop an algorithm for the seperation of patients into at least two major groups - those that need only ORS, and those who need additional antibiotic therapy, primarily for shigellosis.

SIGNIFICANCE

The significance of this protocol is that it will allow a field health worker to more appropriately treat diarrhea. In developing the algorithm, we will see how specific and sensitive the current, locally used classification scheme is for identifying patients with shigellosis. In addition we will see if there are other clinical indicators that could be

obtained by the village health workers that would improve the prediction of who has shigellosis and needs antibiotic treatment. Developing a scheme that will let field workers predict more accurately who needs antibiotic treatment should also help to limit the use of antibiotics to those who actually need them. Limiting antibiotic use should both help reduce costs and also decrease the high prevalence of antibiotic resistance that is seen when these drugs are used indiscriminantly.

FACILITIES REQUIRED

The field part of this project will be carried out in the field area of the Rangpur Dinajpur Rural Services Health Programme. The microbiology tests will be done by the Microbiology Branch of the ICDDR,B. Both programs will use existing facilities. No additional facilities will be required.

COLLABORATIVE ARRANGEMENTS

This study will be done in collaboration with the Medical Programme of Rangpur Dinajpur Rural Services and Medicine Sans Frontiers - Netherlands - Belgium.

BIBLIOGRAPHY

1. Bennish ML, Eusof A, Kay B, Wierzba T. Multiresistant Shigella Infections in Bangladesh. Lancet 1984 ii 462
2. Wierzba T, Bennish ML, Paramanik P, Alam N, Das J, Islam N. Interventions to Reduce Deaths from Dysentery in Rural Bangladesh. Abstract submitted for presentation at the IX International Congress of Infectious and Parasitic Diseases.
3. A Manual for the Treatment of Acute Diarrhea - For Use by Physicians and Other Senior Health Workers. Program for Control of Diarrhoeal Diseases, World Health Organization WHO/CDD/SER80.2 REV. 1 (1984)
4. The Management of Diarrhoea and Use of Oral Rehydration Therapy. A Joint WHO/UNICEF Statement. World Health Organization, Geneva, 1983
5. Diarrhoea Training Unit - Director's Guide. World Health Organization Draft, September 1985
6. Management and Prevention of Diarrhea - A Physician's Manual Kabalikat Ministry of Health Office of the Minister Republic of the Philippines
7. International Training Course on Diarrhoeal Disease Clinical Aspects for Nurses. October 1985. International Centre for Diarrhoeal Disease Research, Bangladesh
8. Treatment and Prevention of Acute Diarrhoea - Guidelines for the Trainers of Health Workers World Health Organization, Geneva, 1985

All of these references, except for No. 2, are available in the ICDDR,B library.

ABSTRACT SUMMARY

1. The population enrolled in this study will be persons who are regularly visited by an RORS family health worker. They will be identified as part of the active surveillance for diarrhea that is currently being carried out. Children five years of age or less will be chosen because they are the persons at highest risk of morbidity and mortality from diarrheal illness, and thus it is most important to develop an algorithm for this group.
2. There are no risks to the patient in this study, which will involve routine diagnostic stool tests.
3. As noted above, there are no risks to the patients in this study.
4. The information that is gathered will be used in part to care for the individual child. That information that is used in analysis will be coded by laboratory number, so that individual identities will not be known when the analysis is done.
5. As there is no risk to the patient, and there is no invasion of privacy, but rather what is being done is part of the care of patients with diarrhea, no written informed consent will be obtained.
6. The interview is as attached. It will essentially consist of the routine questioning that a village health worker would do for a patient with diarrhea. The time required should be five to ten minutes.
7. The patient will receive care for their episode of diarrheal illness. This includes supplying ORS if the patient has watery diarrhea, and offering antibiotics if it is suspected that the patient has shigellosis. Society stands to gain because we will hopefully develop from this study an improved means of managing diarrheal illness in field conditions - conditions that are representative of the way that the majority of the population lives.
8. The study does not require the use of stool for diagnostic purposes. No other specimens are required.

BUDGET (Detailed)

1. Personnel Services

Person	% time	# of Months	Total Cost
Dr. Rosenmans	110	6	0 (Paid by MSF)
Mr. Wierzba	10	12	0 (Paid by RDRS)
Field Staff			0 (Paid by RDRS)

2. Supplies and Materials

ITEM	COST/ITEM/\$	# REQUIRED	TOTAL COST
Laboratory costs:			
Cary-Blair	.10	400	\$40
BGS	.23	400	\$92
PBS	.08	400	\$32
Formalin	.50	400	\$200
MacConkey Agar	.47	400	\$188
SS Agar	.47	400	\$188
Campy Culture	5.28	400	\$1,584
ST & LT Pick	1.98	300	\$594
LT & ST Testing	3.96	300	\$1,188
Rotavirus Elisa	3.30	300	\$990
Vibrio Culture	2.47	300	\$741
Sal, Shig Culture	3.66	600	\$2,196
Stool Microscopy	1.72	300	\$516
Rectal Swab Sticks	.08	1,500	\$120

TOTAL LABORATORY COSTS	\$8,549
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Miscellaneous Supplies (Paper, Pencils, etc.)	\$150
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Total Supplies and Materials	\$8,699
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3. Equipment

Computer: 1 Radio Shack HD 1200	\$2,400
Printer: 1 Epson RX 80	\$325
Uninterruptable Power Source - TQPAZ 400 VA	\$750

\$3,475

4. Patient Hospitalization	No Charge
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5. Outpatient Care	Paid by RDRS
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6. ICDDR.B Transport	No Charge (Transport provided by RDRS)
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7. Travel and Transportation of Persons

12 Roundtrips to Saidpur x \$30/trip	\$360
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8. Transportation of Things	Paid by RDRS
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9. Rent, Communications and Utilities	No costs
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10. Information Services	No costs
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11. Printing and Reproduction	No costs
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12. Other Contractual Services	No costs
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13. Construction, Renovation and Alterations	No costs
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SUMMARY BUDGET
(Only line items with costs are listed)

2. Supplies and Materials	\$8,699
3. Equipment	\$3,475
7. Transportation	\$360
TOTAL	\$12,534

PRELIMINARY QUESTIONARRE (Still has to be field tested)

Identifying information:

1. Patients Name
2. Patients Fathers Name
3. Patients age in years and months
4. Sex
5. Uapzilla
6. Union
7. Village
8. Bari #
9. House #

History

10. Who was the History Taken From: A. Mother B. Father 3. Both Mother and Father 4. Other person
11. What type of diarrhea does the child have now
 - a. patla paikana
 - b. rokto amasha
 - c. shadder amasha
12. How many days has the diarrhea lasted for?
13. When the diarrhea began, what was it like:
 - a. patla paikana
 - b. rokto amashi
 - c. shaddar amasha
14. How many stools has the child had in the last 24 hours?
15. Has the child had a fever during this illness?
16. Has the Child been vomiting?
17. Which started first - the diarrhea or the vomiting?
18. How many times in the 1st 24 hours has the child vomited?
19. Is the child sleeping more than usual?
20. Is the child playing less than usual?

21. Has the child taken medicine in the last 7 days?

1. No
2. Yes, allopathic
3. Yes, homeopathic
4. Yes, ayurvedic or herbal

Examination:

22. weight

23. Height

24. Arm circumference

25. Is the child dehydrated:

- a. No
- b. Yes, mild
- c. Yes, moderate
- d. Yes, severe

26. Is the child's pulse:

- a. normal
- b. weak or feeble
- c. can not feel

27. Is the child

- a. alert and playful
- b. irritable and crying
- c. not active

28. Does the child feel feverish?

29. Did you examine the stool? yes , no

30. If you did examine the stool was it:

- a. normal
- b. patla paikana
- c. rokto amasha
- d. shaddher amasha

31. What treatment did you give the child?