tachment 1.

REVIEW BOARD ON THE USE OF HUMAN VOLUNTEERS
CRL

Date_____

rincipal Investigator_____ Trainee investigator(if any)_____

pplication No 77-017 Supporting Agency(if Non-CRL)_____

itle of study Survival vs Mucosal Electrolyte Oral Solution-Alkaline Diarrhea of Infants

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 possibly 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

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 Board for review.

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

Principal Investigator

Trainee

Please return 2 copies of entire protocol to Chairman, Review Board on Use of Human Subjects

Attachment 1a

INFORMATION TO INCLUDE IN ABSTRACT SUMMARY

The Board will not consider any application which does not include an abstract summary. The abstract should summarize the purpose of the study, the methods and procedures to be used, by addressing each of the following items. If an item is not applicable, please note accordingly:

1. Describe the requirements for a subject population and explain the rationale for using in this population special groups such as children, or groups whose ability to give voluntary informed consent may be in question.

2. Describe and assess any potential risks - physical, psychological, social, legal or other - and assess the likelihood and seriousness of such risks. If methods of research create potential risks, describe other methods, if any, that were considered and why they will not be used.

3. Describe procedures for protecting against or minimizing potential risks and an assessment of their likely effectiveness.

4. Include a description of the methods for safeguarding confidentiality or protecting anonymity.

5. When there are potential risks to the subject, or the privacy of the individual may be involved, the investigator is required to obtain a signed informed consent statement from the subject. For minors, informed consent must be obtained from the authorized legal guardian or parent of the subject. Describe consent procedures to be followed including how and where informed consent will be obtained.

   (a) If signed consent will not be obtained, explain why this requirement should be waived and provide an alternative procedure.

   (b) If information is to be withheld from a subject, justify this course of action.

6. If study involves an interview, describe where and in what context the interview will take place. State approximate length of time required for the interview.

7. Assess the potential benefits to be gained by the individual subject as well as the benefits which may accrue to society in general as a result of the planned work. Indicate how the benefits outweigh the risks.

8. State if the activity requires the use of records (hospital, medical, birth, death or other), organs, tissues, body fluids, the fetus or the abortus.

The statement to the subject should include information specified in items 2,3,4 and 7, as well as indicating the approximate time required for participation in the activity

Rcd. Sept. 5, 77
77-017

SECTION I - RESEARCH PROTOCOL

1) Title: Sucrose vs Glucose Electrolyte Oral Solution - In the Diarrhea of Infants.

2) Principal Investigator: David A. Sack, M.D.

3) Starting Date: July, 1977

4) Completion Date: December, 1978

5) Total Direct Cost: $36,939

6) Abstract Summary: (250 words or less)

We plan a double blind trial to compare the effectiveness of an oral glucose electrolyte solution (WHO formula) with sucrose electrolyte solution in the hydration of infants with cholera, rotavirus, E.coli and other severe watery diarrheal diseases in Bangladesh. Approximately 100 patients with cholera, 100 patients with rotavirus and 100-200 patients with other watery diarrheal diseases, with ages between 3 months and 4 years will be admitted into the study. Because of the seasonal nature of many of the diarrheal diseases, most of the cholera cases will be selected during the cholera season (October, November) and most of the other cases will be selected during January, February and March. The primary determinant of failure of a treatment will be the need to begin (or resume) I.V. hydration; however, other factors such as absorption of sugars and patient's acceptance of therapy will also be examined.

7) Reviews: (leave blank)

a) Research Involving Human Subjects: _____

b) Research Committee: _____

c) Director: _____

d) BMRC: _____

e) Controller/Administrator: _____

SECTION II - RESEARCH PLAN

A. INTRODUCTION

1. Objective: To help eliminate morbidity and mortality resulting from diarrheal disease in infants by developing effective, economical oral hydration fluid.

2. Background: The complications and mortality resulting from syndromes of watery diarrhea are almost exclusively limited to those of dehydration. The primary therapy therefore in the watery diarrhea syndromes is that of rehydration and maintenance hydration. In severe diarrheal states this can only be accomplished with intravenous fluids; however, most diarrheal episodes can be managed successfully with oral therapy. Documentation of the effectiveness of oral GE solution has been established in Calcutta, Dacca as well as in the United States, in both cholera and non-cholera diarrhea.

The rationale for using an oral electrolyte-solution is as follows. In cholera and E.coli diarrhea the diarrhea results from an activation of cyclic AMP with resulting massive outpouring of fluids and electrolytes from the mucosal cells of the small bowel. Absorption however, remains normal throughout the small intestine.

There are three primary modalities through which electrolyte and water are absorbed by the small intestine:

1) the sodium pump system which carries water along with sodium.
2) Passive absorption of water.
3) Glucose facilitated absorption.

It is this glucose facilitated absorption which is utilized in the oral glucose-electrolyte rehydration therapy.

The advantages of oral solution for the treatment of watery diarrheal syndromes are several:

1) The volume of sterile intravenous solution is greatly decreased. This is of very particular importance in the areas where intravenous solutions are limited either by facilities or by economic considerations.

2) Intravenous solutions may be avoided altogether in some patients thus avoiding complications of intravenous infusions.

3) This may be a very practical form of therapy in which hydration canbbe carried out in the home without the use of hospitals and it is especially useful in epidemics of watery diarrhea where logistics probibits wide use of intravenous solutions.

Although the oral glucose electrolyte solution has been documented to be effective in both cholera and non-cholera diarrhea, the experience with this solution has been primarily carried out in patients above the age of two years. The epidemiology of watery diarrheal syndromes however, is that infants less than three years of age are the persons who are at highest risk of diarrheal disease. In many parts of the world the etiologic agent responsible for the watery diarrheal syndrome in this age group has been shown to be the rota-virus. This virus has also been demonstrated in Bangladesh, however the relative importance of this pathogen has not yet been established here. The pathogenesis of rota-virus infection, unlike cholera or E.coli, does involve invasion of mucosal cells by the pathogen. We cannot assume therefore, that the absorption, especially the glucose facilitated absorption, is normal in the rota-virus infection as it is in E.coli

and cholera diarrhea. In fact, absorption of d-xylose and lactose have been found to be abnormal in infections of the Norwalk agent, another viral diarrhea. It is therefore necessary to establish the efficacy of the GE solution in diarrhea caused by rota-virus.

Recently a study was carried out in Dacca comparing the effectiveness of the sucrose-electrolyte solution with the glucose-electrolyte solution in patients over the age of six years with watery diarrhea. In this study the two solutions were shown to be equally effective. However, because of the age group studied in this previous protocol, we do not have information on the efficacy of the sucrose-electrolyte solution in infants especially those infants with rota-virus infection.

In order for sucrose-solution to be effective the sucrose must first be hydrolized by a sucrase in the small intestine, thereby releasing free glucose and fructose. Glucose is then utilized in the glucose facilitated transport. It is known however, that diarrheal syndromes are often associated with a temporary decrease in disaccharidase levels in the small intestine; therefore, it is possible that sucrose would not be effective especially in rota-virus. The importance of this question is a very practical one; since in many countries of the world, glucose is not available, while sucrose is nearly always available. In those situations where glucose is not available; sucrose, if effective, would be very useful in the oral hydration therapy solution.

Several technological advances in the last few years have made the study possible at this time, where it was not possible earlier. These

advances consist primarily of the ability to detect the rota-virus antigen as well as E.coli heat labile toxin by means of an enzyme linked immunosorbent (Elisa). This assay now makes possible the study of large numbers of cases of diarrhea while determining the responsible etiologic agent.

3. Rationale: It is necessary to determine the efficacy of both GE and SE in the diarrhea of infants with respect to etiologic diagnosis so that a decision can be formulated as to the adequacy and limitations of these solutions as oral hydration solutions in this age group.

B. SPECIFIC AIMS

1. To determine the efficacy of GE in the hydration therapy of infants less than four years of age with rota-virus diarrhea.

2. Compare the effectiveness of a SE with GE in the hydration of patients with diarrhea due to rota-virus, cholera and E.coli as well as diarrhea of unknown etiology.

C. METHODS OF PROCEDURE

1. Patient population. A sample of patients - 3 months to four years of age, weighing 1 Kg being admitted to the Cholera Hospital [illegible] of uncomplicated acute watery diarrhea (1 week) who have not received previous antibiotic during last two weeks and whose parents have given informed consent will be studied. Because some of the diseases which will be studied are seasonal, we will need to sample patients over a long period of time in order to have adequate numbers

of patients with rotavirus, cholera and E.coli diarrhea. We plan therefore, to admit patients into the study during two study periods; one corresponding to the "cholera season" and one the "non cholera season".

Cholera Season Study. When the apparent cholera season begins, during the fall of 1977 (approximately October), we will accept the first four patients admitted to the hospital each day who meet the above criteria. Patients will continue to be admitted to the study until 100 culture proved cholera patients have been included in the study.

Non Cholera Season. Beginning during the 1st week in January 1978 the study will resume, again selecting the first 4 patients each day who meet the above criteria. Patients will continue to be admitted to the study until 100 patients with rotavirus diarrhea have been included.

It is expected that a total of 300 to 400 patients will be included in the study in total in order to insure 100 cases of each of cholera and rotavirus. Comparison of the two treatment solutions will be by etiology and severity, but not by season so that patients with rotavirus admitted during the cholera season would be included with the rotavirus patients admitted in February. Likewise, patients with cholera admitted in February would be included in the cholera patients admitted in November.

Clinical Information. All patients will receive a standardized physical

examination including an admission weight. Physical examination will note specifically signs of dehydration. Blood will be drawn for a CBC electrolytes, blood sugar, creatinine, specific gravity, and an acute sera for antibody determination. A stool specimen will be obtained for culture, for microscopic examination, for sodium and potassium determination, for sugar determination, and two aliquots of stool will be frozen (to be examined for rotavirus antigen and heat-labile enterotoxin). Urine will be obtained for routine urinalysis, for sodium, potassium, osmolarity and specific gravity.

Treatment of Patients. Each child will be stratified as to the clinical degree of dehydration (moderate or severe) and randomized in a double blind manner to one of two treatment groups.

Group I (Glucose-Electrolyte Solution) will be treated as follows. The initial replacement therapy for patients who are severely dehydrated will be by intravenous fluid using standard I.V. solutions (70 ml/Kg over 1 hour). The I.V. will then be removed. Oral fluid will begin when tolerated to complete the rehydration (30 ml/Kg over 4 hours). Initial hydration for moderately dehydrated patients will be with oral fluid alone (70 ml/Kg over 4-6 period).

Maintenance Therapy of Group I will be by ad lib oral hydration using GE to replace stool losses. A goal for hydration will be to replace oral solution on an approximately one to one and a half basis, volume for volume. Stool passed during the initial rehydration period will also be replaced during this time.

Group II (Sucrose-Electrolyte Solution) will be treated exactly as Group I except that sucrose will be substituted for glucose in this solution.

Fluids to be used will be as follows:

Glucose Electrolyte Solution		Sucrose Electrolyte Solution	
Na^+	90 meq/liter	Na^+	90 meq/liter
K^+	20 meq/liter	K^+	20 meq/liter
Cl^-	80 meq/liter	Cl^-	80 meq/liter
HCO_3	30 meq/liter	HCO_3	30 meq/liter
Glucose 111 mM/liter		Sucrose 111 mM/liter	
which is made by:		which is made by:	
NaCl	3.5g/liter	NACl	3.5g/liter
$NaHCO_3$	2.5g/liter	$NaHCO_3$	2.5g/liter
KCl	1.5g/liter	KCl	1.5g/liter
Glucose	20g/liter	Sucrose	40g/liter

Follow up evaluations will be made as shown on the enclosed chart.

Maintenance replacement therapy will continue until the diarrhea stops. This is defined as a 24-hour period during which no watery stool has been passed. Oral feedings may begin at 12 hours. Breast feeding may resume whenever the baby is able.

Antibiotics will not be used unless specifically indicated. Intake and output records will be maintained on a 4 hourly basis during the

first 4 hours, then every 8 hours using cholera cots or ileostomy bags. If children are vomiting, oral fluids will be given by small amounts frequently: however, nasogastric tubes will not be used for vomiting. They may be used however, to allow patients to sleep if necessary. All oral intake will consist of the oral solution for the first 12 hours (except for breast milk), then water will be available ad lib. Patients will be discharged roughly 24 hours after diarrhea stops.

Failure of the oral solution will be either a failure to rehydrate or maintain hydration, or failure to maintain electrolyte balance. Failure of hydration will be based on objective criteria which will require the use of I.V. therapy (for moderate dehydration). Decision to use (or resume) I.V. therapy will be based on the following.

1. Failure of initial hydration; that is, failure of the patient to take oral fluid in quantity to match the estimated initial dehydration within 6 hours of admission, and associated with other clinical and laboratory signs (e.g. fall in body weight, poor skin turgor, rising pulse rate, increasing plasma specific gravity).
2. Failure to maintain hydration as shown by an increase in pulse rate, decrease in pulse volume, loss of body weight and an increase in plasma specific gravity of $\geq$ 1.029.
3. Deterioration of the general condition of the patient from the time of admission.

Patients who are restarted on I.V. fluids will again be tried on the oral-electrolyte solution which they previously received.

If electrolyte imbalance develops during therapy (Na $<$ 125, $>$ 155; K $<$ 2.5, $>$ 5.0) patients will be discontinued from the study and considered a treatment failure.

Patients will be asked to return 10-14 days after discharge for repeat serum specimen.

Special Lab. Studies:

Microbiology - E.coli from the admission stool culture will be tested for heat labile enterotoxin using the adrenal cell assay (or Elisa assay), and for heat stable toxin using the infant mouse assay. Antibodies to heat labile toxin will be determined by the microtiter adrenal neutralization assay.

Rotavirus antigen from stool will be determined using an Elisa assay. Antibodies to rotavirus will be determined using a complement fixation test.

Biochemistry - Stool sugars will be determined by measuring reducing substances in the stool, before and after hydrolysis, using clinitest tablets.

After the study is completed it should be possible to compare the sucrose with the glucose groups as follows:

1) Admission values: objective evidence of the severity of the disease should be same in both groups. Pathogens isolated from both groups should be the same.
2) Failure of oral fluids: defined as necessitating return to intravenous fluids or dropping patient from study because of electrolyte abnormality.

3) Duration of diarrhea.

4) The volume of diarrheal stool.

5) The amount of fluids given, both intravenous and oral.

6) Any adverse reactions during therapy.

7) Ease of fluid administration, including acceptance of oral fluid by patients.

Because many of the etiologic agents causing watery diarrhea are seasonal in nature this study will need to be carried out over a several months time period, or until there are 50 patients in each of the diagnostic categories (rotavirus, cholera) treated with each oral fluid regiment.

Randomization to either GE or SE will be done in a double blind manner. Mr Akbar Ali, Biochemistry Branch Chief, will prepare the two solutions and mark one solution "A", the other "B" for each one week treatment period. The code for "A" and "B" will be changed randomly between treatment periods. Prospective stratification of patients will be by degree of dehydration; however, stratification by etiologic agent will be by retrospective analysis. The data will be transferred to IBM cards for data storage and analysis.

D. SIGNIFICANCE

From the results of this study, it should be possible to determine the efficacy of the sucrose-electrolyte solution in the treatment of watery diarrhea, and to determine the efficacy of both glucose and sucrose electrolyte solutions in rotavirus diarrhea. This is important in the treatment of watery diarrheal syndromes throughout the world, especially in rural or under-developed countries where medical facilities are limited.

E. FACILITIES REQUIRED

1) Office for principle investigator. Office for study ward physicians in the ward area.

2) Laboratory space: the routine bacteriology, biochemistry and immunology laboratories will be utilized. In addition one laboratory will be necessary for the development of the Elisa assay for rota-virus and for testing of specimens for rota-virus and enterotoxigenic E.coli heat labile toxin. (See protocol Seaton, et. al. Development of Elisa).

3) Hospital Resources - the study ward will be used. Maximum of 35 hospital beds will be used during each study period. [redacted]. Study physicians will need to be present on the ward 24 hours per day during each study period to admit new patients and monitor therapy. A study nurse will be necessary 24 hours/day during the study periods.

It should be noted that these patients would be hospitalized regardless of the study, and no "extra" patient days are planned.

4) Animal Resources - E.coli from approximately 300 specimens will be tested for heat stable toxin which will require approximately 5400 infant mice.

5) Logistical Support - We will need assistance from the epidemiology Branch to help secure the convalescent serum specimen. Also 4 hours of computer time is anticipated.

6) Major items of equipment - A colorimeter suitable for microtiter plates will be needed in this study. This is included in a separate protocol.

7) Other specialized requirements -- The two oral solutions will be prepared by biochemistry branch.

Sucrose vs Glucose Study

Patient Name _____

Hosp. Number _____

Study Number [1 2 3] [A] [4]

Date of Admission [ ] day [ ] mo. [ ] yr [6 7] [8 9] [10 11]

Time of Admission [13 14] [15 16]

Age [ ] [18 19] months

Duration of diarrhea [21 22] hours

Description of stool [24] (1 watery, 2 liquid, 3 soft, 4 formed, 5 dysentery)

Vomiting [26] (1 yes, 2 no)

Oral Solution [28] (A 1, B 2, C 3, D 4)

Initial Clinical Assessment (to be completed on admission)

Dehydration [30] (1 severe (10), 2 mod-sev (7.5), 3 mild (5), 4 not apparent)

Rehydration fluid requirements [32 33 34 35] I.V. (ml.)

[37 38 39 40] P.O. (ml.)

Admission Weight [42 43] . [45] Kg.

Discharge Assessment

Stool Output during first 24 hours [47 48 49 50] ml/Kg

Total Diarrheal stool [52 53 54 55] ml/Kg

Total I.V. fluid given [57 58 59 60] ml/Kg

Oral solution used [62 63 64 65] ml/Kg

Overall assessment [67] (1 succeeded, 2 failed)

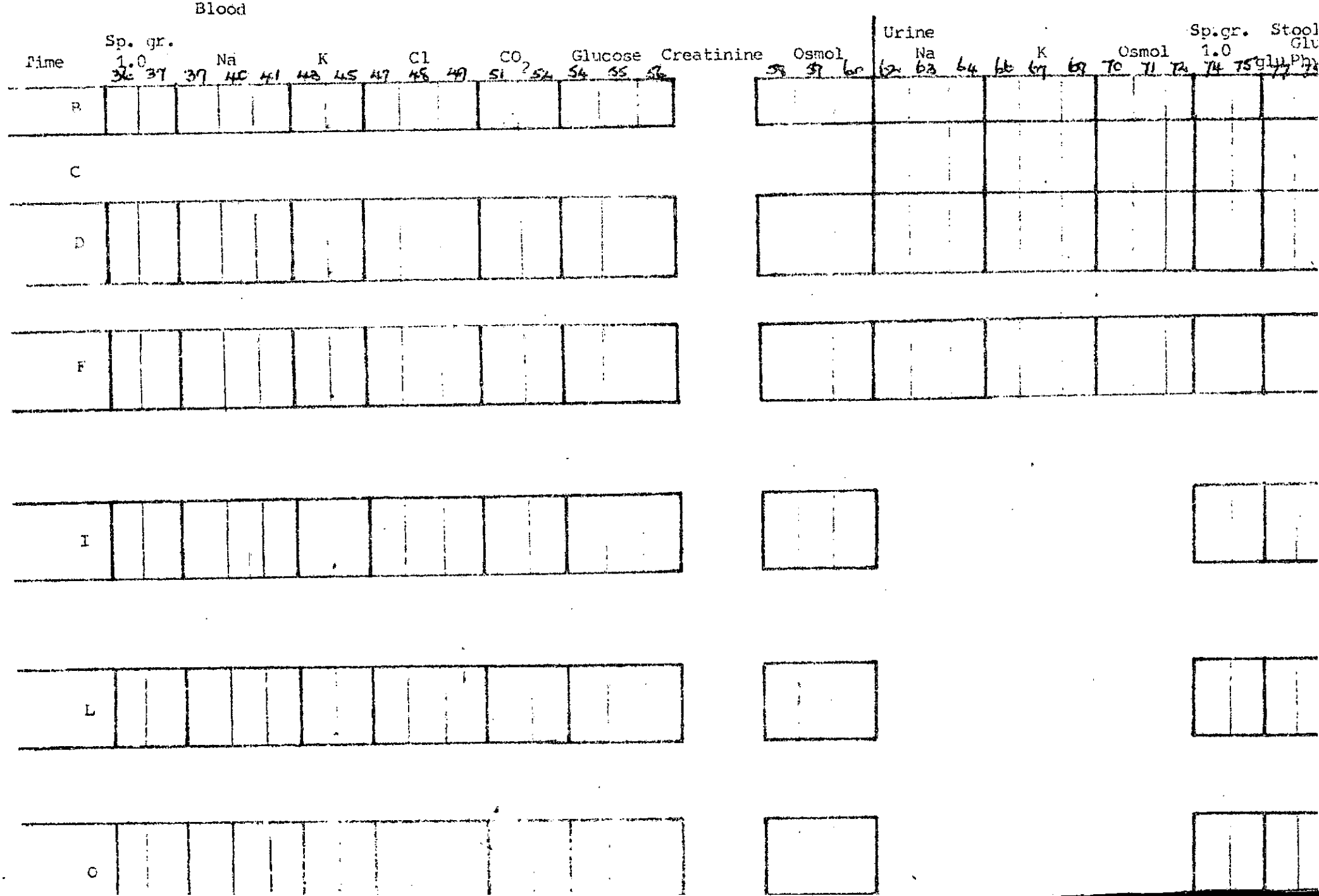
Patient Number [1 2 3]

Date	Hours from Admn	Study Schedule	5 Eyes	6 Skn	7 MM	9 10 12 13 14 15 Body Wt(kg)	P	BP	R	17 Pat Acc	20 21 22 Stool per period	OUTPUT cum stool	23 stl des	Ur	25 26 Vomit	28 29 30 32 33 34 Input I.V.	PO SOL	Cum	PO other
B	0																		
C	4	CBC stool sp gr glucose																	
D	8	Elec stool osmol glucose sp. gr. glucose																	
E	16																		
F	24	sp. gr. stool Elect. Rm107 glucose osmol glucose																	
G	32																		
H	40																		
I	48	sp.gr. stool elect Rm107 glucose glucose osmol																	
J	56																		
K	64																		
L	72	sp. gr. stool elect Rm107 glucose glucose osmol																	
M	80																		
N	88																		
O	96	sp. gr. stool elect Rm107 glucose glucose osmol																	

* 1 = normal
2 = mild dehydration
3 = severe dehydration

** 1 = needs IV replacement fluid
2 = PO

*** 1 = watery
2 = liquid (stains container)
3 = soft
4 = formed


Blood
Time
Sp. gr. 1.0
Na
K
Cl
CO2
Glucose
Creatinine
Osmol
Urine
Na
K
Osmol
Sp.gr. 1.0
Stool
B
C
D
F
I
L
O

Patient identification [ ] [Z] (1 2 3 | 4)

Admission Single Lab. Values

Blood

- Hct [ ] (6 7)
- WBC [ ] (9 10 11 12 13)
- Creatinine [ ] (15 17)

Urinalysis [ ] (19) 1 - normal, 2 - abnormal

Stool

nE [ ] (21 22) rbc/hpf

[ ] (24 26) fecal leukocytes/hpf

[ ] (27) Giardia (1 - yes, 0 - no)

[ ] (28) Ameba (1 - cysts only, 2 - trophs, 3 - trophs with rbc, 0 - neg.)

[ ] (29) Trichomona (1 - pos., 0 - neg.)

[ ] (30) Trichuris

[ ] (31) Hookworm

[ ] (32) Ascaris

[ ] (33) F.buski

[ ] (34) Other _____

Stool Chemistry

Na [ ] (35 36 37)

K [ ] (39 40 41)

Cl [ ] (43 44 45)

CO_2 [ ] (48 49 50)

Osmolality [ ] (52 53 54)

Darkfield [ ] (36) 1- pos., 0 - neg.

Culture [ ] (57) Vibrio (1 - pos., 0 - neg.)

[ ] (58) NCV

[ ] (59) Shig. (0 - neg., 1 - S. dys. I, 2 - S. dys. II, 3 - S. flex. 4 - S. boyd, 5 - S. sonnei

[ ] (60) Salmonella

[ ] (61) E.coli (0 - neg., 1 - LT, 2 - ST, 3 - LT-ST)

[ ] (62) other pathogen _____

Stool Antigen [ ] (64) Rotavirus (0 - neg., 1 - pos.)

[ ] (65) LT (0 - neg., 1 - pos.)

SECTION III

1. Personnel Services

Name	Position	% of Effort	Annual Salary	Taka	Dollars
Dr David Sack	Principal Investigator	30%	$ 34,750		10,425
Dr Shiraz	Co-Investigator	20%	Tk.36,384	7,277	
Dr Rabbani	"	20%	Tk.27,084	5,417	
Dr Asma	"	20%	Tk.27,084	5,417	
Dr Brown	"	10%	$ 20,000		2,000
Additional Study Physician	"	20%	Tk.27,084	5,417	
Epidemiology Technician		25%	Tk.20,484	5,121	
8 Study Nurses	Study Nurse	25%	Tk.16,284	32,568	
Akbar Ali	Study Technologist	10%	Tk.32,076	3,208	
Key Punch Clerk	5 days @Tk.32/day			160	
Mr Rahman	Biochemistry Technician	40%	Tk.27,084	10,834	
Dr Mahmud	Veterinarian	5%	Tk.32,880	1,644	
Animal house Technician		20%	Tk.20,000	4,000	
				81,063	12,425

2. Supplies

	Unit Cost	Amount required		
Office Supplies, misc.			1,000	
IBM Cards	$8/10,000	10,000		8
Computer Tapes	$8.19	2		16
Plastics, glassware				2,000
Infant mice	Tk3/-	5,400	16,200	
Tb syringes	$0.26	2,000		520
Needles, 27g.	$0.05	2,000		100
BHI media	Tk0.16	1,800	288	
1½ ml vials; polypropylene		1,800		100
Nutrient agar, 1lb	$10.00	1		10
Clinitest tablets	$10/bottle	42		420
Computer time	Tk650/hour	4 Hours	2,600	
			20,088	3,174

3. Equipment

4. Hospitalization 1200 patient days 162,000
   Routine tests (See attachment #1) 17,850
   179,850

5. Outpatient follow up 15,000

6. CRL Transport 700 miles 890

7. 0

8. Transport of things 800

9. 0

10. Printing

Printing forms	Stencil 1,000 pages	200	
	Publication		300
	Xerox	500	
	Sub Total:	700	300

11. Contractual Services Tk.20 x 300 (patient follow up pay) 6,000

12. ?

Attachment to Budget # 1

ROUTINE TESTS

Biochemistry Lab	# tests required	Cost/test(Tk)	Cost Total
Serum Na^+	1500	0.5	750
K^+	1500	0.5	750
Cl^-	1500	0.25	375
CO_2	1500	1.0	1500
Glucose	1500	1.0	1500
Creatinine	300	1.0	300
Urine Na^+	600	0.5	300
K^+	600	0.5	300
Osmolality	600	1.0	600
Stool Na^+	300	0.5	150
K^+	300	0.5	150
		Total Biochem	Tk.6675

Clinical Pathology

Blood CBC	300	5.5	1650
Hct	1200	2.0	2400
Urine urinalysis	300	4.0	1200
Sp. Gravity	1500	0.25	375
Stool Micro exam	300	2.00	600
Dark field	300	1.0	300
	Total Clin. Path.	Tk.	6525

Bacteriology

Culture of stool	300	15.50	4650
	Total of Routine tests	Tk.	17,850

B. BUDGET SUMMARY

Category	Year 1 Taka	Year 1 Dollars	Year 2 Taka	Year 2 Dollars	Year 3 Taka	Year 3 Dollars
1. Personnel	81,063	12,425	None		None	
2. Supplies	20,088	3,174				
3. Equipment	-	-				
4. Hospitalization	179,850	-				
5. Outpatients	15,000	-				
6. CRL Transport	890	-				
7. Travel Persons	-	-				
8. Transportation things	-	800				
9. Rent/Communication	-	-				
10. Printing/Reproduction	700	300				
11. Contractual Service	6,000	-				
12. Construction	-	-				
Total:	303,591	16,699				
Total $	36,939					

Conversion Rate $1.00 = Tk.15/-

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Consent Form - Sucrose vs. Glucose Electrolyte Oral Solution in the treatment of Diarrhea of Infants.

The Cholera Research Hospital is carrying out studies to determine the most effective way to treat diarrhea in infants. We would like your child to participate in a study which is attempting to determine the effectiveness of two different sugar-salt solutions, given by mouth, in the treatment of diarrhea in infants. Both of these solutions are effective in adults and older children. This study is being carried out by Drs. Sack, Shiraz, Rahbani and Asma. If you decide to have your child admitted into the study you can expect the following:

1. Your child will be treated for diarrhea.

2. Your child would need to remain in the hospital until he/she has stopped having diarrhea for one day.

3. He (she) will receive as part of his treatment one of two oral sugar-salt solutions, which you will help give. The solution will be marked either "A" or "B".

4. While your child has diarrhea, he will need to have blood tests each day. These are all routine tests and no special or hazardous tests will be done.

5. While diarrhea can be dangerous for an infant, there is no extra risk from participation in this study. If the oral solution is not adequate treatment for your child, we may have to give intravenous solution.

6. You do not have to include your child in the study. If you decide against admitting him (her) to the study, he (she) will be treated at CRL for his (her) diarrhea.

7. You may ask questions about the study at any time.

8. You may withdraw your child from the study at any time, without jeopardizing his (her) medical care.

9. The medical records of your child will be kept confidential.

10. We would like your child to return for a blood test 10 days after he/she is discharged. You will be paid Tk. 15/- plus transportation costs to return for this test.

If you agree to allow your child to participate in this study, please sign your name here.

_____

Date _____

_____ Investigators signature.

Review Board on the Use of Human Volunteers

ABSTRACT SUMMARY

Sucrose vs Glucose Electrolyte Oral Solution
in the Treatment of Diarrhea in Infants

1. Approximately 300 children, aged 3 months to 4 years, of greater than 4 Kg. with uncomplicated watery diarrhea will be admitted into the study. Children must be used in this study because this is the only age group infected with rota-virus which is a major cause of diarrhea in infants. Also infants are the major target group for oral hydration therapy.

2. Risks of this study are very small. While dehydration and electrolyte imbalance are possible complications resulting from diarrhea, patients will be closely followed, 24 hours per day, by physicians to avoid these complications. Venapuncture blood samples will be required daily; this is a discomfort but not a significant risk.

3. Physicians will be present 24 hours daily during the study to detect any treatment failures at an early stage and take necessary action.

4. Patients will be identified by number. All records will be kept in a locked office. At the end of the study, identifying information will be removed from study data sheets.

5. Signed informed consent will be obtained from the parent(s). The study will be explained to the parent(s) in Bengali and consenting parents will sign (or thumb print) the Form. They will also be given a copy of the consent Form.

6. N.A.

7. The patient will benefit by the treatment of his diarrhea, society, especially of rural or under developed countries, will benefit by determining the efficacy of the oral solutions in the treatment of diarrhea of infants.

8. Data will be collected from the patients hospital record. Blood, stool, urine will be collected from patients for study.

PROCEDURES FOR MAINTAINING CONFIDENTIALITY

Patients admitted to the study will be given a study number; records will be kept according to study number and all data will be kept in a locked file in the investigator's locked office. Following completion of the study, all identifying information will be cut off from the data sheet and the clinical information only will be kept at the Cholera Research Laboratory in a locked storage office. Results of the study will be published in a medical journal and no identifying information will be included in the report of this study.