ment 1. Revised

ETHICAL REVIEW COMMITTEE, ICDDR,B.

Date 31/8/88
20.9.88 (Rev. Date)

Principal Investigator Dr. N.H. Alam

Trainee Investigator (if any) _____

Application No. 88-024(Revised)

Supporting Agency (if Non-ICDDR,B) _____

Title of Study "Evaluation of trimethoprim sulphamethaxazole in the treatment of infants and children with persistent diarrhoea"

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 an overview (all other requirements will be submitted with individual studies).
   ✓ Protocol (Required)
   ✓ Abstract Summary (Required)
   ✓ Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw (Required)
   ___ Informed consent form for subjects
   ✓ Informed consent form for parent or guardian
   ___ Procedure for maintaining confidentiality
   ___ Questionnaire or interview schedule *

* If the final instrument is not completed prior to review, the following information should be included in the abstract summary:
1. 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.

(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.

Principal Investigator

Trainee

SECTION I - RESEARCH PROTOCOL

Title: "Evaluation of trimethoprim-sulphamethaxazole in the treatment of infants and children with persistent diarrhoea"

Principal Investigator: Dr. Nurul Haque Alam

Co-Principal Investigator: Dr. Rukhsana Haider

Co-Investigators: Dr. P.K. Bardhan
One person from L.S.D.
(nominated by Dr. Tzipori)

Consultants: Dr. D. Mahalanabis
(Project Coordinator)
Dr. Chris Wanke
Dr. S.K. Roy

Starting Date: As soon as approval is obtained.

Completion Date: Two years from the starting date.

Total direct cost: US$ 93,655.00

Name of the Division: Clinical Sciences Division

Signature of CSD Head .....

Date: 20th September 88

Abstract Summary

Persistent diarrhoea is one of the common clinical problems seen in developing countries. Relatively few studies have been directed towards the recognition, treatment, and prevention of this entity. Among the postulated mechanisms involved in the pathophysiology of persistent diarrhoea, smallbowel bacterial

overgrowth is an important one. In a double blind, randomised controlled trial this protocol proposes to study 52 patients of both sexes in two groups aged 3-24 months, with history of diarrhoea for 14 days or more. One group will receive an antibiotic, trimethoprim-sulfamethaxazole for 7 days, along with a modified diet and a vitamin mineral mixture whereas the other group will receive a placebo instead of the antibiotic. After completion of the study, the clinical responses amongst the two groups will be compared.

After being discharged the patients will be seen every two weeks in the hospital for a period of one month or longer till they can go back to their previous normal diet.

Research Review Committee .....

Ethical Review Committee.....

Director.....

1. A study in Lima, Peru showed that 49% of the deaths in children under 5 years of age were associated with diarrhoea; however, half of those who died had diarrhoea for more than 2 weeks prior to death;

2. In rural Bangladesh, dysentery and chronic diarrhoea accounted for nearly 16% of all childhood deaths (Black et al). Another study in the same area showed that 17% of all under five deaths were due to diarrhoeal illness and 58% of all diarrhoeal deaths were attributable to persistent diarrhoea (Chowdhury M.K. et al);

3. In a study in India 52% of diarrhoeal deaths were associated with persistent diarrhoea although only 5% of all episodes lasted longer than 2 weeks. The case fatality rate was 14% in this group compared with 0.7% among those who had diarrhoea for less than two weeks; i.e. nearly 50% of diarrhoeal deaths could be associated with persistent diarrhoea (Bhan M.K. et al).

The distinction between acute and persistent diarrhoea is somewhat arbitrary because available information suggests that the frequency distribution of diarrhoeal duration is continuous. Most authors have used a duration of 2 to 3 weeks or more to indicate persistent diarrhoea. In India and Peru, persistent diarrhoea has generally been found more frequently in the first year of life. A later peak occurrence has been observed in

SECTION II - RESEARCH PLAN

A. INTRODUCTION

1. Objective:

The major objective of this study is to evaluate the efficacy of an absorbable antimicrobial agent trimethoprim-sulphamethoxazole (TMP-SMX) in the management of children with persistent diarrhoea.

For meaningful interpretation of the results of this study, microbial flora of upper smallbowel and faeces will be evaluated for type, quantity and antibiotic sensitivity.

2. Background

The term "persistent diarrhoea" is meant to define episodes of diarrhoea that begin acutely but persist beyond the expected time period for the usual self limited disease. Many of the patients with prolonged periods of diarrhoea may experience a significant decrease in nutritional status during and following the episode; in some instances a persisting diarrhoea may end fatally. Relatively few studies have been directed towards the recognition, treatment and prevention of this entity. A substantial proportion of the diarrhoea associated deaths in young children are in those with persistent diarrhoea. Examples are:

1. A study in Lima, Peru showed that 49% of the deaths in children under 5 years of age were associated with diarrhoea; however, half of those who died had diarrhoea for more than 2 weeks prior to death;

2. In rural Bangladesh, dysentery and chronic diarrhoea accounted for nearly 16% of all childhood deaths (Black et al). Another study in the same area showed that 17% of all under five deaths were due to diarrhoeal illness and 58% of all diarrhoeal deaths were attributable to persistent diarrhoea (Chowdhury M.K. et al);

3. In a study in India 52% of diarrhoeal deaths were associated with persistent diarrhoea although only 5% of all episodes lasted longer than 2 weeks. The case fatality rate was 14% in this group compared with 0.7% among those who had diarrhoea for less than two weeks; i.e. nearly 50% of diarrhoeal deaths could be associated with persistent diarrhoea (Bhan M.K. et al).

The distinction between acute and persistent diarrhoea is somewhat arbitrary because available information suggests that the frequency distribution of diarrhoeal duration is continuous. Most authors have used a duration of 2 to 3 weeks or more to indicate persistent diarrhoea. In India and Peru, persistent diarrhoea has generally been found more frequently in the first year of life. A later peak occurrence has been observed in

other countries. However, wherever it has been studied, persistent diarrhoea occurs primarily during the first three years of life. At ICDDR,B a majority of the patients with persistent diarrhoea admitted to the treatment centre are aged 3 months to 18 months.

Clinical Categories of Persistent Diarrhoea

Two broad clinical categories of persistent diarrhoea are seen by paediatricians in the developing world (Bhan M.K. et al unpublished). Among the first category are those who pass several liquid stools in a day but without much dehydration. This category is nevertheless important in that growth failure may occur and adverse nutritional consequences may contribute to increased susceptibility to infections and increase the risk of death. The second category is of infants and young children who have severe and persistent watery diarrhoea and in whom maintenance of hydration without intravenous fluid is difficult. In this group the deterioration in nutritional status is rapid, and mortality is high even under reasonable medical supervision. These two categories probably represent a broad spectrum of severity; whether important etiological and patho-physiological difference exists between these groups is not known.

Oral rehydration Therapy is well established for acute diarrhoea. In persistent diarrhoea cases of mild to moderate severity, oral rehydration therapy using ORS is still highly effective. On the other hand in severe persistent diarrhoea among infants a net secretory state exists in the jejunum and this is associated with impaired glucose malabsorption. Oral glucose electrolyte solutions are usually not effective in these patients. Therefore, parenteral fluid and electrolyte therapy often play an important role in their management.

Drug Treatment of Persistent Diarrhoea

Treatment of persistent diarrhoea is broadly based on dietary management, fluid therapy and general supportive care. Antibacterials and other antidiarrhoeal agents have not been evaluated extensively or properly. Patients investigated in the few published studies differ with respect to clinical severity, duration of illness, age and nutritional status. Also, few of these studies used an appropriate control group. At present, routine use of antibiotics in patients with persistent diarrhoea is not recommended except when specific pathogens like Shigella are isolated.

Clinical Experience and Antimicrobials

Usefulness of antimicrobial agents in persistent diarrhoea was suggested in an early report; a combination of oral gentamicin, metronidazole and cholestyramine therapy was effective in terminating persistent diarrhoea in a majority of treated infants (Hill D. et al). The study, however, lacked a control group and it was difficult to identify which of these agents contributed to this apparent clinical effect. Recently the efficacy of oral gentamicin, metronidazole and cholestyramine in persistent diarrhoea was evaluated in a controlled trial by Hill and colleagues. Using a 2x2x2 factorial design forty patients between 6 and 12 months of age were randomised to 8 treatment groups: gentamicin (G) + metronidazole (M) + Cholestyramine (C), G+M, G+C, M+C, and G, M, and C alone. For each drug used in the study, 20 patients receiving a particular drug were compared with 20 not receiving it. Cholestyramine had significant efficacy on stool output only for first 24 hours. However, gentamicin showed a significant decrease in stool output for 3 consecutive days except for first 24 hours of therapy. A recent study in the USA (Craft C et al, Unpublished), comparing oral gentamicin to placebo, showed gentamicin to be effective in shortening the duration of illness, but only in patients who harboured enteroadherent/enteropathogenic E.Coli in the small

bowel (about 50% of patients studied). Additional controlled trials of oral gentamicin therapy for persistent diarrhoea are underway in Guatamala and India.

Tropical Sprue

This syndrome of chronic diarrhoea of unknown etiology, with intestinal malabsorption, and often with multiple nutritional deficiencies in adults and older children is endemic in this subcontinent. These patients usually respond to a course of antibiotic therapy, mainly to Tetracycline (French J.M. et al, O'Brien W et al, Shefy T.W. et al, KLipstein F.A. et al.). Rationale for this treatment approach, however, remains empirical. Although small bowel overgrowth with enteric flora has been demonstrated in them, a convincing difference from the controls taken from the same socioeconomic group could not be demonstrated (Gorbach S.L. et al.).

Intestinal Microflora and Persistent Diarrhoea

Most enteropathogens that cause acute diarrhoea have also been associated with persistent diarrhoea, notable exceptions being vibrios and viruses, especially rotavirus. Those organisms that are isolated with about equal frequency from episodes of acute and persistent diarrhoea include non-typhoid Salmonella, enterotoxigenic E.Coli, Campylobacter Jejuni, and

aeromonas hydrophila. Their continued presence in episodes of persistent diarrhoea probably reflects an impaired ability of the host to terminate infection. Organisms isolated with greater frequency for episodes of persistent diarrhoea include Shigella, enteroadherent E.Coli (EAEC) Enteropathogenic E.Coli and Cryptosporidium (Black, Penny - Unpublished; Bhan et al - Unpublished).

Epidemiological studies at ICDDR,B suggest (Black et al) that 7% of episodes of acute diarrhoea associated with enterotoxigenic E.Coli persisted for longer than 3 weeks compared with 3% of episodes of rotavirus diarrhoea.

The association of EPEC and EAEC with persistent diarrhoea is of particular interest and requires further investigation. Enteroadherent strains, some of which are also of EPEC serotypes, are characterised by their capacity to adhere to cells in tissue culture (E.g. HEP-2 cells). E.Coli with localised and autoaggregative types of adhesion are associated with persistent diarrhoea. The latter type which usually does not belong to EPEC serotypes may play an important role in persistent diarrhoea. In India, for example, they were isolated from 2% of healthy controls, 9% of children with acute diarrhoea and 26% of children (under age 3 years) with persistent diarrhoea (Bhan et al - Unpublished).

In most studies, less than half the children with persistent diarrhoea have recognised enteric pathogens in their faeces. However, a few studies such as the one in Peru (Penny et al) have shown that patients with persistent diarrhoea have increased number of aerobic and anaerobic fecal bacteria in the small bowel in comparison to findings in healthy controls from developed countries in whom the upper small bowel only contains very small numbers of respiratory-type commensal bacteria. However, studies in children with acute diarrhoea and in locally recruited healthy controls in Lima showed similar results as those in persistent diarrhoea patients, raising doubts as to their significance in relation to the pathogenesis of persistent diarrhoea.

Finally, preliminary data from culture of small bowel fluids in infants and children with persistent diarrhoea admitted to ICDDR,B treatment centre showed predominantly E.Coli and Klebsiella when enteric bacteria were isolated. Majority of the coliforms isolated are sensitive to cotrimoxazole.

Combination of trimethoprim and sulfamethoxazole (cotrimoxazole) is a widely used antimicrobial agent and has been described in most standard text books. It is based on the principle that when two drugs, with action

on sequential steps in the pathway of an obligate enzymatic reaction in bacteria, are combined, they become synergistic. The antibiotic activity of the combination of trimethoprim and sulfamethoxazole results from its actions on two steps of the enzymatic pathway for the synthesis of tetrahydrofolic acid. The optimal ratio of the concentrations in vivo of the two agents for synergism for the greatest number of organisms is 20 parts of sulfamethoxazole to one part of trimethoprim. The combination is thus formulated to achieve a sulfamethoxazole concentration in vivo 20 times greater than that of trimethoprim. When 800 mg of sulfamathoxazole is given with 160 mg of trinmethoprim to an adult (5:1 ratio) twice daily the peak concentrations of the drugs in plasma are stated to be approximately 40 and 2 ug/ml i.e. 20:1 ratio. Trimethoprim is rapidly distributed in tisues. High concentrations of each component of the mixture are also found in bile. Cotrimoxazole is available in tablet form (400 mgm sulfamethoxazole plus 80 mgm trimethoprim or 800 mgm sulfamethoxazole plus 160 mgm trimethoprim) and as an oral suspension (200 mgm sulfamethoxazole plus 40 mgm trimethoprim per 5 ml). The usual daily dose for children is 8-10 mgm/kg/day of trimethoprim in two divided doses every 12 hours. Usual adult dose is 800 mgm sulfamethoxazole plus 160 mgm trimethoprim every 12 hours.

In routine use, the combination appears to exert little toxicity. About 75% of untoward effects involve the skin which are typical of those known to be produced by sulfonamides.

3. Rationale

Persistent diarrhoea in infants and children is associated with adverse nutritional consequences and high mortality. Recent studies suggest that antimicrobials such as oral gentamicin shorten diarrhoea duration in such patients and thus may reduce adverse nutritional consequences and associated mortality.

In the absence of clear understanding of the underlying mechanism for persistent/prolonged diarrhoea in infants, therapeutic approaches are understandably empirical. Although, it is postulated that small intestinal colonisation with enteric bacteria may in some way be related to pathogenetic mechanism, the small bowel flora has not been shown to be significantly different to controls taken from the same socioeconomic group. In light of the above we offer the following rationale for this study: a) persistent diarrhoea in infants is a potentially serious disease with serious consequence; therefore, clinicians confronted with this difficult clinical syndrome often use antibiotics; a controlled clinical trial such as this will offer a sound basis for using or for not using an antimicrobial agent; b) as stated earlier, recent reports indicate that judicious use of an antimicrobial agent used for infection with gram negative bacteria such as cotrimoxazole, if found useful, should be of considerable usefulness; c) a similar

syndrome of chronic diarrhoea malabsorption in adults and older children (i.e. tropical sprue), widely prevalent in this subcontinent, often respods to a course of antibiotic tetracyrline; a similar approach to treat infants with prolonged diarrhoea may be fruitful; d) This study also offers opportunity to understand the pathogenetic mechanism of this syndrome; e) in view of the fact that co-trimoxazole is being seriously considered by WHO and other relevant agencies for use as a first line drug for use in the case management strategy for the control programme of acute respiratory infections (ARI), demonstration of its usefulness in persistent diarrhoea may be of added advantage from public health point of view.

B. SPECIFIC AIMS

1. To determine whether treatment with TMP-SMX reduces the stool output, duration of diarrhoea and improvement of intestinal function as measured by breath hydrogen test and intestinal permeability test in children with persistent diarrhoea.

2. If TMP-SMX is shown to be effective in the treatment of persistent diarrhoea how this effect relates to upper small bowel bacterial flora and their sensitivity to antimicrobials.

C. METHODS OF PROCEDURE

Inclusion criteria:

a. Age 3 months to 24 months of either sex.

b. History of diarrhoea for 14 days or more but less than 6 weeks (with no more than one diarrhoea free day) and four or more liquid stool during previous 24 hours.

c. Confirmation of diarrhoea being present during initial observation period of 24 hours on ward diet i.e. four or more liquid stool in 24 hours and stool weight is equal to or more than 30 g per kg per 24 hours of observation.

Exclusion criteria:

a. Systemic infection requiring prompt antibiotic treatment e.g. meningitis, pneumonia.

b. Clinically apparent severe marasmus (weight for age less than 55% of NCHS median weight).

c. History of sensitivity to sulfonamides or cotrimoxazole.

d. Stool culture positive for V. cholerae, Shgiella and Salmonella during observation period. They will be treated according to standard hospital practice.

Response variables:

1. Daily stool output in gram per kg per 24 hours over the treatment period of 7 days (for males only).

2. Duration of diarrhoea as defined below.

3. Weight gain or loss at end of treatment

4. Volume of I.V. needed (per kg body weight) during

treatment (a proxy indicator).

5. Improvement in intestinal function as measured by breath hydrogen test after lactose and intestinal permeability test as measured by differential absorption/excretion of lactulose and mannitol after a test dose.

Sample Size

Based on a recently completed study by Craft et al (Clinical trial of Oral Gentamicin in persistent diarrhoea) and for the treatment to be clinically worthwhile we expect that 70% of the patients receiving TMP-SMX should be cured by day 7 of therapy as against 30% in controls receiving supportive therapy with fluids (I.V. and oral) and diet. taking a significance level ( ) of 0.05 and 80% power to detect a diff erence of this magnitude or more between two groups 21 patients are needed in each group. Assuming a drop out rate of 20% the sample size of 52 total will be required.

Randomization

The study group will receive the drug cotrimoxazole (TMP-SMX) every 12 hours starting 48 hours after admission. The drug will be administered in a liquid form. The control group will receive a placebo which is identical in appearance to the drug. The drugs will be dispensed in identical bottles. A master randomization code will be prepared using random permuted blocks. The drug and placebo bottles will be

arranged in a sequence that corresponds to the randomisation code and then numbered sequentially. The bottles will be labelled with the name of the study and the serial number of the bottle only. The serial number of the bottles will correspond to the serial number of the patients enrolled into the study. As an example when a new subject is selected for the study e.g., the fifth patient he/she will be assigned the medicine bottle numbered 5. A careful record will be kept of the treatment numbers assigned to each subject. Therefore randomisation is incorporated in the patient serial number which corresponds to the serial number of the medicine bottles containing either placebo or the drug. The master randomisation code will be prepared by an appropriately trained person who is not connected with the study and two copies will be kept safely away in two different places.

Patient Recruitment

Children presenting at the treatment centre with a history of diarrhoea of 14 days or more but less than 6 weeks who had at least four liquid stools over 24 hours prior to admission will be evaluated and if they fulfil the remaining inclusion and exclusion criteria will be admitted to the study.

Initial evaluation will include history and physical examination including nutrition anthropometry (recorded on pretested forms), stool collection for 48 hours on ward diet (standard milk-rice cereal-oil mixture) and if stool output

is more than 30 gms per kg body weight in 24 hours then the patient will be included into the study. During this initial 48 hours the patient will have the following investigations which are now routinely done for persistent diarrhoea patients at ICDDR,B:

1. Stool microscopy for pus cells, parasites (including G.Lamblia, E. Histolytica and cryptosporidium).

2. Stool culture for Shigella, Salmonella, Campylobacter Jejuni, cholera, E.Coli (colonies will be saved), klebsiella (colonies will be saved), and stool for rotavirus test.

3. Breath hydrogen test after a lactose drink.

4. Intubation for small bowel samples for quantitative microbiology and microscopy (for G. Lamblia, cryptosporidium, strongyloides stercoralis).

5. Blood for electrolytes, urea, glucose, total and differential WBC count, microhaematocrit and plasma total solids (refractometry).

In addition the patients will receive the following test:

6. Small intestinal permeability test.

7. Throat swab culture for enteric organisms, particularly E.coli and klebsiella (colonies will be saved). (Just before intubation).

Informed Consent

If the patient is found to be eligible for inclusion into the study an informed consent will be obtained (Bangla consent

form attached). The consent form indicates in simple words and easily understood by a nonprofessional person, the purpose of the trial, the benefits and any side-effects of the drug in the study group, the fact that the drug and placebo will be randomly allocated, procedures and examinations to be performed including blood samples and intestinal intubations, stool and urine samples etc., and a clear indication that the patient is free to withdraw from the study at any time and will still receive standard treatment used in this hospital for his/her disease. The consent will be administered by the Principal Investigator(s) and then will be witnessed by another staff member.

After six weeks, if the parents are willing, a separate consent form will be provided. to repeat the intubation during non-diarrhoeal state. The purpose of the investigation, will be to compare the parasites and bacteria isolated during the persistent diarrhoea period with those isolated during the non-diarrhoeal phase, each patient acting as his own control.

Controls (for microbial etiology)

Age matched controls will be selected concurrently from among children aged 3-24 months attending the treatment centre with a history of acute watery diarrhoea of 3 days or less and no antibiotics during this illness and no diarrhoea in the previous 2 weeks. Matching for age will be within one month for infants aged 3-12 months and within 3 months for children

aged 13-24 months. A baseline history will be obtained and clinical examination (including nutrition anthropometry) performed and recorded on a pretested form and stool and rectal swab will be obtained for detection of rotavirus and culture for Shigella, Salmonella, cholera, E.Coli (colonies will be saved), klebsiella (colonies will be saved). Also a throat swab will be taken for aerobic enteric pathogens (particularly E.coli and klebsiella species) mainly to evaluate isolates for their identity with strains isolated from small bowel fluid.

These patients will be intubated within 48 hours of admission following procedures similar to the one described for study patients for small bowel samples for quantitative microbiology and microscopy. Appropriate consent will be obtained for these procedures.

Case Management

Fluid therapy

The patients will be maintained in fluid balance using intravenous fluids as needed by the clinical state and purging rate.

Diet.

Initial diet after admission into the study (i.e. on commencement of medicine) will be based on rice, glucose, egg yolk, vegetable oil and salts which is now routinely used for

persistent diarrhoea patients at ICDDR,B. This mixture has an energy density of 70kcalories per 100 grams. On day 1 they will receive 50kcalories per kg per day and from day 2 onwards they will receive 100kcalories per kg per day.

Vitamins and Minerals.

The patients in addition will receive a vitamin mineral mixture at twice the minimum daily requirements for age (to provide for incomplete absorption).

Drug therapy

Drug or placebo will be administered from the numbered bottles containing liquid preparation of drug or placebo assigned to the patient serial number. Dose will be adjusted to give 10 mgm of trimethoprim per kg per day divided into two 12-hourly doses for 7 days. The mixture will contain a mixture of sulfamethoxazole and trimethoprim in a conventional ratio of 5:1.

Definitions

1. Persistent Diarrhoea - diarrhoea persisting for more than 2 weeks following an episode of acute diarrhoea.
2. Cessation of diarrhoea - passage of soft stool or formed stool and no diarrhoea stool (liquid) for 48 hours.
   Liquid stool: The type of stool which can be poured from one container to another. Soft stool usually takés the shape of the container and the formed stool retains its shape.
3. Treatment failure - patients in whom diarrhoea does not stop by 24 hours after cessation of antibiotic treatment.

Withdrawals from the study

1. Non-compliance 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, meningitis, septicaemia etc.);

2. Consideration of withdrawals during analysis. results of all randomised patients will be included in the analysis of the study. Data from patients withdrawn will be included upto the time of withdrawal. A supplemental analysis in which such patients are excluded will also be made.

   Treatment failures will be transferred to the general ward for further investigations and management.

Study Schedule

1. Procurement of supplies and standardization of methods and development of data forms and recruitment and training of personnel - 2 months.

2. Conduct of pretrial of study materials and procedures - 1 month.
3. Conduct of the main trial - 18 months.
4. Analysis of the data and writing up the results - 3 months.

Data Analysis

There would be generally two types of data, pre-intervention data and response data. The study groups will be compared on admission and throughout the pre-intervention period with regard to history and all the variables prior to the intervention. Major outcome variables will be compared after evaluating the descriptive statistics for distribution etc. The quantitative outcome measures will be compared by using students t-test on primary data or after appropriate transformation when indicated, and also by an equivalent nonparametric test e.g. Mann Whitney U test. Dichotomous outcome measures will be compared by X^2 test or Fisher's exact test as appropriate.

Summary of Patient Procedures

Day 1 (Observation):

- History and physical examination
- Nutrition anthropometry
- Stool microscopy
- Stool and rectal swab for culture
- Duodenal intubation for culture and microscopy (after 4 hour fast)
- Input/output measurements 8 hourly
- Blood test
- Throat (post pharyngeal) swab for culture

Day 2 (Observation):

- Breath hydrogen test (after 4 hour fast) with lactose
- Intestinal permeability test (no fasting required) after a dose of lactulose/mannitol
- Input/output measurements 8-hourly

Day 1 of study (i.e. Day 3):

- Nutrition anthropometry
- Commence 12-hourly medicine
- Stool output measurement 8-hourly (in males)
- Intake of food, ORS and I.V. measured 8-hourly

Day 2-Day 7:

- Same as for day 1 except for nutrition anthropometry
- Body weight twice daily

Day 8:

- Duodenal intubation for culture and microscopy
- Intestinal permeability test
- Nutrition anthropometry
- Summary assessment of improvement

Day 9:

- Body weight
- Follow-up weekly: General examination
  Follow-up body weight

ANNEXE

DESCRIPTION OF PROCEDURES

Duodenal Intubation

This procedure is routinely performed at ICDDR,B for persistent diarrhoea patients. Intubation of the duodenum will be carried out with a sterile polythylene tube (diameter 1.5 mm) with a small mercury-filled tip. To facilitate the procedure the children will be premedicated 1/2 hour before intubation with syp, promethazine 1mg/kg and syp. metoclopramide 1mg/kg. The tube will be introduced per orally. The passage of the tube through stomach and pylorus into the duodenum will be facilitated by changing the position of the child from left to right side and vice versa. The final position of the tip of the tube will be confirmed by checking the pH of aspirate, which is usually above 6.5. The first sample will be examined microscopically for parasites, particularly G. lamblia and S. stercoralis and cryptisporidium and the next portion will be used for aerobic culture. Appropriate dilution of the duodenal juice will be immediately plated into Blood agar chocolate agar and McConkey's agar media for quantitative counts. The organisms isolated will be identified upto genus and if possible upto species level. E.coli isolated will be tested for production of enterotoxins and enteropathogenicity. Drug sensitivity tests for the predominant organisms isolated will be carried

out.

Breath Hydrogen Test

After a 4-hour fast (sips of plain water will be allowed), a fasting breath sample will be collected. Then lactose (2g/kg) will be given to the child and thereafter intermittent breath samples will be collected every 30 minutes after 3 hours. A portion of the collected samples will be aspirated from the collection bag into a plastic syringe, and hydrogen concentration in ppm will be determined with a gas chromatograph after calibrating with a commercial standard of 97 ppm hydrogen in air. A rise in hydrogen concentration of 20 ppm over baseline will be considered as indicative of lactose malabsorption. All expired samples will be collected by allowing the child to breathe through a face mask (paediatric size) and a two-way valve into a rubber anaesthesia bag.

Permeability test

Small intestinal mucosal damage will be assessed by a nononvasive permeability test. Patients will be offered a freshly prepared drink containing 5g lactulose with 0.5g lactose (Duphalac 7.5ml) and 1g mannitol in 20ml of 1% chlorofom water. No fasting is necessary; rather breastfeeding and fluid intake will be encouraged. Urine will be collected for 5 hours in paediatric urine collection bags. One drop of 20% chlorohexidine gluconate will be added

to each bag before collection. Urine volume will be measured and recorded. Lactulose and mannitol will be measured using an automated enzyme assay system utilising Cobas-bio. Results will be expressed as lactulose/mannitol excretion ratio, higher the value more extensive the apparent "damage" to smallbowel mucosa. Normal ranges are available from ongoing studies at ICDDR,B.

REFERENCES

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ABSTRACT SUMMARY FOR ETHICAL REVIEW COMMITTEE

1. This protocol aims to evaluate the efficacy of Trimethoprim-Sulphamethoxazole in the treatment of persistent diarrhoea in children in the vulnerable age group of 3-24 months.

   Since small bowel bacterial overgrowth is one of the postulated mechanisms involved, this protocol proposes to study 52 patients of both sexes, with history of diarrhoea of more than 14 days, in a double blind randomised controlled trial. One group will receive an antibiotic, trimethoprim-sulphamethoxaxole for 7 days, along with a modified diet, and another group will receive a placebo instead of the antibiotic. The patients will be followed up for one month or longer if required.

2. The investigations will not cause any risk to the children.

3. Informed consent will be obtained from the parents or the legal guardians.

4. A short interview will be taken to obtain the clinical history.

5. There will be immediate benefit to the patient, by investigation results, special care, constant monitoring, and appropriate dietary and treatment measures.

6. The amount of blood required will be 3 ml. Stool, urine, and breath will be collected for necessary investigations. Small intestinal fluid will also be obtained for microscopy and culture.

7. Patients' records will be necessary for data analysis.

8. Transport fare will be paid to the parents on follow-up visits.

CONSENT FORM

"Clinical Trial of TMP-SMX in infants with Persistent Diarrhoea"

Your child has been suffering from persistent diarrhoea. ICDDR,B is carrying out a study to evaluate the efficacy of trimethoprim-sulphamethaxazole (an antibiotic) along with a modified diet, in the treatment of persistent diarrhoea. If you agree to enrol your child in this study, the following procedures which are routine investigations for the management of persistent diarrhoea will be carried out.

On the day of admission stool will be examined for microscopy and culture etc. 3 ml of blood will be drawn from a vein for haematocrit, total and differential count, electrolytes and creatinine.

After four hours of fasting, your child will be intubated for the purpose of collection of intestinal fluid for examination of parasites and quantitative culture of bacteria.

During these procedures which are safe, your child will receive a glucose containing intravenous fluid and after completion, he/she will receive the usual hospital milk based diet. On the second day, again after 4 hours fast, breath hydrogen test will be done with lactose. Thereafter intestinal permeability test (no fasting required) after a dose of lactulose/mannitol will be done.

Careful records of total intake and stool and urine output

will be kept. On day 3 your child will either receive the antibiotic or a placebo for 7 days according to a previously prepared randomised table. Then his/her diet will be changed to a special local diet used for persistent diarrhoea in the ICDDR,B hospital.

He/she will receive intravenous fluid if and when required for rehydration. In addition, a vitamin mineral mixture will be given. The intubation will be repeated after 7 days to see the effects of treatment on the bacterial count and the breath H_2 test will be done again before the patient is put back on the milk diet.

After discharge follow up assessment will be done when you will bring your child every two weeks to the hospital for six weeks. If at any time you wish to withdraw your patient from the study, you are free to do so, and even then he/she will receive the standard treatment for persistent diarrhoea.

If the above conditions are acceptable to you, please sign or give your thumb impression below.

Signature of the investigator

Signature/thumb impression of the parent/guardian

Witness: _____ Date: _____

শিশুর দীর্ঘস্থায়ী ডাইরিয়ায় "ট্রাইমিথোপ্রিম ও সালফা-মিথোক্সাজোল" ঔষধের কার্যকারিতা পরীক্ষা

সম্মতি পত্র

আপনার শিশু দীর্ঘস্থায়ী ডায়রিয়া রোগে ভুগছে। আই. সি. ডি. ডি. আর. বি. শিশুদের দীর্ঘস্থায়ী ডাইরিয়া রোগে 'ট্রাইমিথোপ্রিম ও সালফামিথোক্সাজোল' ঔষধের কার্যকারিতা পরিক্ষার জন্য গবেষনা চালিয়ে যাচ্ছে। যদি আপনি আপনার শিশুকে এই গবেষনায় অংশগ্রহন করাতে রাজী থাকেন, তাহলে আমরা নিম্নলিখিত পরীক্ষাগুলো করব, যা প্রথমে এই রোগে সচরাচর করা হয়ে থাকে।

ভর্তির প্রথম দিনে পায়খানা অনুবীক্ষন যন্ত্রের দ্বারা পরীক্ষা করা হবে এবং কালচার করা হবে। রক্তের হিমাটোক্রিট, টোটাল ও ডিফারেনসিয়াল কাউন্ট, ইলেকট্রোলাইট ও ব্লিডিং টাইমের পরীক্ষার জন্য শিশুর শিরা থেকে ৩ মি: লি: পরিমান রক্ত নেয়া হবে।

চার ঘন্টা খাওয়া বন্ধ রাখা হবে, এবং ক্ষুদ্রান্ত্রের রস কালচার ও অনুবীক্ষন যন্ত্র দ্বারা পরীক্ষার জন্য একটি সরু নল মুখ দিয়ে প্রবেশ করিয়ে ক্ষুদ্রান্ত্র থেকে রস সংগ্রহ করা হবে। এই পরীক্ষা সম্পূর্ন নিরাপদ, এবং এই পরীক্ষার সময় আপনার শিশুকে শিরার মধ্যে দিয়ে গ্লুকোজ-স্যালাইন দেয়া হবে। পরীক্ষা শেষ হবার পর শিশুকে হাসপাতালের দুধ-মিশ্রী সারিয়ন খাবার দেয়া হবে। খাওয়া এবং পায়খানা ও প্রস্রাবের হিসাব সংরক্ষন করা হবে।

ভর্তির দ্বিতীয় দিনে আবার ৪ ঘন্টা খাওয়া বন্ধ রেখে সকালের খাবার দিয়ে শ্বাসের হাইড্রোজেন গড়াস পরীক্ষা করা হবে। তারপর ল্যাকুলোজ ও ম্যানিটোল মিশ্রিত জুসের পারমিয়াবিলিটি পরীক্ষা করা হবে।

ভর্তির তৃতীয় দিন আপনার শিশু পূর্ব-নির্ধারিত হিসাব মতে হীরাবুদ্ধিপ্রীয় ঔষধি অথবা প্লাসিবো (অকার্যকরী পদার্থ) পাবে। প্রতি সপ্তাহে সাথে তার সকালের খাবার পরিবর্তন করে বিশেষ খাবার দেয়া হবে যা এই হাসপাতালে দীর্ঘস্থায়ী ডায়রিয়া রোগে দেয়া হয়। একই সাথে ভিটামিন ও মিনারেল মিক্সার দেয়া হবে। এবং পাতলা পায়খানার পরিমাণ অনুযায়ী কিছু ম্যাগনেসিয়াম দেয়া হবে।

৭ম দিন আবার মুখের ভিতর দিয়ে সরু কল প্রবেশ করিয়ে জুসদ্রবণের রস সংগ্রহ করা হবে।

পুনরায় দুই মিশ্রিত খাবার দেয়ার আগে ল্যাকটোজ যুক্ত শ্বাসের হাইড্রোজেন পরিমাপ করা হবে।

রোগীর ছুটির আর কয়দিন ও সম্ভব পর্যন্ত আপনার শিশুকে ৭ দিন পর পর হাসপাতালে নিয়ে আসলে পরীক্ষা করে দেয়া হবে।

যদি কোন সময় আপনি আপনার শিশুকে গবেষণা হতে তুলে নিতে চান, তা আপনি করতে পারবেন। এতেও আপনার শিশু এই হাসপাতালের প্রদত্ত

চিকিৎসা পাবে।

যদি আপনি উপরোক্ত বিষয়ে সম্মত হন,
তাহলে নীচে স্বাক্ষর অথবা টিপসই দিন।

গবেষকের স্বাক্ষর

অভিভাবকের স্বাক্ষর /
টিপ সই

সাক্ষী _____

তারিখ _____

CONSENT FORM

Clinical Trial of TMP-SMX in infants with Persistent Diarrhoea

ACUTE DIARRHOEA

Your child has acute diarrhoea. The International Centre for Diarrhoeal Disease Research, Bangladesh is carrying out a study to compare the parasites and bacteria present in the intestinal fluid of persistent diarrhoea, with those present in acute diarrhoea. If you agree to enrol your child in this study, routine investigation, namely stool microscopy and culture will be done. In addition, your child will be kept fasting for four hours and a thin sterile plastic tube will be passed through the mouth into the stomach, for the purpose of collection of intestinal fluid. This is a safe procedure, and during this period, your child will receive a glucose containing intravenous after which, he/she will receive the usual hospital milk based diet. A throat swab will also be done to compare the organisms with those obtained from intestinal fluid. All records will be kept confidential. The results of these investigations will help us in understanding better the mechanisms of the diarrhoeas which become prolonged.

If the above conditions are acceptale to you, please sign or give your thumb impression below.

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Signature of the investigator	Signature/thumb impression of the parent/guardian
Witness: _____	Date: _____

ਕਿਰਤੀਆਂ ਤੇ ਮੱਧਵਰਗੀ ਪਰਿਵਾਰਾਂ ਲਈ ਸਿੱਖਿਆ
ਯੋਜਨਾਵਾਂ ਦੀ ਕਾਰਜਕੁਸ਼ਲਤਾ ਦਾ ਮੁਲਾਂਕਣ

ਸੁਖਦੇਵ ਸਿੰਘ ਪਰਿਵਾਰ ਦਾ ਸਮਾਜਿਕ ਅਤੇ

ਆਰਥਿਕ ਪਿਛੋਕੜ ਪੇਂਡੂ ਹੈ। ਆਤਮ-ਨਿਰਭਰ
ਉਦਯੋਗਾਂ ਦੀ ਸਥਾਪਨਾ ਲਈ ਮੱਧਵਰਗੀ ਪਰਿਵਾਰਾਂ ਨੂੰ ਵਿੱਤੀ
ਸਹਾਇਤਾ ਅਤੇ ਸਿਖਲਾਈ ਦੇਣ ਲਈ ਸੁਖਦੇਵ ਸਿੰਘ ਪਰਿਵਾਰ
ਯੋਜਨਾ ਅਧੀਨ ਸਹਾਇਤਾ ਲਈ ਅਰਜ਼ੀ ਦਿੱਤੀ ਸੀ। ਇਸ ਯੋਜਨਾ
ਦੇ ਅਧੀਨ ਉਨ੍ਹਾਂ ਨੂੰ ਕਰਜ਼ਾ ਮਨਜ਼ੂਰ ਹੋਇਆ ਸੀ ਅਤੇ
ਉਨ੍ਹਾਂ ਨੇ ਇਸ ਰਕਮ ਨਾਲ ਇੱਕ ਛੋਟੀ ਜਿਹੀ ਦੁਕਾਨ ਖੋਲ੍ਹੀ
ਸੀ। ਪਰ ਕੁਝ ਹੀ ਮਹੀਨਿਆਂ ਵਿੱਚ ਉਨ੍ਹਾਂ ਨੂੰ ਪਤਾ ਲੱਗਾ
ਕਿ ਉਹ ਕਰਜ਼ੇ ਦੀਆਂ ਕਿਸ਼ਤਾਂ ਨਹੀਂ ਭਰ ਸਕਣਗੇ। ਉਨ੍ਹਾਂ
ਦੀ ਆਮਦਨ ਇੰਨੀ ਨਹੀਂ ਸੀ ਕਿ ਉਹ ਕਿਸ਼ਤਾਂ ਭਰਨ ਤੋਂ
ਬਾਅਦ ਵੀ ਆਪਣੇ ਪਰਿਵਾਰ ਦਾ ਗੁਜ਼ਾਰਾ ਚਲਾ ਸਕਣ।
ਉਨ੍ਹਾਂ ਨੂੰ ਡਰ ਸੀ ਕਿ ਜੇ ਉਹ ਕਿਸ਼ਤਾਂ ਨਹੀਂ ਭਰਨਗੇ
ਤਾਂ ਉਨ੍ਹਾਂ ਦੀ ਜਾਇਦਾਦ ਜ਼ਬਤ ਹੋ ਜਾਵੇਗੀ। ਇਸ ਲਈ
ਉਨ੍ਹਾਂ ਨੇ ਆਪਣੇ ਪਰਿਵਾਰ ਦੇ ਕੁਝ ਮੈਂਬਰਾਂ ਨੂੰ ਵਿਦੇਸ਼
ਭੇਜਣ ਦਾ ਫੈਸਲਾ ਕੀਤਾ।

উপরোক্ত কাগজপত্রাদি যাচাই আপনার পক্ষে সুবিধাজনক হলে অনুগ্রহ করে নিম্নে স্বাক্ষর করুন অথবা ঠিকানা উল্লেখ করুন।

আবেদনকারীর স্বাক্ষর

জিজ্ঞাসাধীন অথবা আউটসোর্সিং
স্বাক্ষর / ঠিকাদারি সংস্থার নাম

তারিখ

তারিখ:

Follow Up Consent Form

Your child had been suffering from persistent diarrhoea. After carrying out some routine investigations her/his diarrhoeas was successfully managed. If you permit us we would like to intubate your child again to see how the parasites or bacteria isolated during the diarrhoeal episode differ from those which are normally present, without producing diarrhoea. This will help us in improving the understanding and treatment of persistent diarrhoea.

If you agree please sign or give your thumb impression below.

Signature of the investigator

Signature/thumb impression of parent/guardian

Witness: _____

Date: _____

ফলো-আপ সম্মতি পত্র

আপনার কিডনি প্রতিস্থাপন অস্ত্রোপচার হয়েছে। কিডনি নিয়মিত পর্যবেক্ষণ করে সফলভাবে আমরা আপনার চিকিৎসা করা হয়েছে, আমাদের যদি আমাদেরকে অনুমতি দিন তবে আমরা শুনতে আপনার কিডনির স্বাভাবিকতা দল চুক্তির দেখাবো যে অস্ত্রোপচার প্রতিস্থাপনের যে সব সমস্যাদি ও জটিলতা সিয়াজুল তারা অস্ত্রোপচার না হওয়া-স্থানীয় অথচ্ছায় আমরা প্রয়োজনে ও জটিলতা থেকে কথাগুলি দিচ্ছেন, এবং প্রতিস্থাপন অস্ত্রোপচার ভাল করে বুঝাতে পরে এর চিকিৎসার উন্নতি করতে আমাদের সাহায্য করবে।

আমাদের যদি সম্মত হন তা হলে নিচে স্বাক্ষর করুন অথবা টিপসই দিয়ে দিন।

রোগী/রোগীর স্বাক্ষর

রোগী-মাতা অথবা অভিভাবকের স্বাক্ষর/ টিপসই দিয়ে

সাক্ষী

তারিখ

1 ICDDR,B
1988 BUDGET PROPOSAL (IN US $)

DIVISION NAME: CLINICAL SCIENCES DIVISION
PROTOCOL/BRANCH NAME:CLIN. TRIAL OF TMP-SMX IN INF. WITH PERSISTANT DIAR.
NAME OF P. I./BRANCH HEAD/DIVISIONHEAD: DR.N.H.ALAM
BUDGETCODE: STARTING DATE:
PROTOCOL NO: COMPLETION DATE:
DONOR NAME: GRANT AMOUNT:

A/C Code	EXPENSE CATEGORY	Refer to Page No.	Column A Actual Jan.-	Column B Estim. Whole	Column C Proposed 1989	+ Proposed 1990
3100	Local Salaries	02			23548.2	28271.4
3200	Intl. Salaries	08	0		0	
3300	Consultants	14	0		0	
3500	Travel Local	15	0		500	500.0
3600	Travel Intl.	16	0		0	
3700	Supplies & Mat.	18	0		942.5	942.5
4000	Other Costs	19	0		275	275
4900	Inter Deptl. Ser.	21	0		15350	16650
	Total Direct Operating Cost		0	0	40615.7	46638.9
0300	Capital Expenditure (P.22)				6400	0
	TOTAL DIRECT COST		0	0	47015.7	46638.9

TOTAL = US $ 93655 00

318.88

Reviewed by B & F Office

PERSONNEL REQUIRMENT (LOCAL STAFF) 1988 PAGE 2 OF 22

Description	No. of Positions	No. of Man Months	$ Amount	1990
A. Direct Project/Protocol/ Branch Staff at 01.01.1988 (Source: Page 3)	0	0	0	
Add:				
B. New Recruitments (Source: Page 4)	7	80.4	18421.2	22120.8
C. Staff allocated from other area (Source: Page 5)	3	7.2	5127	6150.6
(i) Sub Total	10	87.6	23548.2	28271.4
Less:				
D. Separations (Source: Page 6)	0	0	0	
E. Staff allocated to other area (Source: Page 7)	0	0	0	
(ii) Sub Total	0	0	0	
(i) - (ii) TOTAL	10	87.6	23548.2	28271.4

NEW RECRUITMENT (LOCAL STAFF) - 1988

	A	B	C	D	E	F=(D x E)	
Job Title	Level	Start Date	No. of positns	No. of Man Mnth	Rate Per Month	$ Amount 1989	1990
1.MEDICAL OFFICER	MO-A		1	12	624	7488	8988
2.SR.HEALTH ASST.	GS-4		2	24	263	6312	7584
3.DATA ENTRY TECH.	GS-4		1	6	263	1578	1896
4.DICTICIAN	GS-6		1	2.4	518	1243.2	1492.8
5.URBAN VOLUNTEAR	"		3	36	50	1800	2160
6.						0	
7.						0	
8.						0	
9.						0	
10.						0	
11.						0	
12.						0	
13.						0	
14.						0	
15.						0	
16.						0	
17.						0	
18.						0	
19.						0	
20.						0	
21.						0	
22.						0	
23.						0	
24.						0	
25.						0	
26.						0	
27.						0	
28.						0	
29.						0	
TOTAL			7	80.4		18421.2	22120.8

MANPOWER-ALLOCATED FROM OTHER AREA (LOCAL STAFF) - 1988

	A	B	C	D	E	F=(D x E)	
Job Title	Level	Budget Code Of Other Area	No.of Positn	No.of Man Months	Rate Per Month	$ Amount	1990
1.DR.M.H.ALAM	NO-B	11 01 10	1	3	867	2601	3120
2.DR.R.HAIDER	NO-A	11 01 10	1	3	636	1908	2289
3.RESERCH OFFICER	GS-6	13 10 10	1	1.2	515	618	741.6
4.						0	
5.						0	
6.						0	
7.						0	
8.						0	
9.						0	
10.						0	
11.						0	
12.						0	
13.						0	
14.						0	
15.						0	
16.						0	
17.						0	
18.						0	
19.						0	
20.						0	
21.						0	
22.						0	
23.						0	
24.						0	
25.						0	
26.						0	
27.						0	
28.						0	
29.						0	
TOTAL			3	7.2		5127	6150.6

Job Title	Travel From To-From	No.of Persn	Estim. Days of Travel Per Person	Person Days (A)	PerDiem Rate (B)	PerDiem Amount (C=AXB)	Transport Air (D)	Transport Ground (E)	Other Cost (F)	Total $ Amount 8= (C+D+E+F)	1990
1. TRANSPORT COST FOR F.UP AT PTS.						500				500	500
2.						0				0	
3.						0				0	
4.						0				0	
5.						0				0	
6.						0				0	
7.						0				0	
8.						0				0	
9.						0				0	
10.						0				0	
11.						0				0	
12.						0				0	
13.						0				0	
14.						0				0	
15.						0				0	
16.						0				0	
17.						0				0	
18.						0				0	
19.						0				0	
20.						0				0	
21.						0				0	
22.						0				0	
23.						0				0	
24.						0				0	
25.						0				0	
26.						0				0	
27.						0				0	
28.						0				0	
29.						0				0	
TOTAL						500				500	500

A/C Code	Item Description	$ Amount	1990
3701	Drugs (used for medicationin the hospitals and field stations)		
3702	Glassware (bottle, beaker, cylinder, petridish, aluminium seal, slides stopper, tube etc.)	50	50
3703	Hospital Supplies (bandage, gauge blade, bowl, catheter, cotton, needle syringe, solution, leukoplast, towel etc.)	125	125
3704	Stationery and Office Supplies (Battery, book register, binders, files, pencil, fastener, paper, ribbon, stapler etc.)	250	250
3705	Chemicals and Media (Acid, reagent dextrose, sodium, bactoagar etc.)	75	75
3706	Materials for Uniform (Cloth, button etc required for making uniforms)		
3707	Fuel, Oil and Lubricants (Diesel, mobil, petrol, kerosene etc.)		
3708	Laboratory Supplies (Aluminium foil, bag blade, brush, cap, container, X-ray etc.)	100	100
3709	Housekeeping Supplies (Aerosol, battery, wiping cloth, duster, lock and key etc.)		
3710	Janitorial Supplies (Bleaching powder, brush, detol, detergent, insecticide, soap etc.)		
3811	Tools and Spares (Automobile spares, tyres, tubes, battery, stores required for maintenance services etc.)		
3712	Non-stock Supplies (Materials not normally kept in stock and purchased only against specific requisitions)	125	125
	Sub Total	725	725
3713	Freight and other charges (Add 30% to above sub total)	217.5	217.5
	TOTAL	942.5	942.5

A/C Code	Item Description	1989 $ Amount	1990
3800	Repairs and Maintenance (Maintenance and repairs of vehicles, equipments, furniture and building)	50	50
3900	Rent, communication and utilities (Postage, telephone, telegram, electricity etc.)	75	75
4100	Bank charges		
4200	Legal and Professional Expenses (Professional membership fee, legal fee, audit fee etc.)		
4300	Printing and Publication (Printing of forms, books, journals, reprints etc.)	150	150
4400	Hospitality and Doantion (Guest house accomodation, donations, hospital food, lunch, refreshment etc.)		
4500	Service Charges (porter, labour, washing, laundry and other misc. expenditure)		
4600	Staff Development and Training (Training course fee, training materials, stipend, scholarship, subsistance paid to the staff)		
	TOTAL	275	275

INTER-DEPARTMENTAL SERVICES - 1988 PAGE 20 & 21 OF 22

A/C Code	Service Area	1989 $ Amount	1990
4801	Computer	0	1250
4802	Transport Dhaka	50	50
4803	Transport Matlab		
4804	Water Transport Matlab		
4805	Transport Teknaf		
4806	Xerox and Mimeograph	250	250
4807	Pathology	900	900
4808	Microbiology Tests	4525	4525
4809	Biochemistry	875	875
4810	X-Ray	100	100
4811	I.V. Fluid		
4812	Media		
4813	Patient Hospitalization study	8600	8600
4814	Animal Research		
4815	Medical Illustration	0	100
4817	Telex		
4818	Out Patient Care		
4819	Maintenance Charges		
4820	Vehicle Maintenance Charges		
4821	Library Service Charges		
4822	Staff Clinic Charges - Dhaka		
4823	Staff Clinic Charges - Matlab		
4824	Bacteriology Test		
4830	Transport Subsidy	50	
	TOTAL	15350	16650

Item Description	Manufacturer	No.of Units	Cost+Freight $ Amount
1.GAS CHROMATOGRAPH		1	3000
2.FACE MASK & AIR BOB			200
3.DEEP FREEZER			1850
4.FILE CABINET		1	150
5.METABOLIC BEDS		2	1000
6. OTHERS			200
7.			
8.			
9.			
10.			
11.			
12.			
12.			
13.			
14.			
15.			
16.			
17.			
18.			
19.			
20.			
TOTAL			6400

1990

Nil