

achment 1.
CE SHEET)

Date 07.02.91
21-5-91

ETHICAL REVIEW COMMITTEE, ICDDR,B.

Principal Investigator Dr. M. Aminul Islam

Trainee Investigator (if any) 21

Publication No. 91-001 (Revised)

Supporting Agency (if Non-ICDDR,B) _____

Title of Study Role of amylase rich

Project status:

Unenriched cereal flour based weaning food (✓) New Study

for the rehabilitation of severely under- () Continuation with change

nourished children aged 5 to 18 months dur- () No change (do not fill out rest of form)

Fill in the appropriate answer to each of the following (If Not Applicable write NA).

Source of Population:

(a) Ill subjects Yes (Yes) No

(b) Non-ill subjects (Yes) No

(c) Minors or persons under guardianship (Yes) No

Does the study involve:

(a) Physical risks to the subjects Yes (No) No

(b) Social Risks Yes (No) No

(c) Psychological risks to subjects Yes (No) No

(d) Discomfort to subjects Yes (No) No

(e) Invasion of privacy Yes (No) No

(f) Disclosure of information damaging to subject or others Yes (No) No

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) No

(c) Use of organs or body fluids Yes (No) No

Are subjects clearly informed about:

(a) Nature and purposes of study (Yes) No

(b) Procedures to be followed including alternatives used (Yes) No

(c) Physical risks NA Yes No

(d) Sensitive questions NA 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 NA

5. Will signed consent form be required:

(a) From subjects Yes No NA

(b) From parent or guardian (if subjects are minors) Yes No NA

6. Will precautions be taken to protect anonymity of subjects Yes No NA

7. Check documents being submitted herewith to Committee:

NA Umbrella proposal - Initially submit an overview (all other requirements will be submitted with individual studies). Protocol (Required)

✓ Abstract Summary (Required)

✓ Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw (Required)

NA Informed consent form for subjects

✓ Informed consent form for parent or guardian

NA Procedure for maintaining confidentiality

✓ Questionnaire or interview schedule *

* If the final instrument is not completed prior to review, the following information should be included in the abstract summary:

1. A description of the areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy.

2. Examples of the type of specific questions to be asked in the sensitive areas.

3. An indication as to when the questionnaire will be presented to the Cttee. for review.

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

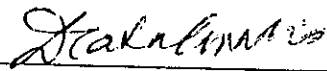
Principal Investigator

A-032082

SECTION I: RESEARCH PROTOCOL

90-001 (Revised)
21.5.91

1. Title : Role of amylase rich germinated
cereal flour based weaning food
in the rehabilitation of
severely undernourished children
aged 5 months to 18 months during
convalescence from diarrhoea.
2. Principal Investigator : Dr. M. Aminul Islam
Co-Investigator(s) : Dr. Mujibur Rahman
Ms. Esther Biswas
Ms. Nasheha Majid
Mr. M. A. Wahed
Project Coordinator : Dr. Dillip Mahalanabis
3. Starting date : As soon as approval is obtained
4. Completion date : One year from the date of
starting
5. Total direct costs : US \$ 42,905.00
6. Possible source of funding : SDC - DANIDA
7. Scientific Division : This protocol has been approved
by the Clinical Sciences Division


Signature of the Associate Director,
Clinical Sciences Division

Date: 07.02.91

ABSTRACT

To evaluate the role of liquefied energy dense diet in increasing the energy and nutrient intake in young children of 5 months to 18 months who are severely undernourished, patients will be randomized to receive either of the three diets in the nutrition rehabilitation unit (NRU) of ICDDR,B:

(1) the study group receiving an energy dense porridge of rice and pulse, liquefied by adding amylase rich germinated wheat flour , (2) first control group receiving the same porridge liquefied by adding additional water but not adding germinated cereal flour and (3) second control group receiving thick and energy dense porridge (i.e. without adding amylase rich germinated wheat flour). A total of 102 patients, 34 in each of three groups, will be studied over a period of one year. Along with the usual rehabilitation they will receive four meals of weaning food specified for each group ad libitum (at 10:00 a.m., 12:00 noon, 2:00 p.m. and 4:00 p.m. of the day) for consecutive 5 days. They will receive the usual rehabilitation and follow up after the study. Patients will be kept in NRU althrough. The major response variables will be quantity of food intake (energy and nutrients), its relation with breastfeeding, if any, and recurrence of diarrhoea, if any.

Reviews:

- (1) Chairman, Research Review Committee: _____
- (2) Chairman, Ethical Review Committee: _____
- (3) Director, ICDDR,B : _____

SECTION II: RESEARCH PLAN

A. INTRODUCTION

1. Objectives

- (a) Primary objective: Is amylase rich germinated wheat flour increases the intake of energy dense porridge of rice in the rehabilitation of severely malnourished children of 5 months to 18 months age during convalescence from diarrhoea?
- (b) Secondary objectives:
 - (i) Does it cause recurrence of diarrhoea?
 - (ii) Does this dietary intervention adversely affect breastmilk intake?

2. Background

In its recent report UNICEF reported that 30% of the under five children in 64 developing countries were suffering from moderate malnutrition and about 5% were severely malnourished (UNICEF 1987). Gordon et al. (1967) have found malnutrition at its height during the weaning period and the age group suffered was between 6 months to 30 months. The reason behind it is that weaning practices along with breastfeeding practices are usually regulated by tradition (Jelliffe 1955). In most cultures, traditional weaning foods are non-milk family foods based on local staple -- usually a cereal such as rice, wheat, corn, sorghum or millet.

When a staple is prepared as a weaning food, it is usually made either into a thick porridge or into a soft/liquid gruel. The latter is used as an early weaning food while porridge is introduced to children from about 2 years of age.

In the liquid gruel, staples hold large amount of water and thus become voluminous with a low energy density. Svanberg (1987) found the flour concentration of such gruel can be as low as 5% giving an energy of only 0.2 kcal/g. To be able to meet the daily energy requirements, a young child would have to consume 3-5 litre of such a thin gruel, which is unrealistic. The high energy requirements of the malnourished children together with their limited stomach capacity, make it impossible for them to eat enough of the liquid gruel.

The energy density of a thick porridge may be made up to 1.0 kcal/g, while the stiff and sticky consistency of such a porridge makes it more difficult to consume, especially for children who may not have developed their full capacity to masticate and to swallow stiff and solid foods.

By adding a small amount of a germinated cereal flour to such a weaning food, advantage is taken of the amylolytic enzymes (developed during germination) to hydrolyse the starch granules into maltodextrines and simple sugars that have a low water holding capacity. As a result the porridge liquefies, making it possible to have more solids per unit volume, while maintaining a thin consistency (Brandtzaeg et al. 1981). This amylase rich germinated cereal flour (ARGC) makes it possible to use thin but energy dense porridge as a weaning food for severely malnourished children.

3. Specific aims

- a) Does the use of a porridge liquefied by ARGC to feed severely malnourished children of 5 months to 18 months of age as weaning food increase calorie intake compared to --
 - (i) the same porridge without ARGC i.e. having thick consistency, and
 - (ii) compared to this porridge without ARGC but diluted to the same viscosity as the ARGC treated porridge?
- b) Is there any recurrence of diarrhoea after receiving ARGC treated porridge?
- c) Is the quality of intake of weaning food affected by the type of diarrhoea the children were suffering from?
- d) Does administration of such a porridge reduce breastmilk intake?

B. STUDY SIGNIFICANCE

In developing countries, weaning foods prepared from staples are often dilute and of low energy density. A thick porridge made from cereal staples with sufficient energy density is often too sticky for infants and young children to eat adequate amounts. A cereal gruel can be made energy dense by adding oil. However, oil is expensive and a scarce commodity in developing countries. Many mothers also regard oil unsuitable for use in small children. A cheaper way to prepare energy dense weaning food is to add a small amount of ARGC flour to a thick porridge. The present study will show whether this type of weaning food is suitable for use in severely undernourished children during convalescence from diarrhoea. It will also evaluate whether its intake causes diarrhoea or adversely affect breastfeeding, whether its intake is affected by diarrhoeal type (i.e. dysentery and watery diarrhoea). Results of this study, if positive, may encourage researchers to conduct further studies on the bioavailability of nutrients in such weaning foods, their community acceptance and methods of promotion.

C. RESPONSE VARIABLES

- a) Major response variables (throughout the study):
 - (1) Quantity of food intake.
The volume (and energy) of milk and the weight (and energy) of porridge taken in g/kg/24 h (and kcal/kg/24 h).
 - (2) Frequency and consistency of stool (times/24 h).
How many times stool was passed in 24 hours and what was the consistency (solid, semi-solid, watery, loose, mucoid, bloody) seen in most of the times.
 - (3) Liking/disliking of the experimental porridge by the children and by the mothers/attendant.
The subjective feeling of the children and mother towards the

weaning diet by observation of behaviour of both and by a questionnaire served to mother/attendant.

b) Secondary response variables:

- (1) Weight gain (or loss).
The increase (or loss) in weight from the randomization to the end of trial compared with weight on admission to the study and expressed as a per cent of admission weight.
- (2) Frequency of vomiting (if any).
Total number of vomiting (if any) in 24 hours.
- (3) Breastmilk intake (test weighing).
Total weight (in g) of breastmilk (if breastfed) ingested in 8 hours (9:00 a.m. to 4:30 p.m.) as calculated by weighing the child before and after breastfeeding.

D. METHODS AND PROCEDURES

(1) Eligibility criteria:

- a) Children staying in the Nutrition Rehabilitation Unit (NRU) of ICDDR,B having weight for age <60% or with oedema;
- b) Of either sex aged 5 months to 18 months;
- c) Should have no diarrhoea (as defined by passage of 3/more watery/liquid stool or stool with visible blood) in last 3 days and therefore should have no dehydration;
- d) Should not be a case of persistent diarrhoea i.e. diarrhoea lasting for more than 14 days and managed at the hospital with special diets;
- e) Should not have associated systemic infections (e.g. pneumonia) and/or complications (febrile patients without demonstrable focus of infection will be included, however if found to be infected afterwards will be excluded from analysis);
- f) Guardian should be willing to give informed consent.

(2) Procedure:

The usual practice is that a limited number of undernourished children (especially severely undernourished ones) reporting ICDDR,B for the treatment of diarrhoea and/or associated illnesses are kept in the NRU for nutritional rehabilitation once they are cured from diarrhoeal symptoms. Patients in the target age group (5 m -- 18 m) usually receive milk based diet (formula milk, see Annexure 1) in the first week; in addition, other semi-solid low-cost home based foods are offered; a mixture of rice and gram (chick-pea) is mixed with molasses to make a paste as weaning food (Annexure 1). Milk is offered in measured amount restricting to a fluid load of 100 ml-150 ml/kg/d as two hourly feeding (even hours); while weaning food is offered ad libitum several times (usually 4 times) per day. Gradually milk is reduced and more semisolid foods are encouraged. These children are followed at the Centre once

monthly for 7-8 months.

All children staying in NRU under the target age group (5 months to 18 months and <60% weight for age or with oedema) will be registered in a log sheet (Annexure 2) with the comment whether participated or not participated in the trial and if not participated reasons of nonparticipation. Children fulfilling enrolment criteria who have been observed for 3 days in NRU (this is the usual practice to allow the patient to settle in a new environment and to start with usual diet of NRU); the consent form will be read out to their legal guardian. After receiving verbal consent, each patient will receive an identification number and identification information will be recorded in the identification form (Annexure 3). Then, a baseline history will be obtained and physical examination will be carried out by the investigator and will be duly recorded in the study forms (Annexure 4). Thereafter children will be stratified according to age group (5 m - 11 m and 12 m - 18 m) and whether they had diarrhoea or dysentery prior to admission into NRU (i.e. there will be 4 strata). Then, children will be randomized using permuted blocks of random numbers of variable block lengths (the investigators will not know the length of variable block). This will be carried out by a knowledgeable person not directly supervising the study. The treatment assignment according to the randomisation code will be sealed in serially numbered envelopes; the serial numbers will correspond to the patient serial number in the study. The clinician will open the next envelope in sequence when the patient has formally entered the trial. After randomization, children will be either in (i) study group who will receive ARGC added porridge; or in (ii) control group 1 who will receive porridge having the same consistency as in the study group (by dilution with appropriate amount of water) but without adding ARGC and (iii) control group 2 who will receive the porridge of same energy density as in study group and having thick consistency (as is used in NRU at present).

After the treatment group has been assigned, necessary documentation about the patient identification number and treatment group will be recorded in the log sheet. This is to prevent future change of treatment group during study schedule. Also, the investigator will again check the eligibility criteria to exclude any patient on trial if found to be ineligible. The special feeding will be offered four times in 24 hours (at 10:00 a.m., 12:00 noon, 2:00 p.m. and 4:00 p.m.) ad libitum. In addition the usual milk based diet will be offered in 2 hourly feeding schedule to all even hours except 9:00 a.m. to 5:00 p.m. (when weaning food will be offered and on demand milk may be offered) providing 100-150 ml/kg/24 h. These weaning foods will be kept available for half an hour during each feed and will be given for consecutive 5 days after the enrolment in the study. The composition of the three types of porridge is attached (Annexure 5).

The weight, length and mid-upper arm circumference will be measured as per standard procedure on admission to the nutrition rehabilitation unit, on the inclusion day and at the end (6th day) of the study. Then weight for age and weight for length will be calculated and recorded as of percentage of the NCHS median value (Annexure 6). Intake of porridge will be measured by weighing the containers before and after feeding. Test weighing of the breastmilk intake will be made by weighing the child before and after breastfeeding in between 09:00 a.m. and 04:30 p.m. (Annexure 7a and 7b). Total intake of porridge per day and during the whole illness will be computed by combining the measurements. Twenty-four hourly evaluation will be recorded in predesigned and pretested forms (Annexure 8a for D1 and Annexure 8b for D2 to D5). The number and frequency of stool motions will be recorded each day. Diarrhoea will be defined based on 3 or more loose stools and/or

presence of blood/mucus in the stool in 24 hours.

Mothers' acceptance will be tested by serving a pretested questionnaire (Annexure 9) on the day 1 of study; also by observing the attitude and behaviour of both mother and child during feeding. A tally sheet (Annexure 10) will be maintained to check the day to day works to be done for the study.

The principal investigator with the help of coinvestigators will take care of patients. Diet will be prepared in the metabolic kitchen of the Clinical Research Centre under the supervision of the weaning food laboratory, both for controls and study children. A senior research assistant will be assigned to supervise diet. A pilot phase will be conducted to standardize procedures.

No incentives/rewards will be given for participating in the study and children will receive usual nutritional rehabilitation if guardian does not agree to enroll the child into the study. Also patient will receive continued nutritional rehabilitation beyond the end of the study and will receive usual follow up after discharge.

No additional investigation will be done except that stool will be examined macroscopically everyday during the study period and routine stool microscopic examination and blood total and differential count, if needed.

3. Withdrawal from the study

- a) Noncompliance of the subject -- either because the patient leaves the hospital before the end of the study; or because the patient requires unscheduled treatment for a serious intercurrent illness (e.g. pneumonia etc.).
- b) Dietary failure -- as evidenced by vomiting (one profuse vomiting/>5 times in 24 h) and/or diarrhoea (>3 times watery/loose stool in 24 h) necessitating change in diet and other interventions e.g. i.v. fluid.

But the details of these patients will be recorded duly for consideration during analysis.

4. Sample size estimate

The sample size is being calculated to detect a difference between study group i.e. ARGC treated group versus control group 2 in the quantity of energy and nutrient intake daily. A 35% increase in total food intake daily is expected in the experimental group. This is based on the observation by Svanberg (1987) in a Tanzanian village, where children of 12 months to 36 months of age consumed 35% more of the semi-liquid diet than the stiff diet. Also this is based on our unpublished data on food intake from a single meal of energy dense porridge liquefied by adding ARGC compared with a single meal of semi-solid porridge of the same energy density in children aged 6 months to 12 months. The mean quantity of porridge ingested by the children group receiving energy dense porridge liquefied with ARGC was 41 g and the mean intake in the control group receiving semi-solid porridge of same energy density was 26 g. With a standard deviation of 20, the sample size to detect the difference at 5% level of significance and with a power of 80% was 28 in each group. Therefore, the total sample size for the three groups is 84. We add 18 (around 20%) for deviated course and the total sample size becomes 102.

5. Data collection

The collected data will be entered into a microcomputer using a data entry template. The pre-intervention data will be summarized and compared among the groups. The study group will be compared with the control group 2 for the major response variables. Significance tests will be carried out using standard parametric tests for quantitative outcome variables. The distribution of data will be examined for validity of such tests and if necessary appropriate transformation will be carried out before conducting the tests. Otherwise non-parametric equivalents will be used for comparing the two groups. Exploratory analysis will also be carried out by comparing the study group with the control group 1 (i.e. group receiving porridge of the same consistency) for the same outcome measurements. Mothers' perception and behaviour of child/mother towards the weaning diet will be used in descriptive form if found to be significant.

E. FACILITIES REQUIRED

This study will be conducted in the Nutrition Rehabilitation Unit of ICDDR,B and the existing facilities will be utilized for the purpose.

Two trainee research assistants will be hired for the purpose.

E. FUNCTIONS OF INVESTIGATORS:

Dr. M. A. Islam (MAI) -- will write the project proposal; plan coordinate and supervise the project. He will do the interim and final analyses, write the final report and submit for publication.

Dr. M. Mujibur Rahman -- will help MAI in patient examination, overall supervision, data entry and report write up.

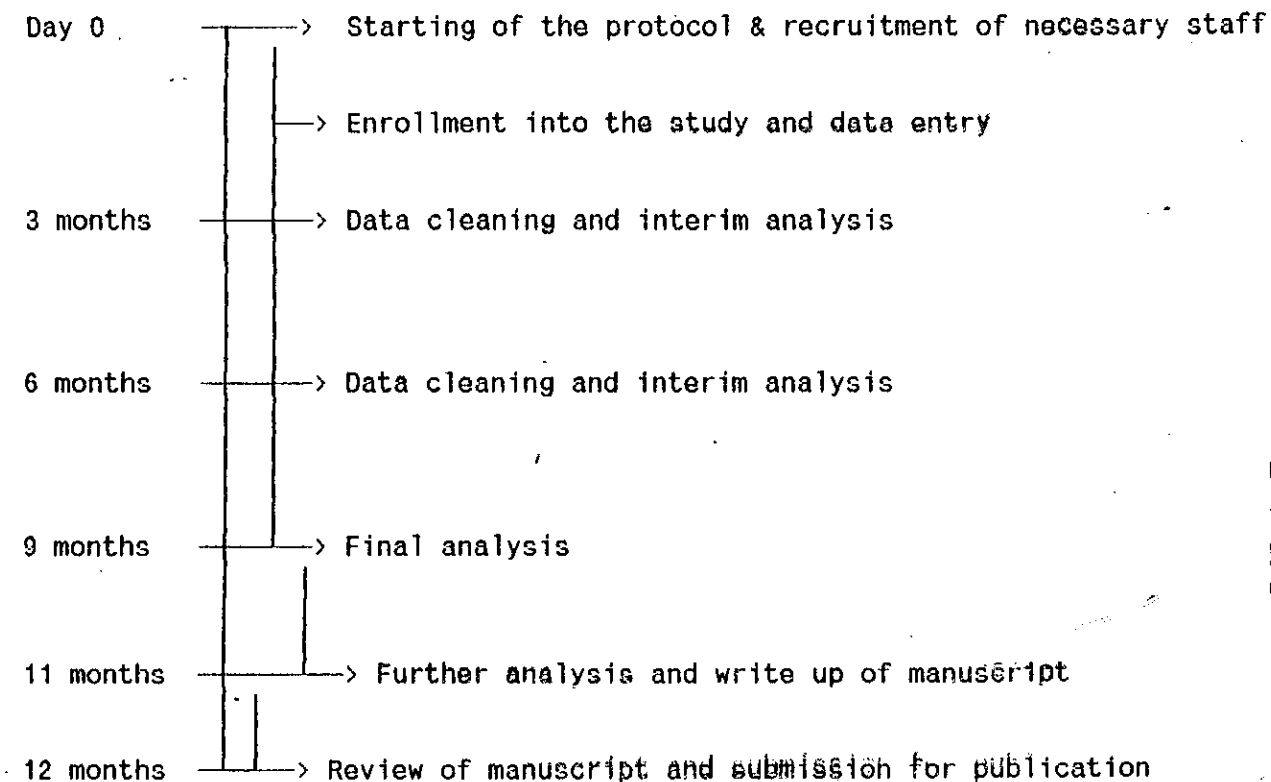
Ms. Esther Biswas -- will select, enrol and take consent of the child. Will supervise weaning food intake and anthropometric measurements, will fill in the questionnaires.

Ms. Naseha Majid -- will be responsible for preparing the weaning food, maintaining its quality and ensuring its proper supply.

Mr. M. A. Wahed -- will be responsible for preparing ARGC based flours, maintaining its quality and ensuring its proper supply.

Dr. Dilip Mahalanabis -- will assist in study design, analysis and interpretation.

F. FLOW CHART:



ANNEXURE 1

Composition of NRU diets

Ingredients	Milk suji	Halwa
Full cream milk powder	40 g	--
Rice powder	40 g	14 g
Lentil	--	6 g
Sugar	25 g	--
Gur (cane)	--	14 g
Soya bean oil	25 g	8 ml
Magnesium chloride	0.5 g	--
Potassium chloride	1 g	--
Water (up to ml)	1000	100
Energy (kcal/100 ml)	67	195
Protein (g%)	1.4	2

ANNEXURE 2

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH

ARGC PROTOCOL: LOG SHEET
(of all eligible patients)

[illegible]

ANNEXURE 3

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH

ARGC PROTOCOL: IDENTIFICATION FORM

Has verbal consent been obtained? Y/N

If [N] do not proceed.

Hospital no.

NRU no.

Child's name: _____ Mother's name: _____

Father's name: _____ Family members (no.):

DOB
dd mm yy

Age (m): Sex: M=1 F=2

Date of admission to hospital:
dd mm yy

Date of admission to NRU:
dd mm yy

Date of admission to study:
dd mm yy

Time of admission to study:
hh mm

Side from which side:

1=OPD 2=TC 3=GW (WATERY) 4=GW (INVASIVE) 5=PERSISTANT

Residence:

☐

1=Dhaka 2=Tongi 3=Joydebpur 4=Zinjira 5=others

Address: _____

Treatment group:

☐

Study group=1 Control group 1=2 Control group 2=3

Type of diet received:

☐

Porridge with ARGC (Study diet)=1
Porridge diluted with water (control 1 diet)=2
Thick porridge without ARGC (control 2 diet)=3.

Child's study No.:

☐☐☐☐

Done by: _____

ANNEXURE 4

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH

ARGC PROTOCOL: STATUS ON NRU ADMISSION

--	--	--

Child's study no.

--	--	--	--

dd mm yy

9=Unknown 8=Not applicable

1. Diarrhoea at home 1=Y 2=N

--

2. If yes, duration (hrs)

--	--	--

3. If yes, frequency (no./24 h)

--	--

4. If yes, stool colour

--	--

1=normal 2=brown 3=green 4=whitish 5=other

5. If yes, stool consistency

--

1=watery/liquid 2=loose 3=semi-solid 4=solid 5=other

6. If yes, stool character

--

1=normal 2=mucoid 3=bloody 4=bloody mucoid 5=other

7. Diarrhoea at hospital 1=Y 2=N

--

8. If yes, duration (hrs)

--	--	--

9. If yes, frequency (no./24 h)

--	--

10. If yes, stool colour (as above)

--

11. If yes, stool consistency

--

12.	If yes, stool character (as above)	
13.	Vomiting at home 1=Y 2=N	
14.	If yes, duration (hrs)	
15.	If yes, frequency (no./24 h)	
16.	Vomiting at hospital 1=Y 2=N	
17.	If yes, duration (hrs)	
18.	If yes, frequency (no./24 h)	
19.	Anorexia at home 1=Y 2=N	
20.	If yes, duration (hrs)	
21.	Anorexia at hospital 1=Y 2=N	
22.	If yes, duration (hrs)	
23.	Fever at home 1=Y 2=N	
24.	If yes, duration (hrs)	
25.	Fever at hospital 1=Y 2=N	
26.	If yes, duration (hrs)	
27.	Paedal oedema at home	
	1=+ 2=++ 3=+++ 0=nil	
28.	Paedal oedema at hospital	
	1=+ 2=++ 3=+++ 0=nil	

29. Paedal oedema at NRU
1=+ 2=++ 3=+++ 0=nil

☐

30. Feeding at home:

Breastmilk 1=Y 2=N

☐

If Y, time/day: _____

Formula milk 1=Y 2=N

☐

If Y, time/day: _____

Cow's milk 1=Y 2=N

☐

If Y, time/day: _____

Semi-solid 1=Y 2=N

☐

If Y, time/day: _____

Solid foods 1=Y 2=N

☐

If Y, time/day: _____

31. Feeding at hospital:

Breastmilk 1=Y 2=N

☐

If Y, time/day: _____

Formula milk 1=Y 2=N

☐

If Y, time/day: _____

Other liquid diet 1=Y 2=N

☐

If Y, time/day: _____

Semi-solid 1=Y 2=N

☐

If Y, time/day: _____

Solid foods 1=Y 2=N

☐

If Y, time/day: _____

32. History of immunization

DPT/OPV ☐ Measles ☐ BCG ☐

0=not immunized 1=dose 1 2=dose 2 3=dose 3

33. Other illnesses at home (if yes, specify)

34. Other illnesses at hospital (if yes, specify)

35. Drugs received at home (with duration, if any):

36. Drugs received at hospital (with duration, if any)

Done by: _____

ANNEXURE 5

Composition of study porridges

Ingredients	Study porridge	Control Gr1 pord	Control Gr2 pord
RF	2 g	--	--
rice powder	16 g	18 g	18 g
bengal gram (dhal)	6 g	6 g	6 g
soyabean oil	3 g	3 g	3 g
ur (cane)	10 g	20 g	10 g
water (up to ml)	100	200	100
energy (kcal/100 g)	150	94	150
protein (g%)	2.6	2.0	2.4
ER	6.8	10.5	6.5
ER	20.7	32.8	20.5
ER	72.5	56.7	73.0

ANNEXURE 6

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH
ARGC PROTOCOL: ANTHROPOMETRY

--	--	--

dd mm yy

Child's study no.

--	--	--	--

9=Unknown 8=Not applicable

1. Weight on admission to hospital (kg)

--	--

 .

--	--
2. Weight on admission to NRU (kg)

--	--

 .

--	--
3. Weight on inclusion to study (kg)

--	--

 .

--	--
4. Weight at the end of study (kg)

--	--

 .

--	--

 (6th day)
5. Length on admission to NRU (cm)

--	--

 .

--
6. Length on inclusion to study (cm)

--	--

 .

--
7. Length at the end of study (cm)

--	--

 .

--

 (6th day)
8. MUAC on admission to NRU (cm)

--	--

 .

--
9. MUAC on inclusion to study (cm)

--	--

 .

--
10. MUAC at the end of study (cm)

--	--

 .

--

 (6th day)
11. Weight for age (NCHS 50th P.C.) on inclusion

--	--
12. Weight for age (NCHS 50th P.C.) at end of study

--	--
13. Weight for length (NCHS 50th P.C.) on inclusion

--	--
14. Weight for length (NCHS 50th P.C.) at end of the study

--	--

Done by: _____

ANNEXURE 7a

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH

ARGC PROTOCOL: WEANING DIET RECORD FORM

--	--	--

Child's study no.

--	--	--	--

dd mm yy

Take the weight of the plate + weaning diet + spoon before and after offering it to the child.

		10 a.m.	12 noon	2 p.m.	4 p.m.
D1	Before				
	After				
D2	Before				
	After				
D3	Before				
	After				
D4	Before				
	After				
D5	Before				
	After				

Done by: _____

ANNEXURE 7b

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH

ARGC PROTOCOL: BREAST-FEEDING RECORD FORM

--	--	--

dd mm yy

Child's study no.

--	--	--	--

Weight will be taken before breast-feeding and just after from 9:00 a.m. to 4:30 p.m.

Day	Time	Before								
		After								
1										
2										
3										
4										
5										
Example	9:20 a.m.	3.140 3.165	11:45 a.m.	3.105 3.160	1:15 p.m.	3.140 3.160				

Done by: _____

ANNEXURE 8a

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH

ARGC PROTOCOL: FEATURES DURING STUDY

--	--	--

dd mm yy

--	--

hr min

Child's study no.

--	--	--	--

9=Unknown 8=Not applicable

Day no. 1 (Weight in kg)

--	--	--	--

1. Stool passed today 1=Y 2=N

--

2. If yes, frequency (no. since 8 am today)

--	--

3. If yes, stool colour

--

1=yellow 2=brown 3=green 4=whitish

4. If yes, consistency

--

1=watery/liquid 2=loose 3=semi-solid 4=solid 5=other (explain) _____

5. If yes, stool character

--

1=normal 2=mucoid 3=bloody 4=bloody mucoid 5=other (explain) _____

6. Vomiting today 1=Y 2=N

--

7. If yes, frequency (no. since 8 am today)

--	--

8. Anorexia today 1=Y 2=N

--

9. If yes, duration in hrs

--	--

10. Fever today 1=Y 2=N

--

11. If yes, duration in hrs

--	--

12. Paedal oedema today

☐

1=+ 2=++ 3=+++ 0=nil

13. Other illnesses, if any (specify)

14. Other investigation and treatment, if any (specify):

15. Write about the attitude of mother and child towards the diet:

Done by: _____

ANNEXURE 8b

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH

ARGC PROTOCOL: FEATURES DURING STUDY

--	--	--

dd mm yy

--	--

hr min

Child's study no.

--	--	--	--

9=Unknown 8=Not applicable

Day no. 2/3/4/5 (put circle) Weight in kg

--	--	--	--

1. Stool passed today 1=Y 2=N

--

2. If yes, frequency (no. in 24 hrs)

--	--

3. If yes, stool colour

--

1=yellow 2=brown 3=green 4=whitish

4. If yes, consistency

--

1=watery/liquid 2=loose 3=semi-solid 4=solid 5=other (explain) _____

5. If yes, stool character

--

1=normal 2=mucoid 3=bloody 4=bloody mucoid 5=other (explain) _____

6. Vomiting today 1=Y 2=N

--

7. If yes, frequency (no. in 24 hrs)

--	--

8. Anorexia today 1=Y 2=N

--

9. If yes, duration in hrs

--	--

10. Fever today 1=Y 2=N

--

11. If yes, duration in hrs

--	--

12. Paedal oedema today

☐

1=+ 2=++ 3=+++ 0=nil

13. Other illnesses, if any (specify)

14. Other investigation and treatment, if any (specify):

15. Write about the attitude of mother and child towards the diet:

Done by: _____

ANNEXURE 9
INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH

ARGC PROTOCOL: MOTHERS' PERCEPTION QUESTIONNAIRE

--	--	--

dd mm yy

Child's study no.

--	--	--	--

Respondent's name: _____ Relation to child: _____

1. What number of alive children do you have? _____
2. What is the age (in months) of this child? _____
3. What do you feed your child? _____
4. How long (in months) have you given your child breastmilk? _____
5. Have you given your child other food? _____
6. If yes, when (at what months of age)? _____
7. What was/should be the initial food other than milk for your child? _____
8. What was/should be the consistency of it? _____
9. Should/did you mix oil to prepare this food? _____
10. How many times you should give/gave this additional food to your child (in a day and night)? _____
11. See this food: is it suitable for a young child? _____
12. If yes, when should it be given (at what month of age) to a child? _____
13. Should breastmilk or milk be continued with it? _____
14. Take its smell: is it suitable for a young child? _____
15. Taste it: is it suitable for a young child? _____

Done by: _____

Date: _____

ANNEXURE 10

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH ARGC PROTOCOL: TALLY SHEET

1. Child staying at NRU -- eligible Y/N; if 'N', do not proceed.
2. History taken on NRU admission -- Y/N
3. Anthropometry done on NRU admission (Wt, length & MUAC) -- Y/N
4. 3rd day of NRU admission/Day 1 of study:
 - a) read the consent form -- Y/N
 - b) fill in the log-sheet -- Y/N, do not proceed if consent is not given.
 - c) if consent is given, sign the consent form -- Y/N
 - d) fill in the identification form -- Y/N
 - e) fill in the status form -- Y/N
 - f) physician's check up of the child (to exclude if pneumonia/complication) -- Y/N
 - g) to record anthropometry (wt, length & MUAC) at 8:45 a.m. -- Y/N
 - h) to open sealed envelope to see treatment group and record in the log sheet -- Y/N
 - i) to fill in mothers' perception questionnaire (before serving weaning diet) -- Y/N
 - j) to give and record weaning diet (10 a.m., 12 noon, 2 p.m. and 4 p.m.) -- Y/N
 - k) to fill in the on-study form (day 1) at 4:30 p.m. -- Y/N
 - l) test weighing of the child and record it, if breast-fed -- Y/N/NA (between 9:00 a.m. to 4:30 p.m.)
5. 4th day of NRU admission/Day 2 of study:
 - a) naked eye examination of morning stool -- Y/N
 - b) to take morning wt (at 8:45 a.m.) -- Y/N
 - c) to give and record weaning diet (10 a.m., 12 noon, 2 p.m. & 4 p.m.) -- Y/N
 - d) to fill in the on study form at 4:30 p.m. -- Y/N
 - e) test weighing of the child and record it, if breast-fed -- Y/N/NA (between 9:00 a.m. to 4:30 p.m.)
 - f) to do stool M/E, R/S or blood tests, if necessary -- Y/N/NA

6. Day 3 of study:

- a) naked eye examination of morning stool -- Y/N
- b) to take morning wt (at 8:45 a.m.) -- Y/N
- c) to give and record weaning diet (10 a.m., 12 noon, 2 p.m. & 4 p.m.) -- Y/N
- d) to fill in the on study form at 4:30 p.m. -- Y/N
- e) test weighing of the child and record it, if breast-fed -- Y/N/NA Y/N
(between 9:00 a.m. to 4:30 p.m.)
- f) to do stool M/E, R/S or blood tests, if necessary -- Y/N/NA

7. Day 4 of study:

- a) naked eye examination of morning stool -- Y/N
- b) to take morning wt (at 8:45 a.m.) -- Y/N
- c) to give and record weaning diet (10 a.m., 12 noon, 2 p.m. & 4 p.m.) -- Y/N
- d) to fill in the on study form at 4:30 p.m. -- Y/N
- e) test weighing of the child and record it, if breast-fed -- Y/N
(between 9:00 a.m. to 4:30 p.m.)
- f) to do stool M/E, R/S or blood tests, if necessary -- Y/N/NA

8. Day 5 of study:

- a) naked eye examination of morning stool -- Y/N
- b) to take morning wt (at 8:45 a.m.) -- Y/N
- c) to fill in mothers' perception questionnaire (Q 7 to Q 15)) -- Y/N
- d) to give and record weaning diet (10 a.m., 12 noon, 2 p.m. & 4 p.m.) -- Y/N
- e) to fill in the on study form at 4:30 p.m. -- Y/N
- f) test weighing of the child and record it, if breast-fed -- Y/N
(between 9:00 a.m. to 4:30 p.m.)
- g) to do stool M/E, R/S or blood tests, if necessary -- Y/N/NA

9. Day 6 of study:

- a) naked eye examination of morning stool -- Y/N
- b) to record anthropometric measurements (wt, length & MUAC) -- Y/N
- c) to send for any investigation, if necessary -- Y/N/NA

10. END of the study.

PREPARATION OF ARGC (from wheat):

1. The cleaned grains of wheat are steeped in excess water (about double volume) in a stainless steel tray for 12 hours.
2. After 12 hours the wheat grains are drained of water.
3. The steeped grains are then wrapped in moist black clean piece of cotton cloth and germinated for 48 hours at room temperature ($\sim 28^{\circ}\text{C}$); the cloth is kept moist by sprinkling water as needed.
4. The germinated wheat grains are spread on filter paper to remove surface moisture and dried for 12 hours under a ceiling fan in a stainless steel tray until dry to the touch. The well germinated wheat grains are then separated from the non-germinated grains manually.
5. The dried grains are again dried in an oven at 50°C for 12 hours; shoots are removed by rubbing.
6. The oven-dried grains are ground to a fine powder in a laboratory blender. The flour is sieved through a local sieve (called 'chaluni'). This germinated wheat flour constitutes the ARGC.
7. The ARGC is stored in polythene bags.

ETHICAL IMPLICATIONS (for Ethical Review Committee)

1. This study aims at evaluating the role of a porridge liquefied by amylase rich germinated wheat cereal flour (thereby energy dense) in increasing the energy and nutrient intake, compared to a thick porridge as such or made liquid (thereby low energy dense), in children aged 5 months to 18 months who are severely malnourished and kept in NRU for nutritional rehabilitation.
2. There is no potential risk involved.
3. Child will be kept in Nutrition Rehabilitation Unit and will not be deviated from usual nutritional rehabilitation as offered by ICDDR,B.
4. The children will be under constant observation of the physicians, health assistants and volunteers.
5. Verbal consent will be obtained from the legal guardians or parents before the patients are included in the study.
6. No blood samples will be taken for the purpose of the study unless it is needed to aid in patient management for concurrent illness.
7. Stool samples will be collected everyday during study and culture will be sent if child suffers from diarrhoea only.
8. All the information will be kept confidential and these will be made available to the legal guardians if they want so.
9. As a part of the standard nutritional rehabilitation of ICDDR,B hospital, all children will receive usual follow-up service after discharge.

REFERENCES

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4. Svanberg U, Fredrikzon B, Gebre-Hiwot B, Taddesse WW. Sorghum in a mixed diet for pre-school children. I. Good acceptability with and without simple reduction of dietary bulk. *J Trop Pediatr* 1985;33:181-185.
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ARGC IN SEVERE MALNUTRITION

BUDGET

PERSONNEL

		US \$
Medical Officer NOA - 1	6 m x 749	4494
Research trainee fellow - 1	12 m x 188	2256
Secretary GS5 - 1	3 m x 422	1266
Data Manager GS5 - 1	3 m x 422	1266
Trainee health asstt. - 2	12 m x 2 x 103	2472
Volunteers - 4	12 m x 4 x 50	2400
Sub-total:		14154

Patient hospitalization

10000

Laboratory

Stool M/E (500 tests)	400
Blood for TC and DC (50 tests)	50
X-ray Chest	100
Sub-total:	550

Equipment

Baby balance	2500
High precision food balance	2500
Sub-total:	5000

Others

Supplies and materials	1000
Printing and publication	500
Xerox	200
Staff clinic	200
Transport	200
Data management	1000
Medical illustration	200
Sub-total:	3300

SUMMARY BUDGET
(Amount in US \$)

Personnel	14,154
Hospitalization	10,000
Laboratory	550
Equipment	5,000
Others	3,300
Total:	<u>33,004</u>
Overhead (30%)	9,901
Grand total:	<u>42,905</u>

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH

ARGC PROTOCOL: VERBAL CONSENT FORM

Appropriate feeding is an essential component of management of severe malnutrition. Children, in practice, fail to get or swallow enough food that is needed for their growth when malnourished. The problem is worsened by loss of appetite and diarrhoea. Use of liquefied energy dense porridge is likely to increase the intake and availability of energy and nutrients by the child.

At ICDDR,B, we plan to add some amount of germinated wheat cereal flour with rice to liquefy the porridge and make it energy and nutrient-dense. Another food will be prepared with the same ingredients but without addition of germinated wheat flour and will be made liquefied. The third food item is also of the same ingredients but is thicker and is presently used in our rehabilitation unit. We like to evaluate the proportion of food and nutrient intake by the children on these three different dietary regimen.

By random selection, your baby may get any of these three types of food. In addition to breastmilk (if breastfed) and other milk, the scheduled food will be served 4 times in 24 hours for 5 days. After admission, a sample of stool will be collected everyday morning. The energy and nutrient intakes will be measured and baby will be weighed everyday morning as it is done to all children staying in this unit. Treatments and medicines appropriate for your child will be provided as usual.

If you allow your child to participate to this study, please give your verbal consent. Even if you do not agree, your child will receive the usual management offered from this hospital.

Witness: _____

Signature of the investigator

আন্তর্জাতিক উদ্যোগ গবেষণা কেন্দ্র, বাংলাদেশ
এ আর-জি জি গবেষণা
মৌখিক অম্মতি পত্র

অসুস্থি জনিত বোগের চিকিৎসায় উপযুক্ত খাবার দেওয়া অপরিহার্য।
(বিশেষতঃ) অসুস্থি বাচ্চারা তাদের সুস্থির চাহিদামত পর্যাপ্ত খাবার খেতে
পারে না। এই অবস্থা আরও জটিল হয় যখন বাচ্চা সুষামতা ও
পাওয়া পর্যাপ্ত খায়। পর্যাপ্ত খাদ্য গ্রহণ হয় নতুন হালুয়া দিলে
বাচ্চা দরকার-মত খাবার খেতে পারে।

আন্তর্জাতিক উদ্যোগ গবেষণা কেন্দ্রে আমরা শক্ত হালুয়ার সঙ্গে
সামান্য পরিমাণে ডিজেনারামের আটা মিশিয়ে নরম করেছি যাতে
খাদ্য গ্রহণ ঠিক থাকে, হালুয়াও নরম হয়। দ্বিতীয় প্রকার-হালুয়া এই
গন্ধের আটা না দিয়ে, পানি দিয়ে নরম করা হয়েছে। তৃতীয় হালুয়াটি
কিছুটা শক্ত যা আমরা এখন এই ওয়ার্ডে ব্যবহার করছি। আমরা
দেখতে চাইছি, বাচ্চারা কোন হালুয়া-কতটুকু খায় এবং তাতে কতটুকু
উপকার হয়।

আপনার বাচ্চাকে এই তিন ধরনের-যে কোন একটি হালুয়া দিলে ৪ বার
করে পর-পর ৫ দিন দেওয়া হবে। সেই সাথে বাচ্চা বুকের দুধ
ও অন্য দুধও পাবে। প্রতিদিন বাচ্চা পর্যাপ্ত খায় দেখা হবে। অন্যান্য
বাচ্চা-মত প্রতিদিন বাচ্চা কতটুকু খেলে তাও দেখা হবে এবং বাচ্চা-
ওজন দেখা হবে। স্বাভাবিক ভাবে, বাচ্চা-কোন ওষুধ দরকার হলে
তাও দেওয়া হবে।

আপনি আপনার বাচ্চাকে এই গবেষণায় রাখতে চাইলে আপনার মৌখিক
অম্মতি দিন। আপনি রাজী না থাকলেও এই হাসপাতালের স্বাভাবিক
চিকিৎসা থেকে আপনার বাচ্চা বঞ্চিত হবেন না।

আপনাকে ধন্যবাদ।

স্বাক্ষর:

গবেষকগণের স্বাক্ষর:

তারিখ:

এ আর জি ডি গবেষণা: মায়েদের বারনার প্রশ্নপত্র।

- ১। আপনার-কয়জন ছেলে মেয়ে বেঁচে আছে? _____
- ২। এই বাচ্চা-কয় কত (মাসে)? _____
- ৩। বাচ্চাকে বাড়ীতে কি খাওয়ান? _____
- ৪। বাচ্চা কয়মাস পর্যন্ত বুকের দুধ খেয়েছে? _____
- ৫। বাচ্চাকে দুধ হাড়া কি অন্য কোন খাবার দিয়েছেন? _____
- ৬। অন্য খাবার দিয়ে থাকলে, কত মাস কয়মাসে প্রথম দিয়েছেন? _____
- ৭। বাচ্চার প্রথম আন্ডা খাবার কি বুকম (হান) ছিল? _____
- ৮। এই আন্ডা খাবারের সঙ্গে কি তেল দিয়েছেন? _____
- ৯। এই আন্ডা খাবার-দিয়ে ওরাতে হোটে কয়বার দিয়েছেন? _____
- ১০। এই খাবারটির দিকে তাকান: এটা কি বাচ্চা খেতে পারবে? _____
- ১১। বাচ্চা খেতে পারলে, কয়মাস কয়মাসে এই খাবার বাচ্চাকে দেওয়া যায়? _____
- ১২। এই খাবারের সঙ্গে কি, বুকের দুধ খাওয়ান উচিত? _____
- ১৩। খাবারটি শুকে (হান নিয়ে) দেখেন: এটা কি বাচ্চাকে খাওয়ান যাবে? _____
- ১৪। খাবারটি খেয়ে দেখেন, এটা কি বাচ্চাকে খাওয়ান যাবে? _____

স্বাক্ষর: _____

তারিখ: _____

Answer to Dr. G. Lawrence's comments:

Quantitation of anaerobes has not been planned as suggested by Dr. Lawrence. This cannot be performed through this protocol, because an enormous number of culture plates would be needed for quantitation with a large number of gas packs and anaerobic jars. In our study design and aim, quantitation is not essential. However we would store all the samples to make quantitative count of the positive samples to make quantitative count of anaerobes and microaerophiles has been planned for jejunal fluids.

The design of the study was made depending on the facilities available at our hospital. For an external reviewer it might be difficult to perceive.

Culture of post mortem specimens has been planned, because in almost each set of culture, some space is available in the anaerobic jar. To utilize the gas pack and anaerobic facility fully we would like to culture post mortem samples.

Quantitation of clostridia would not be done, because of media constrain and laboratory work. The medium suggested by Dr. Lawrence would be tried.

GLC is available at ICDDR,B and underutilized. So we planned to use the GLC in specific cases where justifiable. Direct Gram Staining of the faeces would be done.

Selective enrichment in cooked meat with neomycin and then plating on neomycin blood agar for picking up type *C. perfringens* (Type A & C) would be done.

The procedure for typing of *C. perfringens* will be modified.

There is an anaerobic chamber (Glove box) available at ICDDR,B Microbiology Laboratory. Since the gas mixture had been extremely difficult to procure from the Bangladesh Oxygen Ltd. in the past, an attempt to get the gas mixture from Singapore was made. This worked out much more expensive than the gas packs. However, we would always keep our eye open for the local availability of gas mixture.

With our standard laboratory work load, one lab. person with 100% time should be enough for the bench work.