Attachment 1.

Date 20/7/82

ETHICAL REVIEW COMMITTEE, ICDDR,B.

Principal Investigator Dr. Asma Khanam

Trainee Investigator (if any) 209

Application No. ~~80-050~~ 82-030

Supporting Agency (if Non-ICDDR,B) _____

Title of Study "CLINICAL AND EPIDEMIOLOGICAL STUDIES ON DIARRHOEA ASSOCIATED WITH MEASLES.

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 NA 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 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
   NA 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.

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

Asma Khanam
Principal Investigator

Trainee

82-030

Rec. 22.7.82.

SECTION I - RESEARCH PROTOCOL

1. TITLE: Clinical and Epidemiological Studies on Diarrhoea Associated with Measles

2. PRINCIPAL INVESTIGATOR: Dr. Asma Khanam

   CO-INVESTIGATORS: Drs. G.H. Rabbani , Nigar Shahid

3. STARTING DATE: September, 1982

4. COMPLETION DATE: September, 1983

5. TOTAL DIRECT COST: $17,390

6. SCIENTIFIC PROGRAM HEAD: Dr. Thomas C. Butler

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

Signature of the Scientific Program Head: Thomas Butler

Date: 20/7/82

7. ABSTRACT SUMMARY:

A cohort of 500 children (age 0-4 years) from the village Nandipara will be studied prospectively for a period of one year to determine the incidence and etiology of diarrhoea in children with measles. The effect of both measles and measles with diarrhoea on nutrition will be evaluated by monitoring anthropometric measurements before and after measles. Measles and diarrhoea surveillance

will be maintained by once weekly visit to every child included in the study and twice weekly visit when measles is reported. Rectal swabs for culture will be taken from each child with measles and his controls for a month to identify V. cholera, E. coli (ST & LT), Shigella, Salmonella, Rotavirus and Campylobacter.

8. REVIEWS:

a) Research involving human subjects: _____

b) Research Committee: _____

c) Director: _____

d) BMRC: _____ _____

e) Controller/Administrator: _____ _____

SECTION II - RESEARCH PLAN

A. INTRODUCTION

1. Objectives:

(1) To define the incidence of measles and to identify the enteric pathogens specific to measles associated diarrhoea in children under 4 years of age.

(2) To study the interrelationship between measles infection, diarrhoea and nutritional status.

2. Background:

Measles appears to be a killing disease affecting young children in the tropical and some other less developed countries[1]. Although little is known about the epidemiology of measles in Bangladesh a recent study carried out in Matlab suggests that measles is the number three killer among pre-school children and ranks after diarrhoea and tetanus neonatarum[2]. In another study from Bangladesh, Koster et al recorded a case fatality rate of 3.9% in children under two years of age[3]. Mortality rates vary from country to country. In a study in West Africa, a case fatality rate of 36.6% has been recorded[4]. In the developed countries of Europe and North America the mortality rate ranged between 0.1 and 0.5 per 100,000 population in 1962[4]. In Mexico it was 85 times, in Guatamala 268 times and in Eucador 274 times more than in United States for the same year[5].

The incidence and severity of measles in children also differs between countries. In developed countries like the United States and Europe, where the standard of living is high, the greatest incidence is in children of 3 to 5 years age group and measles tends to be a relatively mild disease[6]. In less developed countries like Nigeria, though still an endemic disease, measles has its major incidence in children under 2 years of age and is a severe disease with unusual clinical features like haemorrhagic skin rash and severe epithelial desquamation[7]. In islands and in truly isolated virgin communities, the disease takes yet another pattern, sweeping through the whole population from the very young to the very old with great rapidity and causing high mortality[8,9].

Children are protected for the first few months of life by transplacental maternal antibody[10]. The level of passive immunity fades steadily after the 5th month when the disease becomes increasingly frequent[11] and by the end of the first year about a third of all children would have suffered from the disease[10]. In a recent study of complication of measles the author has reported that the youngest case to contract the disease was 67 days[12]. This study was based on clinical finding of measles. The present study plans to correlate clinical findings of measles with serology to confirm the diagnosis of measles.

MEASLES AND DIARRHOEA:

Diarrhoea and respiratory tract infections are the commonest complication of measles. The clinical impression is that diarrhoea is common and severe necrotizing gastroenteritis has been described at autopsy. This is probably due to invasion of the lymphoid tissues of the gut by the rapidly multiplying viruses[13]. Morley report from Nigeria that out of a total of 179 attacks of diarrhoea in 256 children with different infections observed for a period of 3 years, 109 attacks occured in children with measles i.e. 60.8% were measles associated diarrhoea[14]. Silhar from India reported that of all diarrhoea cases 21.2% were related to measles[15]. Ghose reported 29.9% cases were associated with measles diarrhoea[16]. Jaspal and Ramkrishnan reported 36-40% of measles patients had diarrhoea[17,18]. The high incidence of measles at 1 to 3 years of age coincides with the age distribution of acute diarrhoeal diseases and with that of malnutrition. Both diseases bear strongly on the severity and frequency of complications and death from measles.

In a case control study of measles, N. Shahid reported that mucoid diarrhoea was significantly more common among cases than controls[12]. Ninety three percent of 426 malnourished Senegalese children with measles had diarrhoea and 57% of 83 malnourished Nigerian children with measles reported diarrhoea[19]. The etiologies of diarrhoea associated with measles were not identified in the African and Indian studies. An unpublished report from the Teknaf project (ICDDR,B) has indirectly shown that measles often produced increased susceptibility to symptomatic Shigella infection.

Fraser reports that measles in one of the many respiratory infections which predispose to bacterial invasion of the respiratory tract, presumably as a consequence of local distruction of mucosa. One related observation is the deleterious effect of measles on tuberculous infection. The causative mechanism is likely to be indirect and probably immunological, along with some other virus infections measles produces a diminution of cell-mediated immunity which lasts for several weeks after the disease is ended[26]. Similarly measles associated diarrhoea may be due to secondary bacterial invasion of the digestive tract as a consequence of the disruption of the gut epithelial continuity and by decreasing cell-mediated immunity by measles virus.

Measles and Mlanutrition

Measles has a deleterious effect on the nutritional status of the child. This is thought to result from a decrease in intake of protein and calories. Appetite is certainly depressed during the infection and soreness of the mouth in breast fed babies may lead to inability to suck and failure of lactation[20]. Creighton describes the measles outbreak in Edinburgh in 1807 and gives the first account of Kwashiorkor in English literature saying that the children recovering from measles were afterwards affected with debility, cough, emaciation and oedematous swelling of face, hands and extremities which proved bery difficult to cure.

A study was carried out in 1977 among the children who had measles but were at different levels of nutrition. Results showed that malnourished children had more severe and prolonged attacks than the well-nourished ones. It was suggested that the malnourished children had depressed immune response which resulted in these severe and prolonged attacks, thus making them more susceptible to intercurrent infection[22]. Another longitudinal study in Imesi, Nigeria showed that children lost more than 10% of their former weight as a result of measles and did not recover their weights quickly after the disappearance of rash but took 7 weeks on an average. Children who had diarrhoea took twice as long to regain their lost weight than children who had no diarrhoea with measles. Many investigators have emphasized that measles has the capacity to precipitate serious nutritional disease in children already suffering from borderline malnutrition (as commonly seen in Bangladesh). Under natural conditions a net deteriorating effect of measles on nutritional status is evident in many ways. Loss of body weight occurs during the acute attack. Several weeks are needed for the weight to return to preceeding level and still longer to regain the expected rate of growth.

3. Rationale:

Measles is one of the important casuses of mortality and morbidity in pre-school children. From this study, knowledge of measles with its complications will be gained prticularly in respect to the

pattern of diarrhoea with specific etiology and nutritional status of the children. This knowledge will be helpful in developing strategies to decrease the morbidity and mortality from measles in rural Bangladesh.

B. SPECIFIC AIMS:

1. To determine prospectively etiologic specific rates of diarrhoea occuring with measles in comparison to a control group without measles.

2. To obtain age specific attack rate of measles over a period of one year in children 4 years and younger.

3. To study the effect of measles with and without diarrhoea, on nutritional status of children.

C. METHODS OF PROCEDURE:

1. STUDY VILLAGE: Nandipara stands at a distance of 2 miles from Bashabo (Madartek) on the eastern outskirts of Dacca city. As of 1978 this village had a total population of about 2000. The census of the village will be done shortly and we expect the population to have increased. The village is easily accessable and takes 30 minutes by a motor vehicle from the centre ICDDR,B. Majority of the population are Muslim who went to Assam during the famine in 1943 and again immigrated from the state of Assam to Nandipara village in early 1965. A large proportion of adult population work as day labourers, carpenters in the surrounding

area (Madertek) while a small proportion work in agricultural land. The village has no electricity and piped water supply.

The advantages for selecting this village are the following:

(a) Easily accessable and saves time and cost of transport by speedboat in contrast to Matlab.

(b) The population is stable.

(c) The centre has successfully utilized this village in the past and has a good understanding with the villagers.

(d) A weekly clinic is available.

(e) We have baseline information on demographic, nutritional, socio-economic and parasitic data of this village.

2. SUBJECTS OF STUDY: A sample size of 500 children aged 0-4 years of either sex without a previous history of measles will be selected and matched for age, sex and socio-economic status. With 500 children of 0-4 years, we know that 36% of 0-2 years children and 24% under one children are attacked annually[12]. From this co-hort, approximately 150 cases are expected to be attacked by measles.

3. MEASLES AND DIARRHOEA SURVEILLANCE: Every child admitted into the study will be visited by the field workers. The field workers will visit the village daily. The mothers and villagers will be trained and instructed to report any case of measles immediately to the field

worker. In addition weekly surveillance of measles and diarrhoea will be performed when the field worker will interview the mother about the child having developed any form of skin rash on the day of visit or during the preceeding week. The form to be used to record this is included as Appendix 1. The diagnosis of measles by the field worker will be confirmed by the investigator within 48 hours and further more by serology. Other data collected on the study children will include presence or absence of diarrhoea (4 or more loose stools in the previous 24 hours), dysentery (mucoid and bloody stool), fever, cough, anorexia, draining ear and vomiting as in Appendix 2. As soon as a case of measles is identified a case control study will be instituted. This will be done by matching each measles child with 2 control children (from among the 500 children in the study) selected one from the closest house and the other from a remote house, in which a child of the same age, sex and income level is present. This data will be available from the census data of Nandipara. Since measles may affect one of these control children in the next of few weeks, therefore a second control child has been chosen. By using the case control method we will be able to distinguish the effect of measles from what is only background infection. Children with measles and their controls will be studied intensively for a 8 week period for the following characteristics:

Fever: Each day all measles cases will have afternoon temperature recorded by the field workers for 2 weeks. Controls, if well will only have temperature recorded at the time of rectal swab. If ill, they will also have a record of daily temperature per rectum.

Anthropometry: Anthropometric measurements weekly for 8 weeks.

Stool M/E: Direct stool examination for the presence of pus cells, red cells and amebae giardia parasites will be done on the first day of onset of measles rash, 1st week, 2nd week, 3rd week and 4th week.

Rectal Swab: 3 consecutive rectal swabs will be taken on the first day of onset of measles rash, at 1 week and 2 week. Thereafter one rectal swab will be obtained on 3rd week and 4th week of measles. Thus we shall be able to know infection versus disease (diarrhoea) produced by enteric pathogens in measles cases and their controls. The following agents will be looked for: Rotavirus, Enterotoxigenic E. coli, V. cholera, Shigella, Salmonella and Campylobacter. This will allow us to analyze the rates of specific infection associated with measles infection compared to the controls. Diarrhoeal episodes occuring four weeks after the onset of measles rash will be labelled "measles associated" diarrhoea.

General Medical Care: Study subjects will not be given any special attention except for the clinical service presently being offered to the whole village by the weekly medical program. Confirmed shigella cases will be treated with ampicillin, X-ray positive cases of pneumonia will be treated with appropriate antibiotic. Children

having diarrhoea will be treated with oral fluid electrolyte solution in their village homes. Only those cases which have failed oral electrolyte fluid therapy and have developed moderate to severe dehydration will be brought to ICDDR,B hospital for appropriate treatment with I.V. fluid and antibiotics. Hospitalization of the cases will be done following a definite clinical criteria. These may include:

(a) moderate to severe degree of dehydration
(b) uncontrolled diarrhoea of more than 15 days duration
(c) severe cases of dysentery with prolapse rectum
(d) increasing respiratory rate, retraction of intercostal or suprasternal muscles, movement of alanasi, obtaining an X-ray and serum electrolytes.
(e) CNS complications following measles.

All children with respiratory distress will be brought to the hospital for a chest X-ray. The following standards will be used to monitor respiratory rate:

New born	-	40/min
2 years	-	25/min
5 years	-	20/min

Anthropometrics: Anthropometric measurements will be performed on all children monthly for a year and weekly for 8 weeks in children with measles and their controls. All nutritional data will be compared to appropriate international standard. Weights of children will be determined using spring scales in kilograms. Scales will be standardized prior to use. All subjects below 18 month will have their lengths measured in centimeters in recumbent position by a portable measuring board and for subjects more than 18 months old, heights will be directly read from a vertical scale with child in erract position. Arm circumference will be measured in centimeters by a simple tape.

Rectal swabs: When a child has diarrhoea (with measles or without measles) 2 rectal swabs will be taken. One will be placed in Cary-Blair transport media and the other in phosphate buffer saline (PBS, PH 7.4). All swabs collected in the village will be brought to the ICDDR,B laboratory in the same evening for plating. Swabs will be plated on Monsoor's agar (SP), SS and MacConkey's agar and the plates incubated for 18-24 hours. The plates will be looked for V. cholerae, Shigella and Salmonella. From the MacConkey's plate 5 lactose positive colonies will be picked that are typical of E. cili and will be stored in blood agar slant for testing of LT by using either chinese hamster ovary cell assay or Y_1 Adrenal cell assay. Two of the colonies will be tested for ST by infant mouse assay. Swabs in the P.B.S. will be preserved frozen until they can be tested for rotavirus antigen by the Elisa assay. Test for Campylobacter will be done in Campy BAP agar (BBL CO).

Serology: 0.2 mls of blood will be required from clinically diagnosed measles children during the acute phase of measles and 14 days after (convulescent phase) to see the rising titre of measles antibody and thus verify serologically the presumptive diagnosis of measles. Blood collection will be done as adopted by CDC Virology Division. Approximately 0.2 ml of blood will be bled by finger or heel prick and allowing the blood to flow filter paper disc of 10mm dimeter. The blood filled discs will be dried thoroughly without allowing the wet spots to touch other surfaces and then put in small labelled plastic bags placed in a flask to be transported from the field to the lab. These samples will be stored in - 50c until assay by direct Haemagglutination inhibition test is performed[25].

COLLECTION OF SPECIMENS

The clinical specimens in the table below will be obtained.

Day	Stool M/E	Rectal Swabs	Serum
0	x	3	x
1 week	x	3	x
2 weeks	x	3	
3 weeks	x	1	
4 weeks	x	1	

D. SIGNIFICANCE

(See Rationale).

E. FACILITIES REQUIRED:

1. Office space. The present office space for Dr. Asma & Dr. Rabbani will be utilized. A file cabinet, one desk and chair will be needed in Nandipara.

2. Laboratory space. ICDDR,B existing lab will be used.

3. Hospital Resources: None.

4. Animal Resources: 15,000 sucking mice for ST assay.

5. Logistic support: Data processing and computer support from computer branch.

6. Major items of equipment:

   weighing scales - 2

   measuring board - 2

   vertical scale - 2

7. Others: none.

F. COLLABORATIVE ARRANGEMENTS:

Serology of measles antibody will be done in I.P.H. by Dr. Farida Haque, Head of Virology Division, I.P.H.

Data Analysis:

It is anticipated that the following analysis and others will be performed.

1. Determination of age specific attack rate of measles in Bangladeshi children below 4 years of age.

2. Diagnosis of the etiological agent of diarrhoea and dysentery associated with measles.

3. Number of diarrhoeal episode per child per year will be compared to children with measles and those without measles.

4. Comparison of growth curves of children with measles and those without measles.

Statistical principles:

Data will be recorded directly on computer formated form to record clinical, nutrition and stool information. After checking the data sheet for obvious recording errots, data will be entered into IBMS/34 computer. The data will then be verified using an edit code. Using the stat pack availabilities of both Fortran and Basic Programmes the data will be tabulated on a monthly basis. At the end of the year, the differences in the two groups will be compared using Chi Square, 't' - test, ANOVA, Paired 't' tests (effect of measles on nutrition) and more sophisticated tests such as analysis of covariance will be included when available.

References

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SECTION III - BUDGET

A - DETAILED BUDGET

1. PERSONNEL SERVICES:

Name	Position	Level/Step	Monthly Rate $	Person Month	Cost $
Dr. Asma Khanam	P I	VII/3 5584	464	6	2781
Dr. Nigar Shahid	C I	VII/1 5078	422	1.2	510
Dr. G.H. Rabbani	C I	VII/3 5584	464	.6	280
Dr. to be named	C I	VI/1 3187	265	12	3,180
Dr. R.H. Gilman	Consultant		No cost to ICDDR,B		
Mr. Maksud		IV/4 2027	169	7.2	1,220
Mrs. Hazera Nazrul		III/4 1706	142	7.2	1,020
Local Boatman 500					
Local Field Asstt. 2 - 1000					
Computer programmer		VI/4 3658	304	1.2	360
Punch operator		III/2 1572	131	1.2	160
Henry Ghose - Study Clerk		III/6 1840	153	1.2	560
					$ 10,970

2. SUPPLIES AND MATERIALS:

Medicine	Syp. Ampicillin	$ 1.00/ph.	800 Ph.	$ 800
	Syp. Crystapen V.	$ .4	800 Ph.	$ 320
	Syp. Paramex C	$ .4	400 Ph.	$ 160
	Syp. Multi vit	$ .5	800 Ph.	$ 400
	Others			$ 500
				$ 2,180
Filter paper:				50
				$ 2,230

3. EQUIPMENTS:

Weighing machine	$ 50 x 2	=	$ 100
Ht. Stick tape length board			$ 50

4. PATIENT HOSPITALIZATION

No. of patients days @ Tk. 150/day	100x3x150	=	$ 2250

5. OUTPATIENT CARE - Nil -

6. ICDDR,B TRANSPORT -- 2600 mile x 3 = $ 390

7. TRAVEL AND TRANSPORTATION OF PERSON = $ -

8. TRANSPORTATION OF THINGS -

9. RENT, COMMUNICATION AND UTILITIES = $ 100

10. PRINTING AND REPRODUCTION

Forms and record sheet	Tk. 4,000		
Publication cost	Tk. 3,000		
Reprint	Tk. 3,000	=	$ 500

11. OTHER CONTRACTUAL SERVICES - Nil -

Computer time @	Tk. 800/hr.		$ 800

	Unit Cost	Amount Required	Project Required	
			Tk.	Dollar
Rectal swab for V. cholera	15	15 x 4400	66,000	3300
Rectal swab for Salmonella/Shig				
Rectal swab for Rotavirus	10	10 x 4400	44000	2200
Rectal swab for Campylobacter	14	14 x 4400	61600	3080
ST assay supplies	14.50	14.50 x 4400	63800	3150
LT assay supplies				
Stool M/E	2.05	2.05 x 2000	4100	205
			Tk.239500	11975

SECTION III - BUDGET

B. BUDGET SUMMARY:

	Taka	Dollar
1. Personnel	-	10,970
2. Supplies	-	2,230
3. Equipments	-	150
4. Hospitalization	-	2,250
5. Outpatient	-	-
6. Transport		390
7. Travel	-	-
8. Transport of things	-	-
9. Rent, communication and utilities		100
10. Printing and Reproduction	-	500
11. Contractual services	-	-
12. Computer time	-	800
		US $17390

Conversion rate $ 1= Tk. 20

Grand Total = US $ 17,390

ABSTRACT SUMMARY FOR ETHICAL REVIEW COMMITTEE

1. This study will be conducted on a cohort of 500 children of both sexes from 0-4 years age at Nandipara for a period of one year. This age group has been selected because measles appears to be most common in this age group and in which both morbidity and mortality is relatively high. History regarding the onset of measles or diarrhoea will usually be gathered from the parents or any other responsible adult member of the family, in addition the sick child will be seen both by the field workers and the physicians. All new births that will occur during this period will be included in the study.

2. This study will mostly collect descriptive, clinical and epidemiological data on measles, diarrhoea and nutrition. These involves no risk as related to the physical, pyschological, social, legal or other aspects of the subject except finger prick blood of 0.2 ml will be taken to confirm the diagnosis of measles rashes and after 15 days to note the rising titre. When a child has measles, simple treatment with paracetamol cough syrup etc may be given and when complicated by diarrhoea or dysentery they will be appropriately treated at their homes or be brought to ICDDR,B hospital in severe cases.

3. Does not apply.

4. Data collected will be computarized and confidentiality will be maintained by locking the files in the cabinet until completion of the study. All data will be abreviated and published without references to subjects name and identity.

5. As the subjects are children under 4 years of age, informed consent (signed or thumb print) will be obtained from the patients or the guardians of the child at the time of admitting the child into the study.

6. Parents or responsible adult family members will be interviewed at their village by the visiting field workers about the history of measles and/or diarrhoea on the day of visit or during the preceeding days. Visits by the field workers will be made weekly and two times a week following measles detection for one year. Informations about the monthly income with occupation will also be obtained.

7. The direct benefit to the subject will be general medical care available to every child at home when they are sick with measles or diarrhoea. Regular visits by the health personnel will make them aware of their health condition which may have long term effect on the community's health in general. Knowledge of the observational data will help in understanding the natural course of the disease in a particular setting which is essential in formulating hypothesis and for the development of projected control programmes.

8. Records of the informations will be preserved after collection from the field by the field workers. No preexisting hospital records will be utilized. Serological verification of the presumptive diagnosis of measles will be obtained by finger prick blood of 0.2 ml twice to observe the rising titre of measles antibody.

CONSENT FORM

The International Centre for Diarrhoeal Disease Research, Bangladesh is carrying out a research project at Nandipara to study the cause of diarrhoea with measles (lunti) and the interrelationship between measles, diarrhoea and nutrition. From this study it will be helpful to develop the standard treatment of the causal agent of diarrhoea associated with measles and thus prevent the sufferings and complications of measles. As you know that measles (lunti) is most common cause of mortality in our children we wish that your child should participate in this study.

You may expect the following examination on your child, if you are willing to participate:

1) Your child will be fully examined by a doctor during the period of measles and in this time 0.2 ml of finger or heel prick blood will be required for confirmation of the diagnosis of measles. Another 0.2 ml blood will also be required after 2 weeks to see the progress of the disease.

2) Rectal swab will also be taken for detecting the causal agent of the disease on the 1st, 2nd, 3rd day of the appearance of rashes and this test will be repeated thrice a week for two weeks and then once a week for another two weeks.

3) Routine anthropometric measurement (height, weight and mid-arm circumference) will be recorded monthly before measles, then weekly after appearance of rashes for 8 weeks. This will help to monitor the nutritional changes following measles.

4) Your child will receive appropriate medical care and facilities.

You are at liberty to withdraw your child from the study at any time. This will not jeopardise the medical care.

If you allow your child to participate in this study please sign your name below.

Signature of the Investigator

Signature of the Legal Guardian

সম্মতিপত্র

আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র নন্দীপাড়ায় হাম (মুন্তি) -এর সাথে সম্পর্কযুক্ত ডায়রিয়ার কারণ এবং হাম, ডায়রিয়া ও পুষ্টির মধ্যেকার সম্পর্ক সম্বন্ধে একটা গবেষণা চালাচ্ছে। এই গবেষণা থেকে হাম-এর সাথে সম্পর্কযুক্ত ডায়রিয়ার কারণ জানা যাবে এবং তার জন্য একটা সঠিক চিকিৎসাপ্রণালী উদ্ভাবন সম্ভব হবে। এইভাবে হামের জটিলতা এবং এর কষ্ট দূর করা সম্ভব হবে। আপনি নিশ্চয়ই জানেন যে হাম (মুন্তি) আমাদের দেশে শিশুমৃত্যুর একটা প্রধান কারণ। আমরা আশা করবো মানবতার খাতিরে আপনি আমাদের গবেষণায় অংশগ্রহণ করবেন।

আপনি যদি অংশগ্রহণ করতে রাজী হন, তাহলে——

① হাম-এ আক্রান্ত হলে আপনার বাচ্চাকে একজন ডাক্তার পরীক্ষা করবেন। এ সময়ে সঠিক রোগনির্ণয়ের জন্য আঙুল কিংবা পায়ের গোড়ালি থেকে সামান্য (০·২ সি·সি) রক্ত নেয়া হবে। ২ সপ্তাহ পরে রোগের অবস্থা জানার জন্য আবার একবার এই পরিমাণ রক্ত নেয়া হবে।

② হামের লক্ষণ দেখা দেয়ার প্রথম, দ্বিতীয়, তৃতীয় দিনে মলদ্বার হতে সামান্য মল নিয়ে পরীক্ষা করা হবে। এই পরীক্ষাটি প্রথম ২ সপ্তাহে তিনবার করে এবং পরবর্তী ২ সপ্তাহে একবার করে করা হবে।

③ মুন্তি হওয়ার আগে প্রতিমাসে একবার শিশুর ওজন, উচ্চতা এবং অন্যান্য দৈহিক পরিমাপ নেয়া হবে। মুন্তি হওয়ার পরে প্রথম ৮ সপ্তাহের জন্য দৈহিক পরিমাপগুলি সপ্তাহে একবার করে সংগ্রহ করা হবে।

④ আপনার শিশুর যথোপযুক্ত চিকিৎসা করা হবে।

আপনি যে কোন সময়ে গবেষণা থেকে নাম প্রত্যাহার করতে পারেন। এতে চিকিৎসার কোন অসুবিধা হবে না।

আপনি রাজী থাকলে নিচে স্বাক্ষর করুন:

MEASLES - DIARRHOEA STUDY

(MEASLES SURVEILLANCE)

Name _____ Study No. / / / (1 2)

Address _____ I D No. / / / / (3 4 5)

Card No. / / (6)

Case type: Case = 1, Control= 2 / / (7)

1. Date of visit (day/month/year) / / / / / / / (8 9 10 11 12 13)

2. No. of visit / / / / (14 15 16)

3. Date of onset of Measles / / / / / / / (17 18 19 20 21 22)

4. Measles rash? (No=0, Yes=1)

5. Fever before rash? No=0, Yes=1, duration? days / / (23) / / / (24 25)

6. Sore throat ? Duration / / (26) / / / (27 28)

7. Nasal discharge ? Duration / / (29) / / / (30 31)

8. Cough? Duration / / (32) / / / (33 34)

9. Day of appearance of measles / / (35)

10. Site of measles rash

Forehead =1, Back of ear = 2, face =3, / / / (36 37)

Arm=4, Leg=5, Chest=6, Abdomen=7,

1+2=8, 1+3,=9, 2+3=10, 3+4=11, 6+8=12

11. Duration of measles rash (days) / / / 38 39

12. Other complains:

a) Nightblindness / / 40

b) Ulceration of gum / / 41

c) " " tongue / / 42

d) Abd pain / / 43

è) Loss of app / / 44

f) Resp distress / / 45

APPENDIX 2

MEASLES-DIARRHOEA STUDY
(DIARRHOEA SURVEILLANCE)

Name _____ Study No. / / / (1 2)

Address _____ I D No. / / / / (3 4 5)

Card No. / / (6)

Case type:
Case =1, control =2, / / (7)

1. Date of visit Day/month/year / / / / / / / (8 9 10 11 12 13)

2. Number of vist / / / / (14 15 16)

3. Date of onset of Measles rash, day/month/year / / / / / / / (17 18 19 20 21 22)

4. Weight Kg. / / / (23 24)

5. Height Cm. / / / / (25 26 27)

6. A.C. (mm) / / / / (28 29 30)

7. Number of stool in 24 hours / / / (31 32)

8. Nature of diarrhoea:

Rice watery = 1, loose =2, liquid = 3 / / (33)

9. Blood and Mucus: Blood=1, Mucus=2
Blood + Mucus =3 / / (34)

10. Dehydration status: mild=1, mod=2, severe =3 / / (35)

11. Other complains: (No=0, Yes=1)

a) vomiting /__/ 36

b) Abdomen pain /__/ 37

c) Loss of appetite /__/ 38

d) Rectal prolapse /__/ 39

e) Tenesmus /__/ 40

f) Fever /__/ 41

g) Cough /__/ 42

h) Drainy ear /__/ 43

i) Pneumonia /__/ 44

j) Nightblindness /__/ 45

k) Ulceration of gum /__/ 46

l) " " tongue /__/ 47

12. Treatment given:

a) Rehydration oral =1, IV=2, Oral + IV=3 /__/ 48

b) Medications: (No=), Yes=1, unk=9) /__/ 49

1) Amp /__/ 50

2) Tetra /__/ 51

3) Cholera /__/ 52

13. Treatment given (contd)

b) Medications: (No=0, Yes=1, Unk=9)

4) Gentamycin / / 53

5) Furoxone / / 54

6) Klion, flagyl / / 55

7) Vit A / / 56

8) Other (specify) _____ / / 57

14. Outcome: Recorded = 1, Died =2 / / 58

15. Number of People in family / / / 59 60

16. No. of living children (under 15) / / / 61 62

17. No. of Cases in the family / / / 63 65

18. Mothers Education (No. of years of schooling) / / / 66 67

19. Fathers occupation:

Detail _____ / / / 68 69

20. Total income of the family in taka.

≤ 500 =1, 501-1000 =2 / / 70

1001-2000 = 3, 2001-3000=4

3001-4000 = 5, > 4000=6

21. Dwelling space < 200 sq ft = 1 / / 71

201-400 Sq. ft. = 2

401 + " " = 3

NAME _____ Study No. / / / (1 2)

I D No. / / / / (3 4 5)

Laboratory Results:

1. Rectal swab culture - (0=neg, 1=pos)

Salmonella typhi	—	/ / (6)
Salmonella other	—	/ / (7)
Shigella flexneri	—	/ / (8)
Shigella dysentereae type I	—	/ / (9)
Shigella dysentereae type II	—	/ / (10)
Shigella boydei	—	/ / (11)
Shigella sonnei	—	/ / (12)
Escherichia coli ST	—	/ / (13)
V. cholerae	—	/ / (14)
Rotavirus	—	/ / (15)
Campylobacter	—	/ / (16)

2. Stool M/E

Parasites

Ameba (0=neg, 1=cyst, 2=troph, 3=troph+RBC)	—	/ / (17)
Giardia (0=neg, 1=cyst, 2=troph)	—	/ / (18)
Hookwarm (=neg, 1=pos)	—	/ / (19)
Ascaris (0=neg, 1=pos)	—	/ / (20)
F. Buski (0=neg, 1=pos)	—	/ / (21)
Trichuris (0=neg, 1=pos)	—	/ / (22)
Strongyloides (0=neg, 1=pos)		/ /

Distribution of Measles Cases Throughout the Year
(Observations of 1 year)

Age Groups of measles children	Spring March-May	Summer June-July	Monsoon Aug-Oct	Winter Nov-Feb
0-6 m				
1 yr				
2 yrs				
3 yrs				
4 yrs				

MEASLES, DIARRHEA AND DEATH OVER 1 YEAR OBSERVATION

		Children with measles			Children without measles		
Age	Total children	No. of children	Cases developed diarrhea	Death occured	No. of child	Cases developed diarrhea	Death occured
0-6 m							
-1 yr							
-2 yrs							
-3 yrs							
-4 yrs							

ISOLATION RATES OF

SHIGELLA, SALMONELLA, E. COLI, V. CHOLERAE, RO

CHILDREN WITH & WITHOUT M

Age	Children with Measles					
	Tot. No. of cases	No. with Shigella/ Salmonella	No. with E.H./G.L	No. with E. coli	No. with Cholera	
0-6 months						
1 yr.						
2 yrs.						
3 yrs.						
4 yrs.						
All ages	Tot. No. of cases	____%	____%	____%	____%	____%

Tot. Nos. of cases ____