Attachment 1. (2)

ETHICAL REVIEW COMMITTEE, ICDDR,B

Date 25/3/86 2/3/86

Principal Investigator Dr. S.K. Roy

Trainee Investigator (if any)

Application No. 86-009

Supporting Agency (if Non-ICDDR,B) The Wellcome Tr

Title of Study "A study of the impact of zinc therapy on intestinal permeability in children with diarrhoea". (collaborative study).

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 Committee:
   - ✓ Umbrella proposal - Initially submit a 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 summar
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 sensitiv areas.
3. An indication as to when the questionnaire will be presented to the Cttee. for review.

(PTO)

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

S.K. Roy
Principal Investigator

Trainee

MAR 2 1986

86-009
2/3/86

SECTION I - RESEARCH PROTOCOL

1.	Title:	A study of the impact of zinc therapy on intestinal permeability in malnourished Bangladeshi children with acute and persistent diarrhoea (collaborative study between ICDDR,B and Dept. of Human Nutrition, LSHTM, London, UK)
2.	Principal Investigator:	Dr. S.K. Roy
	Collaborative Investigator:	Dr. A.M. Tomkins, Dr. R.H. Behrens
	Co-Investigator:	Dr. A.N. Alam
	Consultant:	Dr. A.M. Molla
3.	Starting Date:	May 1986
4.	Completion Date:	April 1988
5.	Total cost:	US $: 84,408
6.	Source of Funding:	The Wellcome Trust (U.K.)
7.	Scientific Programme:	This protocol has been approved by the Pathogenesis-Therapy Working Group

Signature of Associate Director, PTWG _____

Date 15.2.86.

8. ABSTRACT SUMMARY

Children with acute or persistent diarrhoea who are moderately or severely malnourished will be studied at the International Centre for Diarrhoeal Disease Research-Bangladesh (ICDDR,B). Microbiological studies will seek to identify organisms capable of producing mucosal damage or stimulating intestinal secretion. Intestinal permeability will be assessed by measurement of sugars in a 5 hour urinary collection after an oral dose of lactulose/mannitol(L/M). Nutritional status will be assessed by bio-chemical and anthropometric measurements after rehydration.

Children will be randomly allocated to clinical groups in order to receive a zinc supplemented vitamin syrup or non supplemented syrup(control) in addition to oral rehydration and nutritional advice. The duration and severity of diarrhoea and the rate of change in intestinal permeability will be assessed by regular interviews and repeated L/M tests in order to assess the impact of zinc therapy on intestinal function and growth of malnourished children with acute or persistent diarrhoea.

9. REVIEWS:

a. Ethical Review Committee: _____

b. Research Review Committee: _____

c. Director: _____

SECTION II - RESEARCH PLAN

A. INTRODUCTION

1. Objectives:

a. To assess the association between diarrhoeal pathogens, altered intestinal permeability and morbidity among malnourished Bangladeshi children with acute and persistent diarrhoea.

b. To investigate the impact of zinc supplements on the rate of improvement of intestinal permeability and severity of diarrhoea in these children.

2. Background

Diarrhoea is a major problem among children with protein energy malnutrition (PEM). Not only is the duration of symptoms prolonged in children with moderate and severe PEM compared with infection in better nourished children but fluid and electrolyte losses are greater.

The increased severity of diarrhoea in PEM has been attributed to the effect of protein and energy deficiency on the intestinal mucosa but other nutrient deficiencies may also be relevant. Clinical studies in children with severe PEM show the importance of a coexisting zinc deficiency (1). Experimental studies have emphasised the various effects of zinc deficiency on enterocytes - degenerative changes in mitochondria, abnormal desmosome system and increased lateral space between enterocytes - as well as decreased levels of mucosal enzymes and villus atrophy (2). These changes probably account for the diarrhoea and altered rates of intestinal secretion of water and electrolytes when the small intestines of zinc deficient rats are perfused 'in vivo'. Furthermore, the rates of secretion of water and

electrolytes in response to perfusion with cholera toxin are particularly increased if the animals are zinc deficient. These changes are rapidly reversed by the addition of zinc to the diet for 48 hours (3). Our hypothesis therefore is that in children with moderate or severe PEM who develop acute diarrhoea or persistent diarrhoea, zinc deficiency is an important factor influencing the severity and duration of symptoms.

Recent microbiological studies of children with acute diarrhoea (AD) at ICDDR,B have demonstrated a series of pathogens capable of damaging the intestinal mucosa such as Rotavirus, Giardia lamblia, Cryptosporidium, enteroinvasive, E. coli (EPEC), Shigella and Campylobacter. Thre are also several pathogens which stimulate secretion of fluid by means of enterotoxins such as Vibrio cholerae and enterotoxin producing E. coli (ETEC)(4).

Persistent diarrhoea (PD) develops through one or more of a variety of mechanisms including persistent intestinal colonisation by enteropathogens, prolonged mucosal damage associated with food intolerance and delayed mucosal recovery due to malnutrition. The mucosal lesions in PD including villus atrophy and decreased brush border enzymes tend to improve with intensive nutritional rehabilitation, the inference being that nutrient replacement is responsible (5).

However there have been major problems in assessing the mucosal response in children. Sequential assessment of mucosal structure (by examination of biopsy samples) or function (by intubation and perfusion studies) are not feasible on ethical and practical grounds. However a technique for assessment of intestinal permeability in which measurement of urinary sugars were expressed as a ratio, after an oral dose of lactulose (a large dissacharide probe not normally absorbed) and (mannitol a small probe molecule modestly absorbed), has proved acceptable and reproducible method of measuring

intestinal integrity in studies from The Gambia (6). This technique allows measurement of mucosal damage by a non invasive investigation. Correlations between mucosal morphology from biopsy and urinary L/M ratios in both Gambian children with persistent diarrhea with PEM (6) and in children in UK with acute diarrhoea (7), have been used to validate the method. The L/M ratio appears to be sensitive enough to differentiate between infants with normal mucosa and those infected with a pathogen causing mucosal damage i.e., Rotavirus (8). To date there has been no evaluation of the tests efficacy in differentiating between diarrhoea due to mucosal disruptive pathogens or symptoms due to the action of enterotoxins in which the mucosal morphology is relatively preserved.

Current management of AD emphasies the efficiency of oral rehydration therapy (ORT) in replacing fluid and electrolytes for excessive fluid loss. However because the intestinal losses may be significant and duration of symptoms may be longer in the malnourished, we propose that the administration of zinc in addition to ORT could be valuable.

Current management of PD is unsatisfactory despite a variety of antimicrobial and nutritional regimes. This may relfect the heterogenecity of causes and risk factors; the proportion of cases in which a common pathogen is isolated is small though similar organisms to those found in acute diarrhoea may be isolated.

Role of zinc in cell membrane

It has been suggested that zinc has profound effect on stabilization of plasma membrane (9). Serotinin (5-OH Tryptamine) is thought to be an intestinal secretagogue which is inhibited by zinc (10) affecting the cell membrane. Adenosine triphosphates (ATPase) and phospholipase A_2 are

inhibited by zinc which may explain immobilization of energy dependant activity of plasma membrane or increased integrity of the membrane structure. Zinc inhibits calcium ATPase of red cell membrane which serves as calcium pump for the cell. The probable mechanism was explained that zinc competes with calcium and therby inhibit the effect of calcium which controls the intracellular microtubules and microfilaments responsible for the mobility of microorganelles, transport of granules to the membrane as well as the excitability of plasma membrane itself (11).

Abnormalities of zinc metabolism associated with defective transport of sodium has been reported (12). Addition of zinc improved sodium transport in leukocytes of children recovering from malnutrition. Despite of high energy and protein supplementation, intracellular sodium and potassium did not return to normal levels which only returned at physiological level with zinc therapy (13). Sodium transport in uremic cells could be improved by the addition of zinc (14). Zinc has been shown to modify membrane permeability to sodium into dog red blood cells (15). Zinc deficiency was associated with impaired sodium reabsorption in renal tubules (16).

Continued diarrhoeal disorder in zinc deficiency

The most high-lighted human zinc deficiency syndrome associated with diarrhoea, growth retardation, and skin lesion is acrodermatitis enteropathica (AE) and was confirmed in 1974 by E.J. Moynehan (17). Diarrhoea is reversible with zinc supplementation with improvement of other symptoms without delay. Zinc deficiency in AE led investigators to consider the structural changes of intestinal mucosa that might be responsible for altered absorption or increased ultrafiltration into the gut.

Malnutrition in children is associated with zinc deficiency in Bangladesh as has been recently documented (18). About 50 per cent of severely malnourished children presented with diarrhoea and serum zinc level was significantly lower in those children compared to those without diarrhoea.

We propose that the addition of zinc may be important in achieving improved rates of recovery of mucosal structure and propose to investigate this in a collaborative study between the ICDDR,B and the Department of Human Nutrition, LSHTM.

3. RATIONALE

Malnutrition is most often complicated with infections and metabolic derangements of which diarrhoea is predominant in developing countries. In the Gambia, infantile diarrhoea was investigated in relation to intestinal permeability. The findings suggest that there is a significant change in permeability in acute diarrhoea, the changes are more severe in infants with diarrhoea longer than 14 days; on therapy in hospital, the permeability defect improves. The data also shows a significant correlation between weight velocity and gut permeability (19). Of the subjects suffering from chronic diarrhoea a great majority are malnourished. Excess loss of endogenous zinc occurs in prolonged diarrhoea, when malnourished children are zinc deficient. Mucosal permeability is altered in malnutrition in rats, causing higher absorption of macromolecules and foreign proteins, with higher amount of water and electrolyte loss from the experimental intestinal segments (20). This finding is partly confirmed in The Gambian infants, who, had a moderate increase in gut permeability when malnourished with no diarrhoeal disease (19).

The role of zinc on membrane stabilization and repair of mucosal injury is known but it is not known whether zinc could improve permeability of intestinal mucosa sufficient enough for reduction of severity and duration of diarrhoea in the malnourished children who suffer from protracted diarrhoea.

The study examines the potential role of zinc in improving membrane permeability in intestinal mucosa to help development in management of chronic diarrhoea with malnutrition.

B. SPECIFIC AIMS:

1. To investigate the impact of zinc supplementation on the rate of improvement of intestinal permeability in acute and persistent diarrhoea among malnourished children.
2. To relate the association between altered intestinal permeability and morbidity due to diarrhoeal pathogens in the children.
3. To document possible reduction in duration of diarrhoea, stool volume and frequency of stool in acute or chronic diarrhoea by zinc supplementation.
4. To document the effect of zinc supplementation on diarrhoeal morbidity during the follow up period.

C. METHODS OF PROCEDURE:

Children suffering from (1) A.D. (2) P.D. who attend the outpatients department of the ICDDR,B will be eligible for the study. Acute diarrhoea is defined as diarrhoea for less than 3 days. Persistent diarrhoea is defined as diarrhoea lasting for more than 14 days during which there is not more than 3 days without symptoms. The diagnosis of the presence of diarrhoea will be made according to the history given by parent/guardian as previous studies in this community indicate a very close correlation between reporting of diarrhoea and abnormalities on macroscopical examination of stools.

Criteria for selection of children for the study will include:

a. Age range - 3 months to 24 months

b. Sex - Male/female

c. Nutritional status - Weight/age <75% (assessed using a local events calendar and comparing with NCHS standards)or the presence of nutritional oedema

d. Agreement by parent/guardian for child to enter study and to bring child for follow up and receive home visits

A number of measurements will be made:

a. A detailed clinical history, physical examination and socio-economic interview - to assess dietary practice (especially weaning and source/ hygiene of solid foods)

b. Nutritional assessment - weight, height, mid arm circumference, skinfold thickness

c. Blood - plasma zinc, vitamin A, albumin, electrolytes, serum alpha 1- antitrypsin, serum ferritin

d. Mucosal permeability test - measurement of urinary excretion after oral dose of L/M

e. Stool microbiology - culture for Shigella, Salmonelia, V. cholerae, E. coli, (ETEC and EPEC), Campylobacter, Rotavirus, Clostridium defficile

microscopical examination for parasites especially Giardia lamblia and Cryptosporidium

f. Assessment of morbidity - a diarrhoeal history will be obtained by trained fieldworkers

Protocol for acute diarrhoea

Ninety children will be admitted to this part of the study and randomised such that half receive a water soluble vitamin syrup mix of riboflavine, thiamine and ascorbate (but not folic acid) to be taken three times per day. These will act as the control group. The other half will receive the same interim mix to which has been added zinc acetate solution to provide 100 mmol zinc/kg body weight/day.

Clincal Groups

When the results of the microbiological studies are available it will be possible to allocate the children to one of three groups. The number in parenthesis indicate the expected numbers from results of recent studies of children with acute diarrhoea at ICDDR,B.

Group 1. Mucosal damaging pathogen isolated (n=40)

This group will involve those with Rotavirus, Campylobacter, Giardia lamblia, EPEC.

Group 2. Enterotoxin producing pathogen isolate (n=30)

This group will include those with ETEC or Vibrio cholerae.

Group 3. No pathogen isolated (n=20)

Clinical examination and sample collection (L/M test Plasma Zinc, Intestinal Microbiology) will be done under the supervision of the project clinician at ICDDR,B. Parents/guardians will receive payment for transport to bring their

children to the clinic. The role of the fieldworker will be to follow children to their home after the test on day 1 and re-visit on day 3, day 9, and day 13 to remind them to come to ICDDR,B the following day for an examination by the project physician and a further L/M test if diarrhoeal symptoms persist.

Parents will be recalled with child for a control examination and L/M test when the child has been asymptomatic for at least 7 days.

Each parent/guardian will be instructed in the use of oral rehydration therapy (either rice-water oral rehydration solution or electrolytes/salt packets according to the regime in use at ICDDR,B at the time). They will also receive nutritional advice on the importance of continued feeding during and after recovery from diarrhea.

Protocol for persistent diarrhoea

A total of 100 children will be admitted to the study (including some from the AD cohort) and randomised such that half receive the vitamin syrup only and half receive the zinc supplemented syrup as described in the protocol for acute diarrhoea.

Children will be visited at home on days 6 and 13 to remind parents to return to ICDDR,B on the following day for clinical assessment and repeat L/M test (i.e., 1 and 2 weeks following admission to project). The children will then be followed at monthly intervals if symptoms persist for up to three months. Parents will be recalled with child for a control examination when the child has been asymptomatic for at least 7 days.

Clinical Groups

When the results of the microbiological studies are available, it will be possible to allocate the children to one of three clinical groups. There

is inadequate data on the microbiological findings in children with PD at ICDDR,B but extrapolating from studies in Bakau, Gambia, we anticipate a smaller proportion in which pathogens can be identified.

Group 4. Mucosal damaging pathogens isolated (n=20)

This group will include those with Rotavirus, Campylobactor, Giardia lamblia and EPEC.

Group 5. Enterotoxin producing pathogens isolated (n=15)

This will include those with ETEC or Vibrio cholerae.

Group 6. No pathogen isolated (n=65)

Investigations will be performed at ICDDR,B and at home as in the children with AD. Particular attention will be paid towards promoting the use of oral rehydration and appropriate dietary intake.

Indications for treatment

Children with AD are nearly all treated with ORT alone though if the clinical condition merits it, certain antibiotics may be prescribed such as Trimethoprim for severe shigellosis. The present treatment for PD is unsatisfactory - antibiotics rarely produce consistent improvement and efforts at improving dietary intake seem most effective. However there may be indications for specific antimicrobial therapy.

Analysis of data

Data (clinical, nutritional, microbiological, intestinal permeability, morbidity) will be entered on the Microcomputer to be based at ICDDR,B. This will enable the production of crosstabulations for analysis of the considerable number of data sets.

Administration of permeabiliity test

Where required, under supervision of the clinician, infants will be given (preferably by the mother) a freshly prepared drink containing 5g lactulose with 0.5g lactose (7.5ml Duphalac, Duphar Ltd., Southampton, UK) and 1g mannitol in 20ml 1% chloroform water. Breast feeding and fluid intake will be encouraged during the test. Urine samples will be collected for 5 hours into adhesive Uribags (Downs Ltd., London, UK). One drop of 20%V/V chlorhexidine gluconate added to each urine collection. Urine volumes will be measured and recorded. Aliquots (5ml) will be taken and stored at -40C^{O}. Lactulose and lactose can be measured using an automated enzyme assay system described previously (21). Mannitol can be assayed by using a similar assay based on the oxidation of the sugar by mannitol dehydrogenase prepared from Leuconosto mesenteroides as described by Yamanaka(2).

D. SIGNIFICANCE

Zinc supplementation would provide information which will help our understanding of the exact nature of improvement in membrane permeability involved in diarrhoeal state. Data of nutritional indices, diarrhoeal pathogens and altered diarrhoeal morbidity in supplemented and control groups would be available for evaluation of supplementation benefit. The present gap in knowledge about altered intestinal permeability due to diarrhoeal pathogens in acute and persistent diarrhoea will be reduced. The study will be able to develop new knowledge in this field and may indicate zinc supplementation in acute and persistent diarrhoea as a new development.

E. FACILITIES REQUIRED:

1. Office Space - the present office space will be utilized
2. Laboratory Space - ICDDR,B & LSHTM Labs will be utilized
3. Hospital Resource - studyward and outpatient space will be required
4. Animal Resources
5. Logistic Support - set up of micro-computer for data processing
6. ICDDR,B Transport - will be used

F. COLLABORATIVE ARRANGEMENTS

Collaborative arrangements will be made between ICDDR,B and Drs. A.M. Tomkins and Ron Behrens of London School of Hygiene and Tropical Medicine, (University of London) who have done related indepth study and are applicantsfor the grant for the proposed study to the Wellcome Trust (UK).

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ABSTRACT SUMMARY FOR RRC AND ERC

1. Children will be included 3m-24m, in this study because they are the group of high risk with malnutrition and diarrhoea.

2. There is no risk to the subjects for this study rather home follow-up and extensive investigations would help the patients. The permeability measurement is a proven safe procedure.

3. There is no potential risk from the study rather some benefits may be seen during zinc therapy and close-rapporting.

4. Data will be kept under lock and key and will not be available to others.

5. Home follow-time maybe one hour at best - with 15 minutes interview.

6. Patients will be under special care and monitoring. The assessment of nutritional status will help to take measures.

7. The research patients will have their own records. Venous blood (7ml) urine and feaces will be required for investigations.

SECTION III - BUDGET

A. DETAILED BUDGET (For 2 years

1. Personnel Services

Name	Position	% of effort	Project requirement (in US Dollar)
Dr. S.K. Roy	Pr.Investigator	50%	6,450
Dr. A.N. Alam	Co-Investigator	10%	2,290
Dr. A.M. Tomkins	Collaborative Investigator	-	-
Dr. Ron Behrens	" "	-	-
Dr. A.M. Molla	Consultant	-	-
Health worker (3)		100%	9,060
		Sub Total :	17,800

2. Supplies and Materials

Medical supply -	-	1,100
Salter infant scale (25 kg x .1g) @ 45 x 3	-	135
Hardenden Skinfold callipers @ 75 x 2	-	300
Length Board @ 60 x 3	-	180
Automatic pipettes @ 135 x 4	-	560
Calculator @ 50 x 2		100
Microcomputer (CIPROCO TANDY 1200 with supplies) or (Olivetti Desk Top. M24 with supplies)		3,500
	Sub Total :	5,775

3. Interdepartmental cost:

Lab costs	Cost/test ($)	No. of test	
C.B.C.	1.80	240	432
Serum electrolytes	2.72	120	326
Trace element	2.00	240	480
Alk. phosphatase	2.60	240	625
Stool ME	3.00	240	720
Stool C/S	7.00	240	1,680
Stool RV	3.30	120	396
Serum albumin	1.81	240	460
Lactulose/Mannitol	5.0	360	1,600
Campylobactor	8.00	150	1,200
Cl. defficile	8.00	150	1,200

A. Detailed Budget continued

	Patient hospitalization : 500 Taka per day	-	8,500
	Patient transportation	-	1,440
	Transport	-	3,600
	Hostel accommodation (for collaborators)	-	3,000
	Printing, Reporduction, Stationery & Secretarial service	-	4,600
		Sub Total :	31,758
4.	Biochemistry (LSHTM)	-	4,200
5.	International Air-fare	-	2,900
	International Air-freight	-	1,250
	Insurance	-	750
		Sub Total :	4,900

Grand Total :	64,433	US$
Overhead 31%:	19,975	US$
Total cost :	84,408	US$

B. SUMMARY BUDGET

	Description	Project requirement (US Dollars)
1.	Salaries Local	17,800
2.	Supplies & Materials	5,775
3.	Interdepartmental cost	31,758
4.	LSHTM Biochemistry	4,200
5.	International Transport	4,900
	Total:	64,433
	Overhead 31%	19,975
	Grand Total :	84,408

International Centre for Diarrhoeal Disease for Research, Bangladesh

CONSENT FORM (Impact of zinc therapy)

(Statement will be read out clearly and will be explained to the legal guardian when consent is obtained)

ICDDR,B is carrying out research to improve management of malnutrition and diarrhoea in children. For this purpose your child will receive additional vitamins & minerals along with standard treatment for diarrhoea. This research will help us to understand more of the problem and thereby develop better care for the children in risk. If you put your child in the study the benefit may help your child and the rest of the society.

If you decide to participate in the study, you may follow the following procedures.

1. Your child will receive best care possible on our part.
2. You may need to stay 5 hours minimum/or a period required for complete recovery.
3. To understand the illness better and to assess the benifit of the treatment 7 ml of venous blood, stool & urine will be collected for investigations.
4. The child will be allowed to drink a small amount of suger solution (30ml).
5. we shall feed the child adequately during study period.
6. The female health worker will visit your family at subsequent period.
7. We shall like you to bring your child for periodical measurement of improvement of health and nutritional status.
8. You will have full rights to withdraw your child from the study at any time yet he/she will receive all necessary treatment.

Signature of the Investigator

Signature /Thumb Impression
Legal guardian

Date: _____

[illegible]

ZINC

([illegible])

আই সি ডি ডি আর,বি শিশুদের ডায়রিয়া ও পুষ্টিহীনতার বিষয়ে এই গবেষণা কার্য হাতে নিয়াছে। এই গবেষণার কার্যক্রম হিসাবে আপনার শিশুকে সাধারণ চিকিৎসার বাহিরে ভিটামিন বা দস্তার লবণ দেয়া যাইতে পারে। দস্তার উপকারিতা পরীক্ষার জন্য গৃহীত এই গবেষণা হইতে আপনার বাচ্চা সরাসরি উপকৃত হবে উপরন্তু লব্ধ জ্ঞান দ্বারা ডায়রিয়া রোগে আক্রান্ত সকল রোগীর উন্নততর চিকিৎসা বিধি প্রণয়ন করা সম্ভব হইতে পারে।

যদি আপনার শিশুকে এই গবেষণায় অংশগ্রহণ করিতে ইচ্ছুক হন তবে নিম্নোক্ত বিধি গুলি আপনার শিশুর বেলায় প্রযোজ্য হইবে।

১। আমরা আপনার শিশুর জন্য সর্বোত্তম চিকিৎসার ব্যবস্থা করিব।

2। কমপক্ষে ৫ ঘন্টা হাসপাতালে থাকিতে হইবে।

৩। রোগীর চিকিৎসা ও গবেষণার মূল্যায়ন করার জন্য ৭ সি.সি রক্ত, পায়খানা ও মূত্র পরীক্ষা করা হইবে।

৪। শিশুকে সামান্য পরিমাণ জিংক সরবত খাওয়ানো হইবে। (৩০ সি,সি)

৫। পর্যাপ্ত পরিমাণ খাবার দেয়া হইবে।

৬। মহিলা স্বাস্থ্যকর্মী আপনার বাড়ীতে শিশুকে ~~[illegible]~~ পর্যবেক্ষণ করিতে যাইবে।

৭। আপনি মাঝে মাঝে শিশুকে স্বাস্থ্যের উন্নতি পরীক্ষার জন্য হাসপাতালে নিয়ে আসিবেন।

৮। যে কোন সময় আপনি ইচ্ছা করিলে এই গবেষণা হইতে বিরত হইতে পারিবেন তবু আপনার শিশুর চিকিৎসা ব্যাহত হইবে না।

গবেষকের স্বাক্ষর । তারিখ   অভিভাবকের স্বাক্ষর/টিপসই

Name: _____

Patients No.: _____ Father's name: _____

Age: _____ Sex: _____ Occupation: _____

Address: _____ Income/monthly: _____

_____ Source of income: _____

		Duration	Character	Frequency
1.	Diarrhoea:			
2.	Others: a)			
	b)			
	c)			
3.	Past illness: (Diarrhoea)			

4. Dietary practice:

	Yes	No	Stopped	Duration	Frequency	Amount
Breastmilk						
Adequate						
Formula milk						
Cows' milk						
Goats' milk						
Barley						
Rice powder						
Dal						
Vegetable						
Egg/fish/meat						
Rice						

5. Immunization: Measles _____ BEG _____ DPT _____

6. Age of the 2nd youngest child: _____

7. Mother's _____ FP _____/_____

APPENDIX II

PHYSICAL EXAMINATIONS: Date: _____

1. Age: _____ 2. Wt.: _____ 3. Ht.: _____ 4. MAC: _____ SKFT-

5. MK: _____ 6. Kwashiorkor: _____

7. Marasmus _____

Year Month Week

8. Oedema leg: _____ Duration: ____ / ____ / ____

9. Skin change: _____ Duration: ____ / ____ / ____

10. Hair change: _____ Duration: ____ / ____ / ____

11. Eye: _____

12. Ear infection: _____ Rt. _____ Lt. _____ Both _____ No _____

13. Tonsils: _____

14. Dehydration: No _____ Mild _____ Mod _____ Severe _____

15. Liver palpable: _____

16. Lungs: _____

17. HT _____

Others: _____

Others: _____

APPENDIX III

(INVESTIGATIONS)

Date: _____

Patient No.: _____

1. Blood - _____

_____

_____

2. Stool - Protoxoa/Parasites _____

M/E - _____

Organism - _____

3. L/M test - _____

4. Others : _____