

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

HH

Principal Investigator Dr. Eussif
Dr. Sack

Trainee Investigator (if any) _____

Application No. 80-023

Supporting Agency (if Non-ICDDR,B) _____

Title of Study Treatment of Travelers
Diarrhea with Chlorpromazine

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

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
- 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
 - (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.

We agree to obtain approval of the Review Board on the Use of Human Subjects for any changes involving the rights and welfare of subjects before making such change.

Dr. Sack
Principal Investigator

80-023

Rec'd 9/6/80

SECTION I - RESEARCH PROTOCOL

- (1) Title: Treatment of Travelers Diarrhea with Chlorpromazine
- (2) Principal Investigators: Dr Abu Eusof
Dr David Sack
- (3) Starting Date: June 1980
- (4) Completion Date: June 1981
- (5) Total Direct Cost: 17,735
- (6) Scientific Program Head:

This protocol has been approved by the Pathophysiology and Therapy Working Group.

Signature of Scientific Program Head:

L. C. Sack

Date:

3 June 80

- (7) Abstract Summary: This study is designed to determine the efficacy of Chlorpromazine (CPZ), 1mg/kg, taken orally in decreasing the symptoms of purging, cramps, and nausea from an episode of travelers diarrhea. The patients in this study will be newly arrived (within 3 months) expatriates who come to the travelers clinic. Patients fitting the criteria for the study will be given either CPZ or a similiar appearing placebo at the time of their visit for diarrhea and a diarrhea diary will be maintained to record symptoms. Besides the CPZ, patients will be given oral therapy packets but no antibiotics

will be used. If CPZ is effective in alleviating the symptoms of travelers diarrhea, we would have established an effective form of therapy which would not encourage the emergence of antibiotic resistant bacteria.

(8) Review:

(a) Ethical Review Committee: _____

(b) Research Review Committee: _____

(c) Director: _____

(d) BMRC: _____

(e) Controller/Administrator: _____

SECTION II - RESEARCH PLAN

A. INTRODUCTION

1. Objective: The objective of this study is to determine the efficacy of chlorpromazine taken as one dose of 1mg/kg orally in the treatment of acute watery diarrhea of travelers.
2. Background: Several studies have now established that the major cause of "travelers diarrhea" is infection with enterotoxigenic E. coli (ETEC), primarily those E. coli which produce heat labile toxin (LT) with or without heat stable toxin (ST). This has been shown in Mexico,^{1,2} Kenya,^{3,4} Morocco,⁵ Nepal¹ and Bangladesh⁶. This is especially true of the diarrhea episodes which occur within a few weeks of arrival. Those episodes which occur later are less likely to be due to ETEC, perhaps because of acquired immunity to the ETEC organisms or their toxin(s).

The management of travelers diarrhea includes measures to try to prevent the disease and measures to treat. Prevention is through proper hygiene⁷ (since the infection is acquired by eating contaminated food and/or water) and in some circumstances by taking prophylactic antibiotics

such as doxycycline.^{4,5} Treatment of an episode is by maintaining hydration with oral glucose electrolyte solution and, in severe cases, giving an antibiotic - either doxycycline or cotrimoxazole.⁶

Recent studies at ICDDRB and elsewhere have found that CPZ, a non-antibiotic, might be useful in the treatment of diarrhea due to an adenyl cyclase stimulating enterotoxin such as cholera toxin or E. coli LT.^{8,9,10,11} One paper found that CPZ also inhibits the secretion due to ST,¹² though others have not confirmed this. (unpublished data, Jan Holmgren). It seems that CPZ is able to inhibit the stimulation adenylate cyclase and hence decrease the levels of cyclic AMP; however, there may be other actions of the CPZ which also lead to a decrease in secretion since CPZ is able to decrease secretion due to dibutryl cyclic AMP as well. A clinical study in cholera patients have shown a marked decrease in purging rate in patients treated with CPZ¹¹ and another similiar study in patients with LT or LT/ST ETEC diarrhea is also planned.

Treatment of travelers diarrhea is a logical extension of the previous CPZ studies, since it would have obvious advantages over treatment with antibiotics. Though effective currently, antibiotic useage encourages

-3-

the emergence of antibiotic resistant bacteria. If a non-antibiotic, safe drug were available, it would provide the symptomatic relief which would benefit the patient and would do so without encouraging the resistant organisms.

3. Rationale: We plan to determine the efficacy of chlorpromazine in the treatment of travelers diarrhea. If successful, this would establish a safe, non-antibiotic treatment which would alleviate symptoms due to travelers diarrhea.

B. Specific Aims.

1. Determine the efficacy of CPZ in the treatment of travelers diarrhea with special reference to episodes due to ETEC.

C. Methods of Procedure.

Expatriates who have been in Dacca less than 3 months who develop acute watery diarrhea would be invited to attend the "travelers clinic". Patients, of either sex, would be considered for the study if they are

>18 years of age, have taken no Lomotil or other anti-peristaltic drugs, have taken no antibiotics and are suffering from acute watery diarrhea of less than 48 hours duration. Patients with a history of fever greater than 101^oF, blood and/or mucus in the stool, very severe cramps, or prolonged diarrhea (>48 hours) would be excluded. The prospective study patients would be given a pamphlet about travelers diarrhea and the study (enclosed). In addition the study nurse would discuss the study with the patient. If willing to participate and able to complete the follow-up, they will sign the consent form.

When admitted into the study the patients would fill out a questionnaire (enclosed) giving details of the episode before the clinic visit. They would then provide a fresh stool specimen for examination.

The patients would be randomized to one of 8 medications. 4 of which contain CPZ and 4 of which contain a placebo. The randomization will occur by draw from an envelope, and the code will remain blind - i.e. neither the patient nor the nurse will know whether

the drug was CPZ or placebo. A single dose of 1mg/kg will be given orally at the clinic. The patient will then take one form (the diarrhea diary) with him to completely record his symptoms on a 12 hourly basis until he is well. Also the nurse will maintain telephone contact with the patient during the 5 days of the study.

Five days after the initial visit the patient will return to the clinic for follow-up which will include 1) insuring that the diary diarrhea was filled accurately. 2) repeat stool exam. 3) treatment of any pathogens discovered in the initial specimens.

The initial questionnaire, nurses report and diarrhea diary (enclosed) will be used to analyze the clinical response, and this will be correlated with the stool microscopy and bacteriology (forms enclosed).

Handling of specimens: Each episode will be given a study number (T.C. 001, TC 002, etc) which will identify the forms and specimens as being from the travelers - CPZ study. Since patients would bring 2 stool specimens per episode the specimen would be labelled accordingly (TC 001 - 1 and TC 001 - 2, etc). The stool specimens would have a routine microscopic exam (with measurement of pH) and would be tested for bacterial pathogens including ETEC^{14,15} and campylobacter.

Data analysis. From the data forms a comparison will be made of two groups to insure comparability including age, sex, duration of diarrhea symptoms prior to clinic visit, number of diarrhea stools prior to clinic visit, prevalence of vomiting, stool white cell count, stool red cell count, and bacterial pathogens recovered. This comparison will use chi square and T test where appropriate.

The determination of efficacy will be determined comparing the duration of diarrhea symptoms, the frequency of stools per 12 hour period, the severity of cramps (graded subjectively) and the frequency of vomiting in the two groups. A dummy table of the expected clinical measurements is as follows:

Clinical effectiveness of chlorpromazine in the Treatment of Travelers Diarrhea.

	Placebo	CPZ
Duration of diarrhea after treatment(Hrs)	mean±SE	
Number of diarrhea stools after treatment.	mean±S.E.	

Placebo

CPZ

3. Frequency of stools per 12 hours after treatment.

Ist 12 hours period	mean±SE
2nd " " "	"
3rd " " "	"
4th " " "	"
5th " " "	"
6th " " "	"
7th " " "	"
8th " " "	"

4. Severity of Cramps*

a. Severe	%
b. Mod	%
c. Mild	%
d. None	%

5. Number with fever $>101^{\circ}$

6. Number with same pathogen at day 5

*defined on diary

The data analysis will be carried out for both ETEC and non ETEC travelers diarrhea. The sample size will be based however on only ETEC producing LT or LT/ST since the other causes of travelers diarrhea are so unusual that statistically meaningful analysis will not be possible. It is anticipated that 100 episodes of LT or LT/ST ETEC will be needed. This would mean that about 200 episodes would need to be treated. This assumes that some patients will not give sufficient follow-up and about 60% of episodes will be due to ETEC.

.. Since ETEC diarrhea generally produces a stool which is alkaline containing negligible numbers of fecal leukocytes, analysis of this sub-group with response to CPZ will also be carried out to test whether this rapid clinical test can predict response to treatment. Acid stools or stools containing fecal leukocytes represent a different mechanism of diarrhea,¹⁶ hence they would not be expected to respond to CPZ.

- D. Significance: This study should establish the usefulness of CPZ in the treatment of ETEC diarrhea in an out-patient setting. While the results are immediately applicable

to travelers diarrhea, they should also be of value to the treatment of other mild ETEC diarrhea.

E. Facilities Required:

1. The office and clinic space is already provided
2. Lab space is already provided
3. Hospital resources - nil
4. Animal resources - 800 specimens for infant mouse assay.
5. Logistic support - Rarely the study nurse will have to visit a patient for follow-up and will need transport.
6. Major items of equipment - none
7. Specialized requirements - CPZ and placebo.

F. Collaborative Arrangements

The study will be a collaborative study between ICDDRB (Dr Abu Eusof) and Johns Hopkins University Division of Geographic Medicine (Dr David Sack) who will be returning to Baltimore. The details of the collaboration are outlined in the memorandum of understanding between the two institutions.

G. Note on Finances of Travelers Clinic

Some of the expenses of the travelers clinic will be covered by an NIH grant for study of local immunity to enteric diseases (i.e. the nurses salary). Patients coming to the clinic will be charged for the services they receive including laboratory examinations. The payments received from this source could then be used to pay for one administrative assistant and one research assistant in clinical pathology.

SECTION III - BUDGET

A. DETAILED BUDGET

1. PERSONNEL SERVICES

<u>Name</u>	<u>Position</u>	<u>% of effort</u>	<u>Annual Salary</u>	<u>Project Requirement</u>	
				<u>Taka</u>	<u>Dollar</u>
1. Dr Abu Eusof	Investigator	20%	60960	12192	
2. Dr David Sack	Co-Investigator	10%	38000		3,800
3. Mrs Franco	Study Nurse	30%	5000		1,500
4. Mrs Boone	Study Nurse	30%	5000		1,500
5. Daniel Ascension	Admn. Assistant	30%	20700	6210	
6. Mizanur Rahman	Research Tech.	30%	19982	5994	
7. Shafi Ahmed	Sr. Research Tech.	30%	40884	12265	
8. Waseque Uddin Ahmed		5%	45312	2265	
9. A.K.M. Kibriya	Sr. Research Asst.	5%	55980	2799	
10. Animal House Tech.		10%	36000	1800	
11. Computer Programmer				800	
12. Key Puncher				500	
				<u>44825</u>	<u>6,800</u>

2. SUPPLIES

Stool cultures - 400 at Tk.40 each	16000
Stool microscopic exam at Tk.400 at Tk 20 each	8000
Stool cups	1000
Infant mouse assay - 800 assays @Tk.10 per assay	8000

3. EQUIPMENT - None

4. Hospitalization - None

5. Outpatient care - covered under personnel

6. ICDDR,B Transport - 100 miles @ per mile

7. Travel and Transportation of Persons - None

	<u>Project Requirement</u>	
	<u>Taka</u>	<u>Dollar</u>
8. <u>Travel and Transport of things</u>		
Transport of cultures		200
Transport of supplies		500
9. Rent, Communication, Utilities - None		
10. Printing, Reproduction	3000	200
11. Other - Computer time	1000	
12. Construction - None		
13. Indirect Costs 35%	28,288	2695
	<hr/>	<hr/>
	110,113	10395
	(US\$ 7,340)	

Tk. 15.00 = \$1 Total: \$17,735

Expected Income:

Tk 120 x 200 = Tk24,000 (US\$ 1,509)

BUDGET SUMMARY

<u>CATEGORY</u>	<u>TAKA</u>	<u>DOLLARS</u>
1. Personnel	44825	6800
2. Supplies	33000	
3. Equipment	-	-
4. Hospitalization	-	-
5. Outpatients	-	-
6. ICDDR,B Transport	-	-
7. Travel & Transportation	-	-
8. Travel & Transport of Things	-	700
9. Rent/Communication/Utilities	-	-
10. Printing/Reproduction	3000	200
11. Other - Computer time	1000	
12. Construction	-	-
13. Indirect Costs 35%	28288	2695
	<hr/>	<hr/>
Grand Total:	110,113	10395
	=====	=====

Tk. 15.00 = \$1

Total : US\$17,735

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REFERENCES

1. Merson, M.H., Morris, G.K., Sack, D.A., Wells, J.G., Creech, W., Feeley, J.C., Sack, R.B., Kapikian, A.Z., Gangarosa, E.J. Travelers' diarrhea in Mexico a prospective study. *N. Engl. J. Med.* 294:1299-1305, 1976.
2. Gonbach, S.L., et al. Travelers Diarrhea and toxigenic *Escherichia coli*. *N. Engl. J. Med.* 292:933-936, 1975.
3. Sack, D.A., Kaminsky, D.C., Sack, R.B., Wamola, I.A., Ørskov, R., Ørskov, I., Slack, R.G.B., Arthur, R.R., Kapikian, A.Z. Enterotoxigenic *Escherichia coli* Diarrhea of Travelers: A Prospective Study of American Peace Corps Volunteers. *J. Hopk. Med. J.* 141:63-70, 1977.
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9. Lonroth, I., et al. Chlorpromazine inhibits toxin-induced intestinal hypersecretion. *Med. Biol (Helsinki)*55:126-129, 1977.

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11. Rabbani, G.H., et. al. Chlorpromazine reduces fluid loss in cholera. *Lancet* i:410-412, 1979.
12. Abbey, D.M. Effect of Chlorpromazine on the secretory activity of *E. coli* heat stable enterotoxin. *Infect. Immun.* 26:1000-1003, 1979.
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14. Sack, D.A., Sack, R.B., Test for enterotoxigenic Escherichia coli using Y_1 adrenal cells in minuculture. *Infect. Immun.* 11:334-336, 1975.
15. Morris, G.K., Merson, M.H., Sack, D.A., Wells, J.G., Martin, W.T., Dewitt, W.E., Feeley, J.C., Sack, R.B., Bessudo, D.M. Laboratory investigation of diarrhea in travelers to Mexico: an evaluation of methods for detecting enterotoxigenic E. coli. *J. Clin. Microbiol.* 3:486-495, 1976.
16. Sack, D.A., et al. The role of carbohydrate malabsorption in determining the severity of rotavirus diarrhea (In preparation).

ABSTRACT SUMMARY

1. Adult expatriates with travelers diarrhea will be subjects for this study of the effectiveness of chlorpromazine in the treatment of travelers diarrhea.
2. Risks from the study are minimal but consist of the side effects of the drug chlorpromazine. These includes postural hypotension, drowsiness, liver function abnormalities, allergic reactions, and dyskinesias.
3. The patients will be warned about the potential for hypotension and drowsiness and will be cautioned not to drive or operate machinery.
4. The records will be kept in a locked cabinet in the clinic office. Computer identification will be by code number only and after data is entered into the computer, the original data forms will be destroyed.
5. Informed consent will be obtained.
6. There will be a medical history taken.
7. The individual will gain through treatment of his illness and may possibly benefit from a therapeutic effect of the drug. Society will gain if a new form of therapy is developed for travelers diarrhea which does not use antibiotics.
8. Stool specimens will be obtained.

PERMISSION FORM - TRAVELERS DIARRHOEA - CHLORPROMAZINE STUDY

The International Centre for Diarrhoeal Disease is carrying out a study to determine the effectiveness of a medication called Chlorpromazine for travelers Diarrhea. Chlorpromazine is usually used as a tranquilizer however, recent studies have shown it to be effective in treating severe watery diarrhea due to cholera. We are now testing it to see if it is effective in treating travelers diarrhea as well. If you agree to join the study we will ask you 1. Fill out an initial questionnaire, 2. Submit a stool specimen 3. Keep a "diarrhea diary" for 5 days 4. Return for a follow-up visit in 5 days and submit a follow-up stool specimen then. We will also give you a single dose of the study medication. This study medication will be either chlorpromazine (the active drug) or a similiar appearing placebo medication. Neither you nor the investigators are to know which you are taking until after the code is broken in order to keep the information objective.

A common side effect of chlorpromazine is some sleepiness. This means that you should not drive or operate machinery during the next 24 hours. Other side effects of chlorpromazine are extremely rare when taken as a single low dose like this but include low blood pressure when changing position, liver function abnormalities, and allergic reactions (in persons allergic to the medication).

You do not have to participate in the study. If you choose not to participate we will still treat your diarrhea with standard medical treatment. If you wish to withdraw from the study, you may do so. This will not affect the medical care you receive.

Your records will be kept confidential. You may ask questions concerning the study at any time.

If you agree to participate in the study, please sign your name here.

Date:

INFORMATION REGARDING TRAVELERS DIARRHEA

AND CHLORPROMAZINE

Travelers diarrhea is a very frequent problem among visitors to developing countries such as Bangladesh. About 60% of travelers to Dacca have at least one episode of diarrhea during the first month in Dacca. This is caused by an infection with a bacterial germ found in contaminated food and/or water. Theoretically, one could eliminate the possibility of diarrhea by sterilizing all the food and water before they consume it. In reality however, one just has to be as careful as is reasonable and accept some risk.

The most common bacteria causing travelers diarrhea is one called enterotoxigenic E. coli. The enterotoxigenic E. coli (ETEC) are similar to the normal E. coli which everyone has in their intestine except that this one is able to produce a toxin which attaches to the lining cells of the intestine. Through some biochemical changes in the cells the toxin causes them to secrete fluid into the intestine. The infection with ETEC is therefore not like other infections where there is invasion of the bacteria into the tissue. With ETEC, all the symptoms are related to the toxin's action on the cells lining

the intestine. Recently we and other scientists elsewhere have found that a drug called chlorpromazine will reverse the action of the toxin. This was first discovered in laboratory experiments and then in animals (who may also suffer from ETEC diarrhea). This was followed-up by a study at ICDDRB which showed that chlorpromazine is successful in decreasing the secretion in patients with cholera - a disease which produces a similar biochemical change in the intestinal cells. We are therefore now encouraged to test whether the drug will be effective in patients with travelers diarrhea.

The use of a medication like chlorpromazine for diarrhea due to a bacterial infection is a new approach. Usually infections are treated with antibiotics to kill the bacteria and this approach sometimes works in travelers diarrhea. However with time, bacteria may become resistant to antibiotics. With chlorpromazine the antibiotic sensitivity patterns would not be important since the drug would be working only to neutralize the effect of the toxin rather than kill the bacteria.

Actually patients with severe watery diarrhea do not need either an antibiotic or an anti-secretory medication like chlorpromazine. With time the body is able to clear

the germ from the intestine. During the diarrhea however it is important to avoid dehydration since this is the main feature of diarrhea which can lead to serious complications. In very severe diarrhea, such as cholera, intravenous fluids are sometimes necessary to prevent dehydration. In less severe diarrhea, such as the usual travelers diarrhea, dehydration can be prevented simply by drinking a special sugar salt solution. This special solution is specially formulated to replace the fluids being lost. You should drink approximately 1 glass (about 200ml) of solution for each diarrheal bowel movement you have. This will help you avoid much of the weakness and fatigue associated with dehydration, but it will not of course stop the diarrhea.

If you decide to participate in the study on chlorpromazine, we will ask you to fill out some forms ; will ask you to submit a stool specimen for testing and will ask you to return for follow-up 5 days after the first visit. It is very important that you complete the forms accurately since this is how we will draw conclusions regarding the usefulness of the treatment with chlorpromazine. In this study there is a 50% chance that you will receive the real drug and 50% chance you will receive a placebo. In both cases we will give you the oral

rehydration packet which is the "standard" treatment for watery diarrhea. Please DO NOT take any other medication especially DO NOT take Lomotil, Aspirin or an antibiotic. If your stool exam indicates the need for an antibiotic we will prescribe that for you.

Please feel free to call or come back to the clinic if you have any question concerning your illness or the study. The clinic number is 303-593, 300171-8/34

DIARRHEA DIARY: TRAVELERS DIARRHEA - CHLORPROMAZINE STUDY

Since you have taken a study medication for your diarrheal illness, we would like to obtain a accurate and complete record of your response to the medication. Therefore, we would like you to fill out this record of symptoms. For convenience the time periods on the record are 12 hours blocks of time 12 noon to 12 midnight, etc. Its very important that you fill out the record each day since its easy to forget. May be you could keep the form in the bathroom.

Study no _____
(1-3)

Name _____ Patient no TC _____
(4-6)

Date medication given _____ Time given _____ 24 hr clock)
day mo year (7-12) (13-16)

Date											
	Time	0-12	12-24	0-12	12-24	0-12	12-24	0-12	12-24	0-12	12-24
# stools		17	18	19	20	21	22	23	24	25	26
description of stools*		27	28	29	30	31	32	33	34	35	36
Severity of cramps**		37	38	39	40	41	42	43	44	45	46
#Vomiting episodes***		47	48	49	50	51	52	53	54	55	56
Feverish feeling yes/no		57	58	59	60	61	62	63	64	65	66
If, yes, highest temp...											
Changed plans due to illness yes/no		67	68	69	70	71	72	73	74	75	76

*1 - like water
2 - very runny
3 - loose
4 - formed
5 - hard
6 - bloody
7 - other
0 - none

**0-no cramps
1-noticeable cramps
2-moderately severe cramps, but can carry on
3-severe cramps which make you double up

***if none put "0"
fever 77 _____ *1=y, 2=n

Card No 02

STOOL MICROSCOPIC REPORT - TRAVELERS DIARRHEA - CPZ STUDY

Study Number (1-2)

Specimen Number

TC 4-7

Appearance 1=watery 2=very loose, with color
 3=soft 4=formed 5=hard
 6=bloody 7=other 0=none

 8

pH (measured)

 9-10

gross blood 1 = yes 2 = no

 11

gross mucus 1 = yes 2 = no

 12

guaiac (indicate positivity on a 0 to 4 scale)

 13

Fecal pus cells (mean of range)

 14-15

Fecal rbc (mean of range)

 16-17

Fecal macrophages (mean of range)

 18-19

Neutral fat (indicate positivity on a 0 to 4 scale)

 20

parasitic exam

ameba cysts 1 = yes 2 = no

 21

ameba trophs 1 = c̄ rbc 2 = without rbc 3 = neg

 22

giardia cysts 1 = yes 2 = no

 23

giardia trophs 1 = yes 2 = no

 24

trichomonas 1 = yes 2 = no

 25

hookworm 1 = yes 2 = no

 26

Ascaris 1 = yes 2 = no

 27

strongyloides 1 = yes 2 = no

 28

pinworm 1 = yes 2 = no

 29

other worm 1 = yes 2 = no

 30

Card No 04
 79-80

FOLLOW-UP VISIT

Date of Return Visit day/mo/yr _____
(54-59)

Diary checked _____ 1 = found satisfactory
60 2 = deficiencies corrected
3 = diary not reliable
4 = no diary

What is the patients subjective assessment of the effectiveness of the study drug? _____ 61

1. It worked well.
2. It seemed to help at first but then the effect wore off.
3. It didn't help.
4. Other

True or false - I would rather have had the diarrhea than _____ 62
the side effects of the study drug. 1 = T, 2 = F

How do you feel now in relation to your diarrheal illness?

1. I am well now _____ 63
2. I am nearly well now
3. I am about the same
4. I am worse

Follow-up stool specimen obtained 1 = y 2 = n _____ 64

Number of specimen TC _____ 65-68

Date of specimen same as follow-up y = 1 n = 2 _____ 69

Patient did not return for follow-up
1 = returned 2 = did not returned _____ 70

Number of times this patient has been included in this study with previous episodes of diarrhea _____ 71

IF yes, what was episode numbers

STOOL BACTERIOLOGY REPORT - TRAVELERS DIARRHEA - CPZ STUDY

Study No 1-3

Specimen Number TC 4-7

Salmonella	1=yes	2=no	<u>8</u>
Shigella flex	1=yes	2=no	<u>9</u>
Shigella Sonnei	1=yes	2=no	<u>10</u>
Shigella boydii	1=yes	2=no	<u>11</u>
Shigella dys I	1=yes	2=no	<u>12</u>
Shigella dys ≥II	1=yes	2=no	<u>13</u>
Yersinia	1=yes	2=no	<u>14</u>
Aeromonas	1=yes	2=no	<u>15</u>
V. cholerae	1=yes	2=no	<u>16</u>
NAG Vibrio	1=yes	2=no	<u>17</u>
Campylobacter	1=yes	2=no	<u>18</u>
ETEC 1=LT/ST, 2=ST only 3=LT only 0=no			<u>19</u>
If ETEC positive, how many colonies positive out of 5? Put "8"= pool only positive.			<u>20</u>

Sensitivity pattern

Isolate number TC 21-24 25-26 (25-26=# from above li)

Tet	<u>27</u>	Chloro	<u>30</u>	Gent	<u>33</u>
Amp	<u>28</u>	Sulfa	<u>31</u>	Septra	<u>34</u>
Strep	<u>29</u>	Neo	<u>32</u>		

Isolate number TC 35-38 39-40

Tet	<u>41</u>	Chlor	<u>44</u>	Gent	<u>47</u>
Amp	<u>42</u>	Sulfa	<u>45</u>	Septra	<u>48</u>
Strep	<u>43</u>	Neo	<u>46</u>		

Serotype of ETEC

O 44-51 K 52-54 H 55-57

Card No 05
79-80

TRAVELERS DIARRHEA - CHLORPROMAZINE INITIAL QUESTIONNAIRE

This questionnaire is designed to accurately record the symptoms you have had which have now brought you to this clinic. While some questions may seem obvious, it is necessary for us to have an accurate and complete record of your illness.

	Office Use Only
Study number _____	(1-3)
Name _____	Patient number (office use only) TC _____
	4-6
Age _____	7-8
Sex _____	m=1, f=2.
Duration in Bangladesh _____ days	9
Have you visited other developing countries on the way to Bangladesh? _____	10-11
List _____	y=1, n=2
How many months ago did you leave your home country? _____	12
Today's date _____	13-14
	day/mo/yr
Today's time _____ AM, PM. (circle)	15-20
	24hr clock
When did your illness begin	21-24
Date _____	25-30
Time _____	31-34
What was the first symptom (circle)	35
1. nausea and/or vomiting	
2. Cramps and/or diarrhea	
3. Fever	
4. Respiratory symptoms	
5. # 1 and # 2 simultaneously	
6. other _____	
When did the diarrhea begin	
Date _____	36-41
Time _____	42-45
How many times did you pass diarrhea stool the first 12 hours of your illness? _____	46-47
the second 12 hours ? _____	48-49
the third 12 hours ? _____	50-51
the fourth 12 hours ? _____	52-53
Have you changed your plans because of your illness _____	y=1, n=2.
Have you stayed in bed _____	54
	y=1, n=2.
Have you taken any Lomotil or similiar drug for your illness? _____	55
	y=1, n=2-
	56

(over)

Office Use Only

Have you taken any antibiotic during the last week _____ name _____

57 y=1,n=2

Have you taken any other medication during the last week _____ name _____

58 y=1,n=2

Have you seen blood in your stool _____

59 y=1,n=2

Have you seen mucus in your stool _____

60 y=1,n=2

Have you had tenismus _____

61 y=1,n=2

61

(Tenismus is a painful spasm in the rectum after having a bowel movement).

Have you had abdominal cramps which double you up? _____

62 y=1,n=2

Have you had cramps which are not that bad but are painful _____

63 y=1,n=2

Have you had cramps which are noticeable but not bothersome _____

64 y=1,n=2

Have you had fever >101° _____

65 y=1,n=2

Have you had fever between 99 and 101° _____

66 y=1,n=2

Have you had chilly feelings _____

67 y=1,n=2

Have you had shaking chills _____

68 y=1,n=2

Have you had ache all over feeling _____

69 y=1,n=2

Are the others in your group with a similiar illness? _____

70 y=1,n=2

70

How would you describe your diarrheal stool

- 1. like water _____
- 2. very runny _____
- 3. loose _____
- 4. formed _____
- 5. hard _____
- 6. bloody _____
- 7. other _____

71

(med given) _____
72

(card no) _____
01
79-80