1978

ANNUAL REPORT

CHOLERA RESEARCH LABORATORY

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH

BANGLADESH

Dacca, Bangladesh

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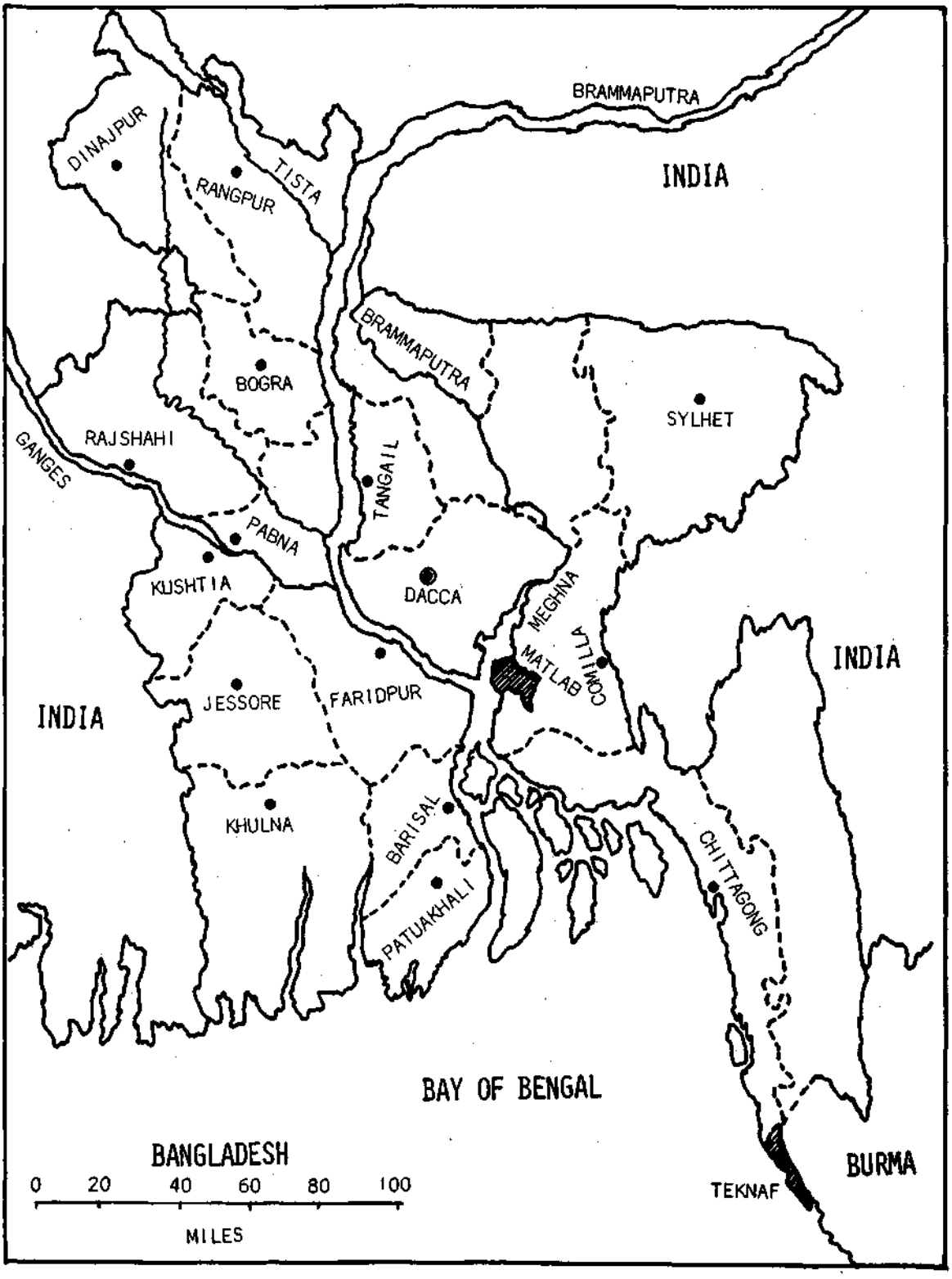
PREFACE

This Annual Report provides a broad overview of the research and training programs and other activities of the Cholera Research Laboratory (CRL) for the 1978 fiscal year (October 1, 1977 to September 30, 1978). The specific research findings and program activities which are considered important are summarized without technical details. Persons interested in obtaining the full technical details of any of the research are invited to communicate directly with the Director.

The Cholera Research Laboratory has operated under a bilateral Project Agreement between the Governments of Bangladesh and the United States of America. The Governments of the United Kingdom and Australia also support the CRL. Special project funds are provided by the International Development Research Center of Canada and the Ford Foundation.

The Cholera Research Laboratory has completed a transformation to the International Centre for Diarrhoeal Disease, Bangladesh during the course of 1978 and early 1979. This is summarized in some detail in this report. All future publications and reports will refer to the institution by its new designation.



Bangladesh showing location of Matlab and Teknaf field research areas.

TABLE OF CONTENTS

TRAINING PROGRAM

Page

INTERNATIONALIZATION

ORGANIZATION

PUBLICATIONS AND PAPERS

INTRODUCTION

This represents the last Annual Report for this institution under the name Cholera Research Laboratory. During the course of FY 1978 the final steps were taken which led to the President of the People's Republic of Bangladesh promulgating an Ordinance on December 6, 1978 establishing the International Centre for Diarrhoeal Disease Research, Bangladesh the successor to CRL. This action was followed by a plenary meeting of an Interim International Committee under the Chairmanship of the United Nations Development Programme which convened at the World Health Organization Headquarters in Geneva on February 13-14, 1979, and endorsed the ICDDR,B, selected the first Board of Trustees and committed support to the new International Centre.

In anticipation of the transformation of the CRL into the ICDDR,B steps were taken to restructure and reorient the scientific program through the establishment of problem-oriented Scientific Working Groups dealing with diarrheal diseases, nutrition, population and training, and through the development of policies and procedures to assure critical scientific and ethical review of all research proposals. Since initiation of these procedures in mid 1977 through the end of 1978, sixty research protocols have been formulated with 43 approved for implementation. The research and training accomplishments are summarized in this report within the framework of the program objectives of the Scientific Working Groups.

There are three Working Groups concerned with diarrheal diseases. Their topics are pathogenesis and therapy, disease transmission and control, and host resistance. The major thrust of the Working Group on Therapy has been to develop cheap, simple, and effective methods of treating diarrhea that can be made widely available in the rural areas. The research program has established that sucrose (table sugar) can be substituted for glucose in oral therapy and that even simpler mixtures using salt and unrefined sugar (molasses) available in the village may be acceptable. Following from this experience, CRL has developed practical procedures for packaging the correct proportions of salt, sugar, and bicarbonate of soda that can be implemented

in any rural health center, and has also devised a simple measuring spoon for household use in preparing oral solutions. The current research now extends to the rural areas where a variety of strategies, including the use of indigenous practitioners or even mothers themselves to provide oral therapy in the villages are being tested.

The Working Group concerned with Diarrheal Disease Transmission and Control began to use for the first time new diagnostic tools that have been developed to detect rotavirus and enterotoxigenic E. coli in large-scale epidemiological studies in the rural areas. These investigations have established that rotavirus alone accounts for 50%-75% of all episodes of watery diarrhea in children under the age of five years seen at the treatment center. Enterotoxigenic E. coli accounts for about 25% of diarrheas in all age groups. With the addition of rotaviruses and enterotoxigenic E. coli to shigella, cholera and the non-cholera vibrios, a specific cause can now be established for more than 80% of cases of diarrhea. A significant fraction of the remainder are due to parasites such as giardia and amoebiasis. This information on specific causes of diarrhea, which had been lacking until the last two years, now permits detailed investigations on the critical biological, social, cultural and environmental factors that facilitate disease transmission and are most amenable to control measures.

The major task of the Working Group on Host Resistance and Immunity relates to development of improved vaccines. CRL in collaboration with Bangladesh Medical Research Council, the Wellcome Foundation (U.K.), and the National Institutes of Health (U.S.A.) is participating in an effort to develop an improved cholera vaccine which is expected to provide a higher level and longer duration of protection, particularly to children. The first stage of field investigations this past year has shown that the vaccine is free from adverse reactions and is an effective immunogen. Coupled with vaccine development are more fundamental studies of the actual mechanisms of intestinal immunity in diarrhea cases. A major advance in the past year has been the successful development of a series of new techniques for measuring specific antibodies to cholera and other enteric diseases in intestinal secretions.

These are being applied to define the natural immune mechanisms following an episode of diarrhea. It is anticipated that this information will provide the foundation for the development of more effective vaccines in the future.

The Working Group on Nutrition has been particularly concerned with the interrelationships of diarrheal diseases and malnutrition. In the past year longitudinal field studies have been initiated to determine both how specific causes of diarrheal disease may lead to malnutrition as well as to what degree this process may be halted or reversed by oral rehydration therapy. In conjunction with these biomedical studies, there are investigations into the social and cultural determinants of the feeding practices which families initiate when a member has diarrhea or another acute illness.

A special area of concern is breastfeeding. Longitudinal field study indicates that breastfeeding is universal among rural women, extending well into the next pregnancy in many cases. A small clinical study clearly demonstrated that breastfeeding was well maintained throughout an episode of diarrheal illness, although supplementary feedings dropped dramatically. Nutritional supplementation studies directed toward lactating women indicated that maternal milk production could be substantially increased by an improvement in maternal diet.

A significant accomplishment of the Population Working Group was the publication of a five-volume series analyzing the 1974 census in Matlab and the vital registration records for the years 1974, 1975 and 1976. Concurrent with this, indepth analyses were completed on some determinants of fertility including seasonality, marriage patterns and traditional contraceptive practices. Studies of patterns of mortality, particularly in childhood have indicated that a few basic immunizations and oral hydration for diarrhea could result in a 41% reduction in infant mortality and a 33% reduction in the 1 to 5 year mortality.

A major component of the population program has been a study of strategies to provide contraceptive services in the rural areas. Initially the CRL investigated the effectivenss of simply distributing oral contraceptives and condoms to 24,000 families in the Matlab area. This

began in late 1975 and by early 1976, 18% of the couples were participating in contraception. Further followup revealed by mid 1977 a declining prevalence of practice, dropping to about 10%. Therefore, in late 1977 a restructured family planning and health services program was developed utilizing more qualified female field workers to provide a comprehensive range of fertility control services including injectible contraception and sterilization as well as maternal and child health care. This restructured effort covering 13,000 couples has so far resulted in a steady rise in the practice of contraception reaching 32% within 15 months after the program was initiated.

Training, extension and staff development are the newest activities to receive systematic attention at the CRL. As in the past staff from the CRL responded to requests for epidemic aid for cholera outbreaks from the Government of Bangladesh and also the Government of Maldive. In addition, however, in anticipation of the mandate of the ICDDR,B to provide training, the CRL took the initiative to reach a formal agreement with the Bangladesh Directorate of Health Services (Preventive) under which the CRL would implement a systematic training program for Rural Health Center doctors. Under this program, the Government sends ten Rural Health Center doctors each week to the CRL, Dacca. The CRL provides accommodations in a trainees' hostel and gives a one-week course of lectures and practical training on the management of diarrheal diseases. Over a one-year period, 500 doctors from throughout the country will be trained.

In addition to practical training, the CRL has embarked upon a program to develop Bangladeshi research manpower. Six research Fellowships were offered to young Bangladeshi scientists for biomedical research training at CRL for a one-year period. In addition, selected mid-level CRL staff are being given fellowships for advanced training abroad. The long-term goal of this effort is to assist in developing scientific leadership needed both for national institutions and for the new International Centre with its expanded research agenda.

In completing the evolution to the new Centre attention is also being directed to research and

training needs in other developing countries, especially in the region. Negotiations are well underway with the World Health Organization, the United Nations Development Programme, and the United Nations Fund for Population Activities for support to assist the Centre in providing research and technical training, and seminars, and workshops for scientists and program administrators for other developing countries in areas of the Centre's expertise.

DIARRHEAL DISEASE RESEARCH

The importance of the diarrheal diseases as a global health problem is highlighted by the fact that in 1978, the World Health Organization made control of diarrheal disease a major priority for a global effort. The WHO Southeast Asia Regional Office anticipating this, declared diarrheal diseases in children a research priority one year earlier, and, in September, 1977, convened an interregional seminar in New Delhi to identify research topics of highest priority for countries in this region. Twenty-one topics were identified. The CFL research program in the past year specifically addressed most of the problems, and, in fact, provided definitive answers to several questions. This research is summarized according to the three major areas of concern of the Diarrheal Working Groups: Therapy; Disease Transmission and Control; and Host Resistance.

I. THERAPY

The highest research priority of the Working Group on Diarrheal Pathogenesis and Therapy has been to develop the technologies and strategies that can lead to the goal of assuring that cheap, simple, and effective means of treating diarrhea can be made available to all individuals in Bangladesh and in developing countries in general. This research effort has had to address a number of fundamental questions that required a series of investigations ranging from carefully controlled clinical trials to large-scale operational research programs in rural villages. The questions needing answering were: Could simpler and cheaper formulations of oral therapy which villagers could prepare themselves be utilized without significant loss in effectiveness? and, What strategies are most practical for introducing oral therapy nation-wide at the village and household level in the rural areas? Research projects addressing specific aspects of these questions are described below.

A. Substitution of sucrose for glucose in oral therapy.

Physiologic studies have established that the essential ingredient in oral therapy is glucose, which is actively absorbed by the intestine even in the presence of

cholera and related diarrheas, and brings with it into the body the salts and water necessary to reestablish and maintain hydration. For some years it has been suggested that ordinary table sugar (sucrose—a disaccharide consisting of glucose and fructose which must be split by an intestinal enzyme before absorption) might be a practical substitute for glucose. Some research had been carried out on this question so that by mid 1977 there were five different published studies on this topic. Each, however, was small scale, using different types of fluids, and patients with different characteristics and different causes of diarrhea, and evaluation techniques were not comparable. As a result, though the general consensus was that sucrose could successfully replace glucose, there were reservations regarding the general use of sucrose except when glucose is not obtainable. CRL, therefore, undertook three large-scale controlled clinical trials and one large-scale comparative clinical study to definitively resolve this question.

1. Sucrose versus glucose in oral therapy in adults with severe watery diarrhea.

This was a carefully controlled clinical trial involving 148 adult male patients; 79 had cholera, 34 had enterotoxogenic E. coli, and the majority of the remainder had diarrhea of unknown causes. The study tested the efficacy of sucrose versus glucose oral solution both in rehydration and maintenance of hydration. In both groups, patients with severe (greater than 10%) dehydration were initially given intravenous fluids to reverse shock and then attempts were made to continue to rehydrate and maintain all patients on oral therapy alone. Failure was defined as the need to give unscheduled intravenous therapy. In this group of patients, the success rate for the sucrose solution was 75% and for the glucose solution, 84%. This study demonstrated that the sucrose electrolyte oral solution can be used almost as effectively as the glucose solution in most cases of severe diarrhea in adults.

2. A comparison of sucrose versus glucose oral therapy in "cholera like" diarrhea in children.

This was a double-blind controlled trial involving 111 children under 5 years of age, 102 of whom had confirmed cholera. The study design was similar to that in adults. The overall success rate for oral therapy with sucrose was

73%, and with glucose 77%. As illustrated in Figure 1, failure with oral hydration is related to the severity of diarrhea. Only in the most severe cases does glucose seem to have an advantage over sucrose. Such severe cases however, are infrequent, and most will require some intravenous fluids in any event. This study, similar to the experience in adults, showed that sucrose solution can be used almost as effectively as glucose in oral hydration of children.

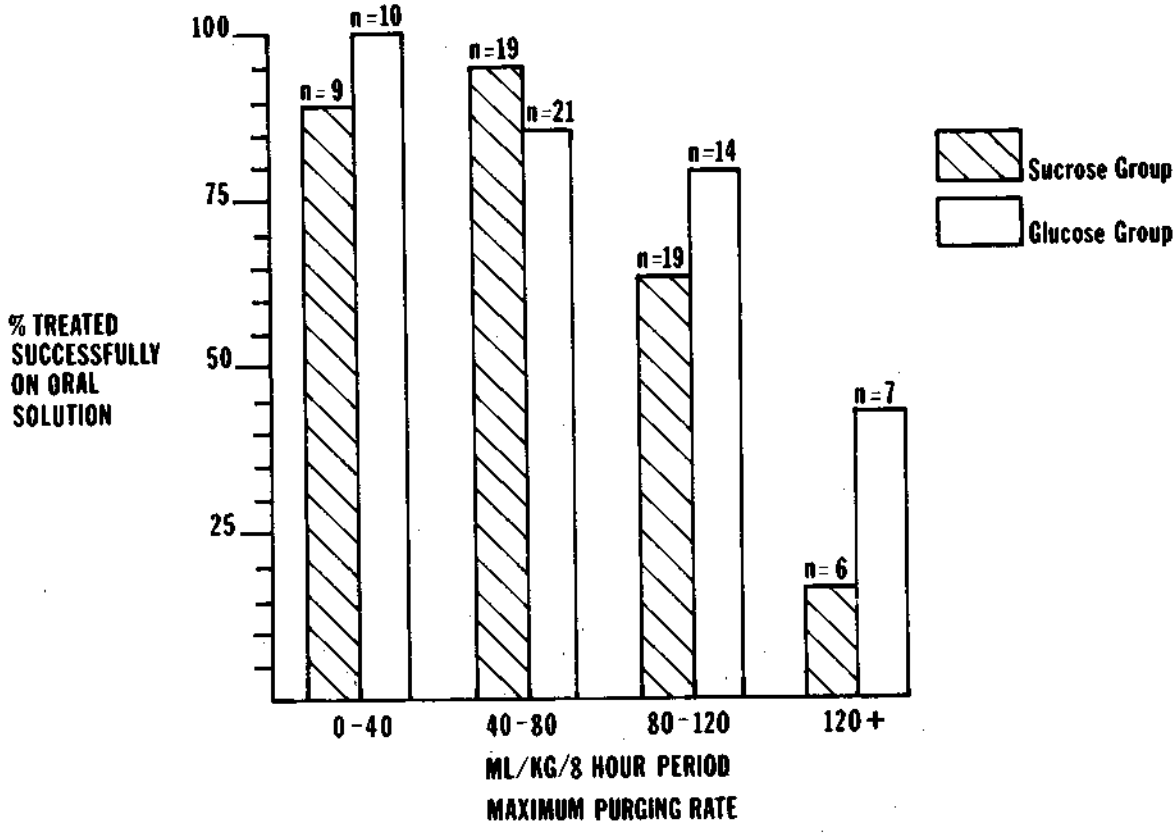


FIGURE 1. The relationship of severity of diarrhea to the successful use of oral therapy with glucose or sucrose based solutions in children under 5 years of age.

3. A comparison of sucrose versus glucose oral hydration in children with rotavirus diarrhea.

Rotavirus is proving to be the single most common cause of diarrhea in infants under the age of 3 years world-wide. Because the pathophysiologic mechanism of diarrhea in rotavirus is different than with cholera or the enterotoxigenic E. coli, controversy had arisen as to whether oral rehydration would be effective in this disease. A controlled clinical trial was carried out in 57 children age 5 months to 2 1/2 years with confirmed rotavirus diarrhea, comparing glucose with sucrose oral therapy. All patients in both groups were successfully treated with oral therapy only without requiring intravenous therapy. A detailed clinical comparison of the sucrose and glucose oral therapy groups showed no difference in the rate of rehydration. A comparison of these oral hydration patients with a similar group treated intravenously showed that the rate of rehydration was slightly slower in the oral therapy group, but the difference was not clinically significant.

4. A large-scale comparative clinical study of sucrose and glucose oral therapy in rotavirus diarrhea.

The Matlab rural treatment center treats approximately 20,000 diarrhea cases anually with the majority of these cases being managed by oral therapy. With the establishment of rotavirus diagnostic techniques in Matlab, a clinical study was carried out on a series of 787 children admitted with rotavirus diarrhea over a 4-month period. For 2 months all cases were treated with an oral glucose electrolyte solution. Subsequently a sucrose solution was used. About 400 children were in each treatment group. Oral therapy alone was shown to be effective in 93% of the children receiving the glucose electrolyte solution and 88% of those receiving the sucrose electrolyte solution. Failures requiring intravenous hydration occurred in that small group of children most severely dehydrated and with frequent vomiting.

5. Practical use of oral sucrose electrolyte solution.

These studies conclusively established that sucrose is a satisfactory substitute for glucose in oral therapy for diarrheal diseases. Based on results of these investigations, the CRL in December 1977, switched to a sucrose-based oral solution for all routine clinical and field use. Since then, more than 100,000 diarrhea patients have been treated in the CRL facilities with the sucrose-based solution with no clinically observable differences in outcome from that previously obtained with the glucose-based oral solution.

B. Effectiveness of locally available village salt (labon) and unrefined brown sugar (gur) in oral therapy.

A simpler innovation in oral therapy that would make it more widely available in the villages is to use the cheapest locally available ingredients in the simplest formulation possible. Some health workers have suggested and are actually using a simplified solution made of locally available salt and unrefined sugar called labon-gur. A labon-gur solution has the advantage of being cheap and widely available in the rural areas. A theoretical concern that has not been tested relates to the fact that it does not contain sodium bicarbonate which is in the current formulations to correct the acidosis associated with diarrhea. Surprisingly, in spite of widespread popular use of this or similar sugar-salt solutions in many countries, it has not been subjected to critical clinical trials.

1. Labon-gur clinical trial in adults.

A clinical trial was carried out on 50 adult patients with moderate dehydration due to diarrhea of various causes to observe the efficacy of the labon-gur solution. Failure in these cases was defined as not correcting the hydration, not maintaining hydration, or developing an electrolyte imbalance during the study period. After initial intravenous rehydration in a few

severely dehydrated patients, all 50 cases were successfully hydrated and maintained on the labon-gur solution. Clinically, these patients did as well as similar cases treated with the usual sucrose electrolyte oral therapy. Serum electrolyte studies revealed that acidosis was more sustained in the labon-gur group however, this electrolyte abnormality presented no clinical problem in these adults.

2. Labon-gur clinical trial in children.

Because acidosis may be a more severe problem in children with diarrhea, this study was extended in a comparative trial involving over 100 children with moderate to severe dehydration due to diarrhea. Most required some initial fluid replacement with intravenous fluids; half were then given a labon-gur oral solution, the other half a labon-gur solution with sodium bicarbonate. Preliminary analysis indicates that both groups are achieving a comparable success rate of about 70%. Sustained acidosis is much more common in children receiving the solution without sodium bicarbonate, however, this does not seem to be presenting a significant clinical problem under these study conditions.

While these investigations were not complete, the data indicate that labon-gur is reasonably effective in oral hydration and that omission of sodium bicarbonate may not create a serious problem in most cases.

C. Practical production of oral hydration solutions.

Up to the present time, in a number of developing countries where oral therapy is being introduced, the glucose based formulation has typically been produced by a single, centralized, large-scale, relatively sophisticated production facility. Having established the efficacy of a sucrose-based solution and the practical utility of labon-gur opens the possibility of village based production of the sugar electrolyte packets, and even homemade solutions. A series of studies were conducted which have led to the introduction of two practical innovations by the CRL.

1. Mass production of sugar-salt-bicarbonate packets.

The CRL has developed a simplified technique to produce packets of the sugar-salt-bicarbonate mixture

required to make up one litre of oral fluid. The procedure involves measurement by volume of the correct proportions of the sugar, salt and sodium bicarbonate using large containers to minimize the error, mixing by hand, and then putting a measured volume of the mixture in a small plastic bag which can be sealed by a candle. A pre-printed label (Figure 2) is stapled to the bag which explains the contents and provides pictorial instructions for mixing and administering.

This production process which is done by illiterate female workers costs 0.85 taka (about 6 U.S. cents) per litre packet. The quality of the product produced by these illiterate workers reasonably approximates that produced by highly trained laboratory technicians utilizing sophisticated balances. Over the past year the CRL has used this production process to make approximately 20,000 packets per month for the Dacca and Matlab operations.

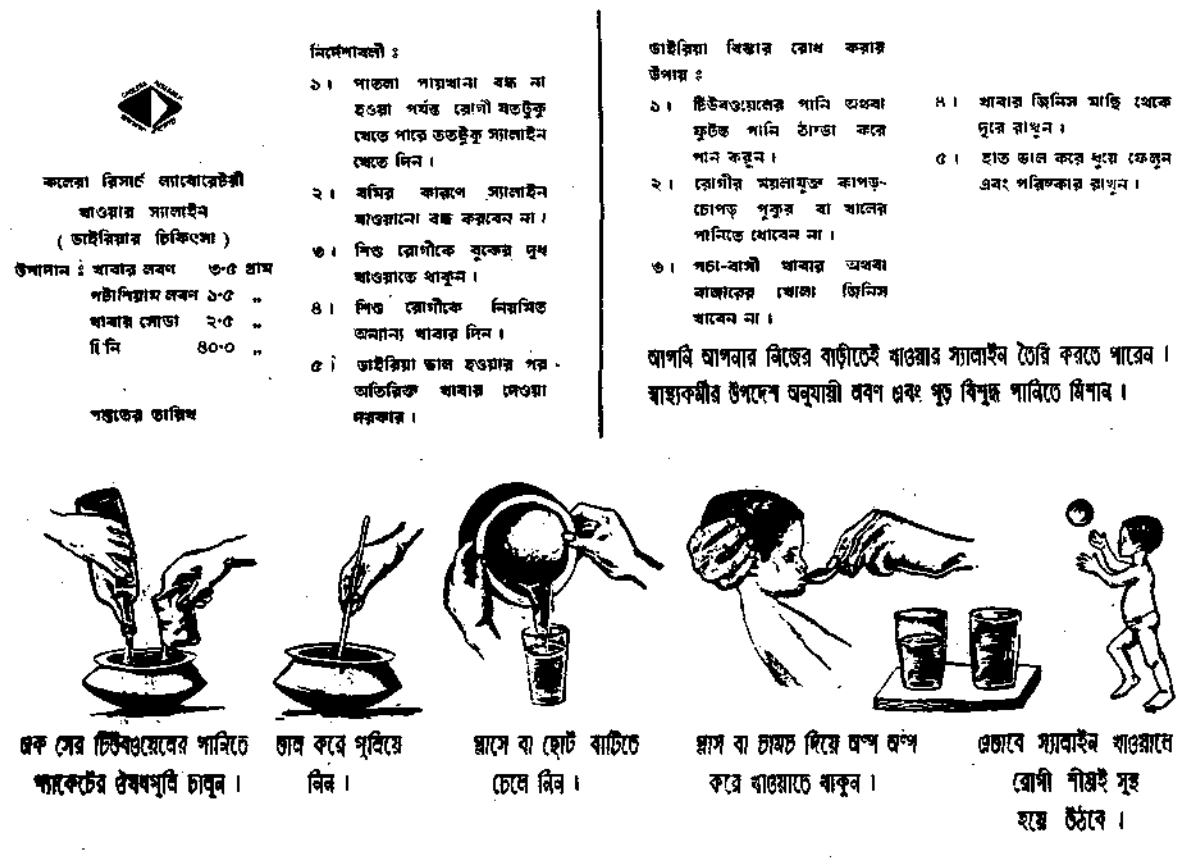


FIGURE 2. Oral therapy packet label. Front (above) and back (below).

2. A measuring spoon for home use for labon-gur.

For the homemade production of a labon-gur solution, the CRL has designed a plastic measuring spoon with cups on both ends, one for measuring the salt and the other for measuring the unrefined sugar. A local manufacturer has produced several thousand of these which are now being distributed with pictorial instructions (Figure 3) in a field test of a home-based treatment program described below. (See page 14.)

In terms of relative cost of the ingredients in Bangladesh, the cost of the constituents for a hundred litres of the glucose electrolyte solution is approximately twelve U.S. dollars, with glucose being the most costly ingredient. If sucrose replaces glucose, the cost falls to approximately seven U.S. dollars, while the ingredients for a similar volume of labon-gur solution would be under two dollars. The ingredient costs do not give the full picture of the relative advantages of simpler formulations, since the widespread availability of sucrose or of labon-gur permits decentralized production utilizing simpler techniques and less skilled workers which would also represent a substantial savings.

FIGURE 3. Poster explaining preparation and use of labon-gur oral therapy with measuring spoon.

D. Oral therapy distribution programs utilizing village-based health workers.

Two different approaches are being examined to determine the effectiveness of a village-based distribution of oral therapy utilizing trained health workers.

1. Female village workers — Matlab.

In the Matlab field study area, 160 female village workers who normally conduct vital registration and other work covering an estimated population of approximately 137,000 were given 2 1/2 days instruction in the indications and use of the oral therapy packets in treating acute diarrhea cases. Because errors in measuring the volume of water for mixing had previously been shown to be a problem, the workers were given discarded I.V. bottles (1 litre size) and instructed to show the mothers the corresponding water level in pots, pans and mugs from households accepting oral therapy. Since this study was conducted in the Matlab area, severe cases and other problems were referred to the Matlab Treatment Unit. There was a comparison population of 134,000 persons where this distribution program was not initiated at the same time as those villagers were to be part of a domiciliary treatment program which was to be initiated after a few months.

Evaluation of this effort over four-month period revealed that the workers distributed 33,000 packets, or about 200 packets per worker. Quality control of the fluid mixture prepared in the field by spot checking showed it to be satisfactory. On the average, approximately 5.5% of the population were treated for diarrhea episodes in a given month. In terms of efficacy, a comparative analysis with the control area indicated that this household treatment program resulted in a 25-35% reduction in hospitalization rates at the central treatment center.

2. Indigenous practitioners — Chandpur.

A different village-based strategy is being tested in thanas adjacent to Matlab in the Chandpur subdivision. In these areas which are not directly served by the Matlab treatment center a survey revealed that most diarrheal cases are treated by indigenous practitioners generally using ineffective methods. The plan is that groups of approximately 25 practitioners will be given a one-week training course at the Matlab treatment center on oral

rehydration and the management of diarrhea. A follow-up evaluation of the impact of these local practitioners is planned for several months after they return to their practice.

E. The efficacy of home-based oral rehydration programs

There are two field investigations looking at the feasibility of oral therapy as a domiciliary program in the rural area.

1. Family depot holders — Teknaf.

In the Teknaf project area in one village of approximately 3,500 persons, 25 families were recruited to serve as depot holders for oral fluid packets and were trained in the proper administration of oral therapy by village-based field workers. In an adjacent village of approximately 1,700 persons, the village-based workers provided oral therapy directly, during the course of their bi-weekly rounds. A two-year follow-up of this activity revealed that the incidence of diarrheal diseases in the two villages was approximately the same. In the village with depot holders more than 90% of the cases received oral therapy, while in the other village only about 30% of the cases were treated, primarily due to the infrequency of field visits. The morbidity and mortality surveillance program being carried out by these field workers showed a marked difference in the diarrhea case fatality rate between the two villages. In the village with depot holders providing treatment, the case fatality rate was only one-fifth the level seen in the adjacent village without the depot holders. These data suggest that the ready availability of oral rehydration at the household level by trained villagers can have a substantial impact on diarrhea mortality.

2. Bari-mothers — Matlab.

In the Matlab area a home-based oral therapy program is being initiated over a much larger area, covering a population of 80,000. In this project, involving 2,000 women, one mother in each bari (a bari is a group of patrilineally-related families) is trained in the correct procedure for mixing and administering oral therapy and provided the materials to treat the family members in her bari. This study additionally involves a comparative trial;

in half the area, mothers are given the sucrose-based oral therapy packets, in the other half they are given containers with the ingredients labon (salt) and gur (brown sugar) and a measuring spoon. The objective is to assess the acceptability and effectiveness of this programmatic approach in terms of reducing the need for hospitalization and intravenous therapy and reducing mortality in mass-scale use under field conditions. The two different solutions are being tried to determine if there is a significant difference in acceptability and effectiveness under field conditions. If not, the use of labon-gur would greatly decrease the cost as well as the technology involved in introducing domiciliary-based oral therapy on a national scale.

As this project has been initiated in late 1978, there is insufficient data to reach any conclusions at this time.

F. Antibiotic trials.

Clinical trials of antibiotic therapy in diarrheal diseases must be a continuing activity. There are generally two objectives. The first is to define what are the simplest yet effective therapies for specific diarrheal diseases. Secondly, because antibiotic resistance develops over time, there must be a regular evaluation of the effectiveness of alternative antibiotics. Two antibiotic studies were carried out in the past year.

The effectiveness of a large, single dose of ampicillin in comparison with a five-day divided dose schedule in the treatment of shigella dysentery was examined. Ninety-one patients with shigella dysentery, 50 adults and 41 children, were included in this randomized comparative study. The single large dose therapy was 100 micrograms per kilogram. For the five-day therapy this same amount was divided into four equal doses given for five days. Approximately half the patients had dysentery due to Shigella shiga with the majority of the remainder due to Shigella flexneri.

The results revealed that both children and adults had a satisfactory clinical response to the single large dose of ampicillin as compared to patients receiving the routine divided dose for five days. Clearing of the organism from stool cultures was better with multiple doses; 97% were clear by the seventh day as compared with 89% with the single dose. Overall, the study indicated the single dose of ampicillin may be used with clinical results as satisfactory as achieved with multiple doses.

Because ampicillin-resistent strains of shigella are beginning to appear, another clinical trial is testing the efficacy of trimethoprim sulphamethoxazole (bactrim) in the treatment of shigella dysentery. A preliminary analysis of data from 23 cases suggests that this will be an effective alternative for shigella dysentery.

G. Chlorpromazine, a diarrhea-inhibiting drug.

The discovery of oral therapy has greatly simplified management of acute watery diarrheas and makes effective therapy potentially available to all. However, the most severely affected patients purge at such a high rate that they will not survive unless they receive intravenous replacement of fluids. Thus, there has been an urgent need to develop drugs that could decrease the rate of fluid loss in cholera and other diarrheas and thus obviate the need for intravenous therapy. In recent years, the enzymatic mechanism by which cholera toxin and the related toxins of E. coli cause fluid loss has been determined, and drugs which reverse this enzymatic stimulation have been sought. One drug, chlorpromazine was shown to be effective in reducing diarrhea in animal models, and so, was selected for clinical trials.

Eleven heavily purging cholera patients were given chlorpromazine either by injection (1 mg/kg or 4 mg/kg) or orally (1 mg/kg) and the clinical course was followed in comparison to an untreated group. The treated cases showed an average 66% reduction in stool output as compared to only a 29% decline over time with the untreated group. These preliminary results require more detailed study before the practical utility of this drug is established, however, it indicates for the first time that there is a prospect of a drug which can stop the diarrhea, and reduce the need for intravenous and oral fluid replacement in cholera and related diarrheas.

II. DISEASE TRANSMISSION AND CONTROL.

The research goals of this Scientific Working Group encompassed three areas. These are: (1) to define the agents responsible for the various kinds of diarrhea seen in Bangladesh and to determine their natural cycles; (2) to delineate the ways in which they have spread in different communities in Bangladesh; and (3) to seek effective and applicable interventions by which the cycles of disease can be interrupted.

The research program encompasses clinical, laboratory and field investigations. Hospital-based surveillance is required as an ongoing activity to detect and monitor the important causes of diarrheal illness in the community. This surveillance not only provides information on the annual incidence of various causes of diarrhea but also gives indicators on the seasonal patterns, geographic distribution, and age and sex characteristics of the cases. These are essential, both for formulating hypotheses for research as well as for rationalizing control programs. Most of the active research is conducted in the community where a multi-disciplinary approach is important since diarrheal disease transmission is as dependent on social and cultural as well as biological and ecological factors. Supportive laboratory investigations are also essential, particularly to develop practical diagnostic tools for large-scale use in field investigations.

A. Diarrhea surveillance — the incidence and causes of acute diarrhea.

The three diarrhea treatment centers operated by the CRL are located in Dacca City; and in the field study areas in Matlab Thana, Comilla District; and Teknaf Thana, Chittagong District. In fiscal year, 1978, these three centers treated a total of 118,421 diarrhea cases; 98,315 were seen in Dacca, 15,597 in Matlab, and 4,509 in Teknaf.

1. Matlab

In the Matlab field study area, which encompasses a population of 269,000 persons in 228 villages under continuous demographic surveillance, a systematic sample of all diarrhea cases seen in the central treatment center was selected for comprehensive microbiological investigations to describe in detail the annual diarrhea incidence by specific cause. Table 1 reveals that in the period

February 1977 through January 1978 the incidence of diarrheal disease seen at the Matlab treatment center was 30.3 per 1,000 persons, or,expressed another way, one out of every 33 persons in this population had an episode of diarrheal disease sufficiently severe to bring them to the treatment center. Overall, a specific agent could be identified in 80% of the cases. It is noteworthy that the two most common causes of diarrhea, accounting for 50% of all of the cases in all age groups, are the enterotoxigenic E. coli and rotavirus. Cholera and the non-cholera vibrios account for almost a quarter of the cases, while Shigella species account for only 5%. With reference to rotavirus, it must be added that this infection is confined almost exclusively to children under the age of three years. Therefore, if one is considering only childhood diarrheas, this agent alone would account for from 50% to 75% of the cases, depending on the time of the year.

TABLE 1

Matlab Treatment Center Surveillance

Annual incidence of diarrhea by etiology,
February 1977 - January 1978

Pathogen	Incidence per 1000 population
V. cholera	3.7
Non cholera vibrios	3.1
Shigella	1.5
Enterotoxigenic E. coli	8.1
Rotavirus*	7.5
Other	6.4
Total	30.3

*Estimated from surveillance November 1977-August 1978

As shown in Figure 4, each of these specific causes of diarrhea has its own seasonal pattern. Cholera typically has the most striking pattern, with a sharp seasonal peak at the end of the monsoon which gradually declines with cases almost absent during much of the rest of the year.

attacks the most susceptible hosts and then produces a permanent immunity. The enterotoxigenic E. coli and noncholera vibrios also have the highest incidence in the first year of life, with a declining rate with age; however, cases are common in adults. This pattern is typically seen with highly prevalent infections where there may be multiple serotypes of the organism, so that new infections can repeatedly occur in the same individual because of continuing susceptibility to different strains of the same organism.

Cholera shows a very distinctive age pattern. Cases are rare in young infants and increase in frequency through early childhood. This picture, coupled with the distinctive seasonal and geographic distribution of cholera is indicative of a very different mode of transmission. Numerous investigations to date point to cholera being acquired primarily by direct ingestion of relatively recently contaminated water, and not easily spread by food or fingers, even in grossly unsanitary environments.

In interpreting the results of diarrhea surveillance in the Matlab area, it should be recognized that this locality was chosen for research by the CRL in 1963 specifically because it was characterized by a very high incidence of cholera from year to year. Ecologically, Matlab is a riverine flood plain with most of the land going under water in the monsoon season and the villages being interlaced with tidal canals and surrounded by multiple shallow ponds in the dry season. Fresh surface water is abundantly available for all uses. In this context, it is not surprising that cholera, a water-borne disease is prevalent. It is interesting to note in addition, however, that among the 15,597 diarrhea cases seen at the Matlab treatment center in 1978, 92% were clinically classified as watery diarrhea and only 7% as dysentery. This pattern is in striking contrast to the diarrhea disease pattern observed at the Teknaf treatment center described below.

2. Teknaf

The research program was initiated in Teknaf, the southern tip of Chittagong District in 1974 because of reports of the high incidence of Shigella dysentery. With the establishment of a treatment center, three years surveillance from 1976 to 1978 have confirmed this to be the case. Among 5,283 patients treated at the center

over the three-year period, 86% presented with the clinical picture of dysentery. Bacteriological examination supported these clinical observations. Various serotypes of shigella were isolated from over 35% of the patients seen at the treatment center during this three-year period. Eighty-eight to ninety percent of the isolations from year to year were Shigella flexneri.

The impact of dysentery on this community is illustrated by Figure 5 which shows the age specific attack rates in 1977. For children under the age of five, about 25% have an episode of clinical dysentery every year and in about one case in five, this will be due to shigella. Case rates are lower in adults but still about one out of every ten to twenty adults will be afflicted with dysentery every year.

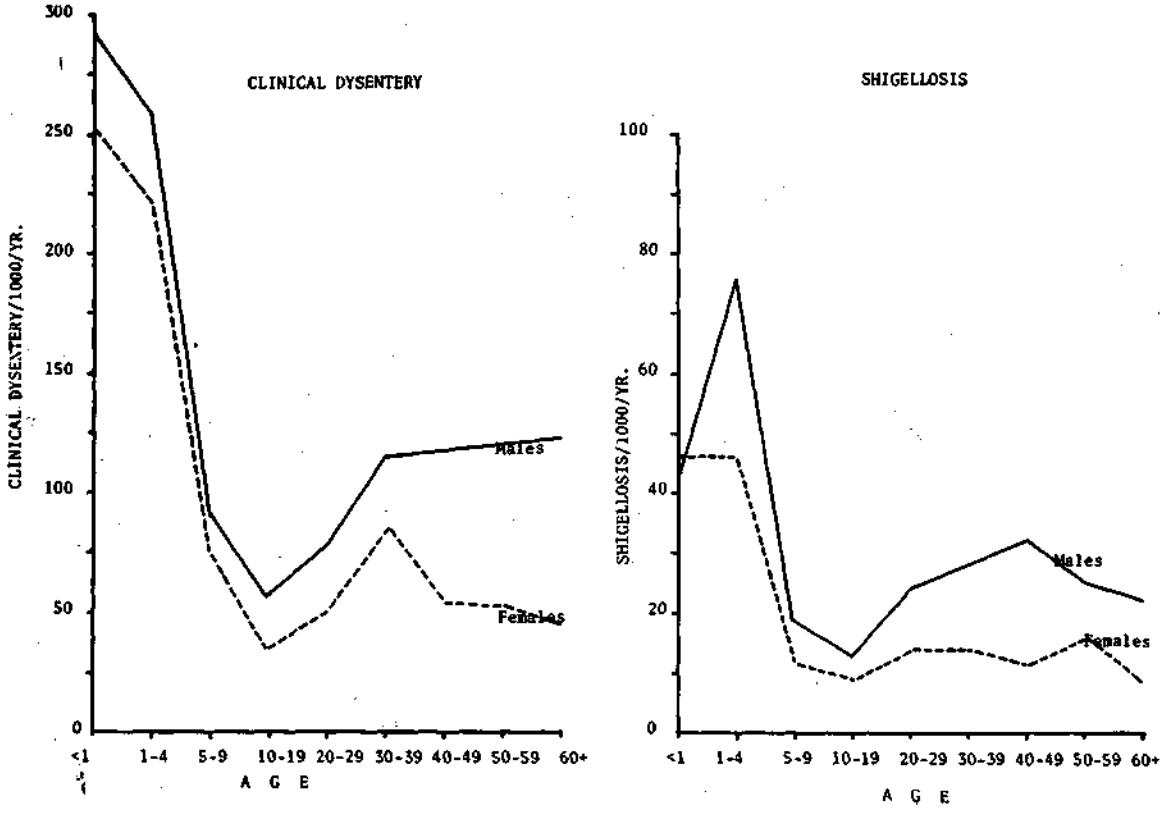


FIGURE 5. Age specific attack rates for dysentery and for laboratory confirmed shigellosis, Teknaf, 1977.

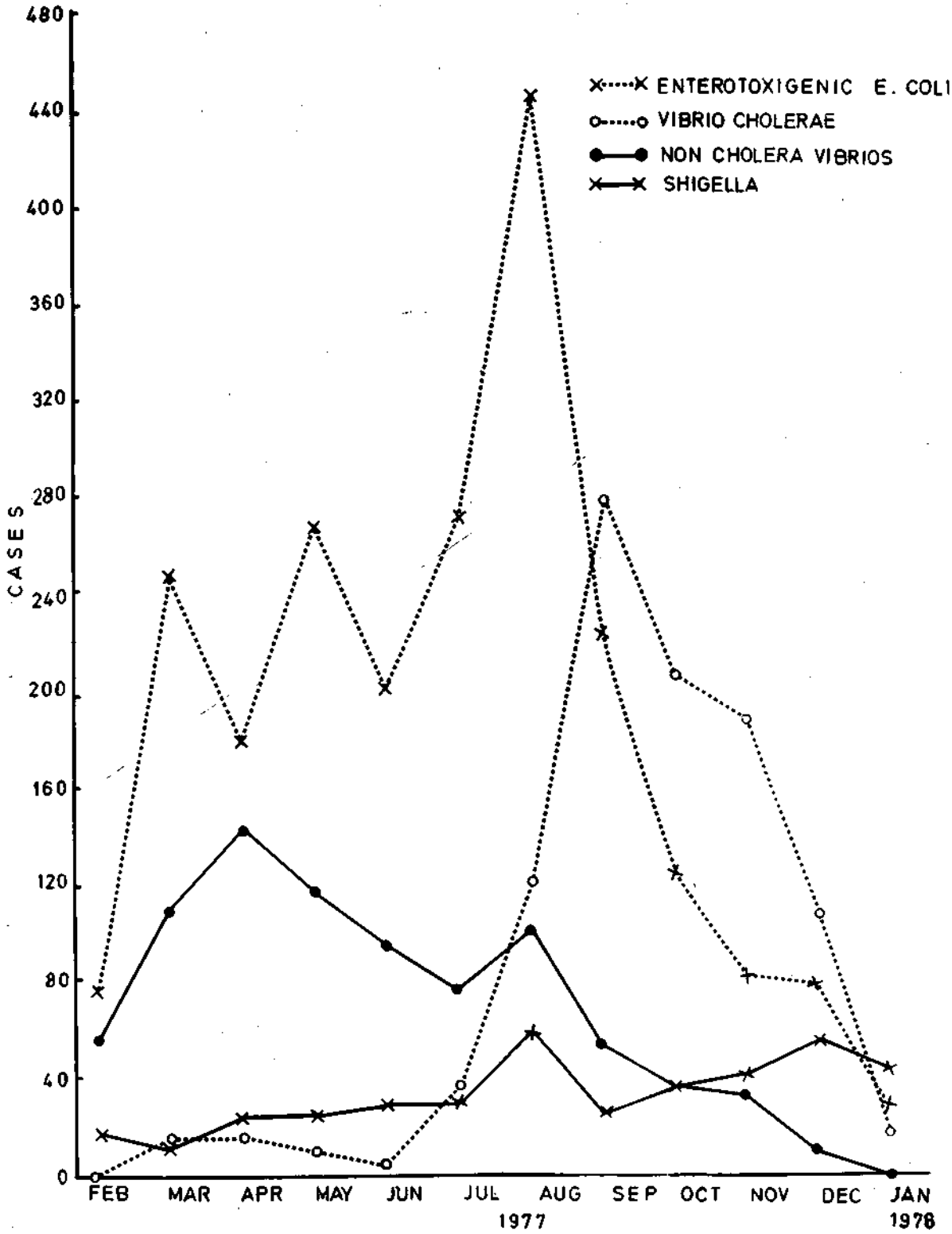


FIGURE 4. Seasonal incidence of diarrhea by cause, Matlab treatment center.

The non-cholera vibrios show almost the opposite pattern, suggesting that there must be quite different ecological factors involved in the transmission of these two diseases. Enterotoxigenic E. coli have a high level of prevalence through the hot summer months peaking in mid-monsoon, while sigella cases maintain a relatively constant low-prevalence throughout the year.

Rotavirus, which is not shown in the figure, has a rather high prevalence throughout the year, but the highest incidence is in the coolest months of the year, suggesting a distinctively different mode of transmission from the bacterial diarrheas.

A critical examination of the age pattern of cases by specific causes reveals additional distinctions that offer clues regarding mechanisms of transmission and the importance of acquired immunity. Table 2, giving the relative frequency with which specific agents were isolated from children with diarrea in the first five years of life illustrates first, the concentration of rotavirus infections in children under three. The virtual absence of rotavirus in older children and adults is indicative of a highly prevalent infection in the population, with an agent having only one or a very few serotypes which

TABLE 2

Matlab Treatment Center Surveillance

Estimated relative frequency by age of isolation of enterotoxigenic pathogens and rotavirus from diarrhea cases among children under 5 years

Age (Years)	Rotavirus	Ent.E. coli	NCV	V. Cholera
	%	%	%	%
<1	48	56	55	5
1	50	28	25	10
2	2	6	10	23
3	-	6	7	32
4	-	4	3	30
All	100	100	100	100

to 11.4% of all diarrheas. Because of the severity of this illness, it is associated with higher mortality as well.

1. Transmission of Shigella dysenteriae infection in urban families.

This epidemic prompted a field investigation of the S.dysenteriae in families in Dacca to determine the relevant epidemiological characteristics. The family contacts of 47 index cases with S.dysenteriae were followed up prospectively for 10 days, with bacteriological cultures and environmental surveys. Analysis of the results revealed that among 240 family contacts, 49 (20%) were found infected with S.dysenteriae. Almost two-thirds of these infected contacts had diarrhea and 10% ultimately required hospitalization. Higher infection rates were associated with poor families living in congested dwellings with open latrines and unprotected water sources. Not unexpectedly, in 20% of these families, some members were found infected with other strains of shigella. This was a further indicator of the poor environmental living conditions of these families. Antibiotic sensitivity studies revealed that 90% of the S.dysenteriae, Type I strains were resistent to tetracycline, the most commonly used antibiotic for diarrheal illness.

2. Personal hygiene and shigella control.

These and other investigations clearly indicate the high risk to shigella infection among family members, particularly, under poor environmental conditions. At the same time, they indicate how impractical and ineffective it would be to try to control the infection by giving antibiotics to family contacts. On this basis, a family study has been initiated to determine how effective the provision of soap, along with instructions in handwashing and other hygenic practices would be in reducing secondary infections and hospitalizations among family contacts of dysentery cases. This is being carried out as a controlled study with alternate families having only regular follow-up examinations with appropriate treatment for symptomatic cases. A preliminary analysis of the data from 15 families indicates that this can be an effective intervention. Family members receiving soap along with detailed hygenic instructions have been demonstrated to do more effective washing than the control families. Further, the secondary infection rate and case rate among

contacts in the treated families is only about one-fifth that observed in the control families.

D. Enterotoxigenic E. coli.

There are a number of special problems that make epidemiological research on the enterotoxigenic E. coli very difficult. First, in contrast to shigella and cholera, many strains of E. coli are normal inhabitants of the human intestine. Thus, special tests are required to specifically detect those strains that are toxigenic and will produce diarrheal disease. This is complicated, first, by the fact that there are (at least) two distinct types of toxin, one that is heat labile (LT) and quite similar to cholera toxin, and another that is heat stable (ST). The toxin problem is further complicated by the fact that the only reliable assays for toxin require either animals (suckling mice for ST) or tissue culture (for LT).

A given E. coli strain may have only LT, only ST or both LT and ST. Toxigenicity, however, may not be stable for any given strain since these characteristics are associated with plasmids (genetic material) which may be transmitted from one strain to another or lost by a given strain

1. Development of practical laboratory diagnostic tests.

The research program of the CRL on this problem has required simultaneous efforts at developing laboratory methodologies in conjunction with surveillance and field research programs. Two basic investigations were important in this regard.

a. Sampling techniques for toxin assays.

Typically, up to 10 individual E. coli colonies on a culture plate from each individual case are separately tested

The distinctively different patterns of diarrheal disease in Teknaf and Matlab presumably relate to different ecological settings. Although a coastal area, Teknaf actually suffers severely from a deficit of fresh water for drinking and household purposes. The tidal river is too salty and much of the sub-surface area is solid rock, making drilled wells extremely difficult. The high prevalence of dysentery in the Teknaf area as compared to the Matlab area is consistent with the characterization of this disease as "water-washed" indicating that transmission is inversely related to the volume of water available for personal use but not strongly related to the quality of water.

3. Dacca

In 1977-78 a 1% systematic sample of the acute diarrhea cases seen at the Dacca Treatment Center was selected for intensive clinical and epidemiological study. Over a twelve-month period, approximately 1,000 patients were selected for a comprehensive microbiological investigation including a search for cholera and non-cholera vibrios, shigella, enterotoxigenic E. coli, rotavirus and parasitic causes of diarrhea. The clinical course was carefully monitored and general epidemiological data on the social and demographic characteristics of the patients were obtained. The study, which is just completed, will provide information on the range of causes of diarrhea prevalent in the Dacca area and the spectrum of the clinical picture given by various agents. Comparing these findings with the results of hospital surveillance in the rural areas can provide valuable clues to the ecological factors that are important for transmission for specific diarrheal diseases in the urban as contrasted with the rural areas.

B. Cholera-changing epidemiological patterns.

Since the opening of the treatment center facilities by the CRL in Dacca in 1962 and in Matlab in 1963, the CRL has maintained bacteriological monitoring coupled with field investigations of the epidemiological pattern of cholera in the urban and rural areas. The most significant change observed over this time period has been the shift in the predominate organism from the Classical biotype of Vibrio Cholerae to the El Tor biotype which occurred between 1972 and 1973. A recently completed review of 10 years of cholera surveillance from the Matlab hospital illustrates this shift.

Between 1968 and 1977, 5,122 cases of confirmed cholera were treated at the Matlab field hospital. From

1968 to 1972 all but 66 of 2106 cases were of the Classical biotype. From 1973 to 1977 all but 6 of 3,115 cases were of the El Tor biotype.

Field studies undertaken by the CRL in the late 1960's revealed large differences in the epidemiological patterns of cholera according to the biotype of the organism. For example, studies of family contacts of cases infected with Classical cholera revealed up to 20% would be infected and from 5% to 10% would ultimately require hospitalization for clinical cholera. By contrast, studies of family contacts of El Tor cholera, while also revealing up to 20% infected, found that only 1% to 2% of the family members would ultimately require hospitalization for cholera. In the vast majority of El Tor cases, the infections were symptomless, or produced only mild diarrhea.

With the change to El Tor as the predominant infecting organism in Bangladesh after 1972, a family study was again initiated in Dacca to determine what were the epidemiological characteristics of the El Tor disease. A recently completed analysis of these data reveals that the spectrum of illness with El Tor cholera in Dacca is much more similar to that previously found for Classical cholera than that previously described for El Tor cholera. Specifically, in the families studied, 31% of the family contacts were infected and 7% required hospitalization for cholera. This high ratio of hospitalized cases to total infections in these family contacts suggests that the El Tor disease now in Dacca is a more severe form of the infection than traditionally associated with the El Tor organism and closely approximates the pattern associated with Classical cholera. Whether this shift in the spectrum of illness relates to characteristics of host susceptibility or microbial virulence remains to be determined.

C. Shigella dysentery — epidemiology and control.

Shigella dysentery is a chronic endemic problem in Dacca. Typically from 3% to 5% of diarrhea cases treated at the CRL will be due to shigellosis. Over the years, the predominant infecting organism has been Shigella flexneri. Beginning in 1970, the much more virulent strain, Shiga dysenteriae, Type I, became more prevalent. The number of cases rose steadily from 26 in 1970 to 1,210 by 1974, representing an increase from 0.6%

for the production of ST and LT. Because toxin assays in animals and tissue culture are expensive and laborious, an investigation was undertaken to determine the efficiency of various sampling procedures for detecting toxigenic E. coli in stool cultures. The study involved comparing the results obtained by testing one, two, a pool of five, or a pool of ten E. coli colonies isolated from 109 cases presenting with severe diarrhea. Stool specimens were taken both in the acute and convalescent stage of the disease. The results revealed that toxin testing of 5 individual isolates or a 10 pool had almost equal efficacy as testing 10 individual isolates. Establishing the efficiency of this procedure facilitated the hospital surveillance study reported above, which required 300 to 400 toxin assays every month over a one-year period.

b. Association of toxigenicity with serological groups of E. coli.

An investigation was undertaken to establish if there were any well-defined relationships between enterotoxigenicity and specific species of E. coli as characterized by serological grouping. This investigation had not only scientific but also practical implications. Serological grouping of E. coli can be performed in any laboratory simply by mixing specific immune sera with a suspension of E. coli taken from a culture plate and looking for agglutination. Over 150 different serogroups of E. coli can be distinguished by this technique. If enterotoxigenicity can be associated with only a few serogroups, this would provide a simple laboratory tool to rapidly identify toxigenic strains for diagnostic and epidemiological purposes.

To carry out this investigation, a large number of E. coli strains were collected from acute diarrhea patients suspected clinically of having enterotoxigenic E. coli, and also from symptomless individuals. All E. coli isolated were tested for both LT and ST toxin production at CRL and then sent to the Central Public Health Laboratory, Colindale, London, for serological testing to determine the O serogroup. The results of testing 740 strains are presented in Table 3. Altogether 266 strains were toxigenic and 474 nontoxigenic. Noteworthy is that 164 (61.7%) of the toxigenic strain fell within eight O serogroups while only 6.4% of the non-toxigenic strain were within the same serogroups. These results are consistent with

earlier observations and indicate that serological screening can be a useful clinical and epidemiological tool for studies of toxigenic E. coli.

TABLE 3

Relationship between O serogroup of E. coli and toxigenicity

O group	Number tested	Toxigenic LT-ST	Toxigenic ST	Toxigenic LT	Non-toxigenic	% Toxigenic
6	43	29	7	1	6	86.0
8	29	24	2	-	3	89.7
15	17	8	-	-	9	47.1
27	9	-	4	-	5	44.4
63	14	1	10	1	2	85.7
78	58	34	24	-	-	100.0
115	17	13	1	-	3	82.4
148	6	-	5	-	1	83.3
Other	547	29	63	10	445	18.6
TOTAL	740	138	116	12	474	35.9
% in specific O Groups Tested	26.2	79.7	45.7	16.6	6.3	

2. Transmission of enterotoxigenic E. coli in rural households.

Beginning with enterotoxigenic E. coli cases detected through hospital surveillance in the Matlab hospital, and utilizing as an indicator the O serogroups 6, 7, and 78 and 115, a household-based study of the pattern of E. coli transmission was carried out in the Matlab area. Eighty-two families were included in this study. The households were visited daily for 10 days and all regular members were cultured each day, and day 1 and day 10 blood specimens were obtained. Bacteriological cultures were also taken from drinking water sources, bathing and cooking water sources, water stored in the house, leftover food, animals and cow dung utilized by the household.

A preliminary analysis of results in 446 household contacts indicate that 53 persons (12%) were infected with toxigenic E. coli with 20 persons symptomatic with diarrhea. Infection rates were highest (30%) in children under 2 years of age and lowest (7%) in adults over age 20. Also, 80% of infected children had diarrhea as compared to only 16% of the infected adults. Water sources were found positive about 5% of the time, while the organism was found in household drinking water and food only about 1% of the time. Environmental contamination was found with less frequency in a group of control families similarly studied but the low rates make interpretation difficult. The data clearly indicates there is effective transmission of E. coli within these rural households with infants and youngest children being the highest risk to infection and illness, but exact routes of spread are not fully clarified.

E. Rotavirus diarrhea.

Only within the last few years has rotavirus been identified as a major causitive agent in childhood diarrheas. Epidemiological investigations, however, have been extremely limited because the virus cannot be isolated by culture techniques and until recently required direct visualization of the virus particle in stool specimens by electron microscopy. The detection of rotavirus in stool specimens has been greatly simplified by a new immunological procedure called the Enzyme Linked Immuno Sorbant Assay (ELISA) technique. In late 1977, the CRL made arrangements in collaboration with the U.S. National Institutes of Health to establish the ELISA technique at both the Dacca and Matlab facilities. The utilization of this technique permitted for the first time the hospital surveillance studies (described above) as well as providing the diagnostic basis for the clinical trials of oral therapy in rotavirus disease.

A community based study of the epidemiology of rotavirus diarrhea in the Matlab area has been undertaken with the following design. Fifty cases of rotavirus diarrhea were selected from the Matlab hospital. In addition to documenting the clinical course, breast milk from lactating mothers of the cases and nasal secretions

from the cases were screened for rotavirus and rotavirus antibodies. All household contacts and neighborhood contacts age five or less of the index cases had stool and serological examinations for rotavirus infection. Animal stools were also obtained for rotavirus detection. The study has been designed to provide information on the ratio of symptomatic to asymptomatic cases in rotavirus diarrhea, the transmission of the organism in the family and the neighborhood, and in man and animals and the relationship of serum antibody to protection from disease. Data collection was completed this past year, but results are not yet available.

F. Non-cholera vibrios — disease characteristics and taxonomy.

The increasing frequency of non-cholera vibrios (NCV) as a cause of acute diarrhoeal disease in Bangladesh has been reported. In the past, the non-cholera vibrio group has been a repository for those organisms which fail to agglutinate in serum specific for V. cholerae. Consequently this group of organisms is heterogenous and frequently contains organisms which should be assigned to different taxonomic groups; some misidentified groups include V. parahaemolyticus, Aeromonas hydrophilia and Pleisomonas shigelloides. A direct result of this clumping of organism under the acronym NCV has been to confuse the clinician in the recognition of NCV diarrhoeal disease. The ubiquitous abundance of NCV in aquatic environments of cholera endemic and cholera free areas of the world has raised doubts on the pathogenicity of these NCV. Diagnostic schemes to distinguish and identify the pathogenic NCV from the free living aquatic NCVs are lacking.

The CRL in direct response to characterise the disease and the organism has initiated a detailed clinical and taxonomic study of the non-cholera vibrios. The purpose of this research has been to characterize and distinguish pathogenic members of the cholera-like group of organisms and establish their taxonomic position; to define the disease process associated with pathogenic strains and its relation to cholera; and develop an identification scheme for clinical use. This study with such a broad

basis has necessitated close collaboration with other centers interested in this field (Department of Microbiology, University of Maryland, U.S.A. and Department of Microbiology, University of Surrey, U.K.).

Preliminary microbiological results of 87 cases of acute diarrhea associated with cholera-like organisms reveal that these organisms belonged to four distinct taxonomic groups: V. cholerae Non O Group I; V. parahaemolyticus; A. hydrophilia and Group F Vibrios. It has only been possible to examine the clinical records of 21 V. cholerae Non O Group I cases and 21 V. Parahaemolyticus because the other cases were mixed infections, mainly toxigenic E. coli. The main clinical features which distinguish NCV disease from cholera include: abdominal pain (76.19%); cramps (33.0%) and fever (38.0%). The duration of diarrhoea after hospital admission and the total stool output are considerably less than that of cholera.

Studies on the experimental pathogenicity of O Group I non-agglutinating V. cholerae reveal a spectrum of biological activity. Isolates were characterised as being able to produce: an LT-like toxin; an ST-like toxin; enteritis without LT or ST; or having no activity in the biological assays. Out of 110 NCV selected from clinical and environmental sources: 19.1% produced at LT-like toxin; 1.8% produced an ST-like toxin and 66.4% produced enteritis in the classic models of enterotoxicity, the infant rabbit and the rabbit ligated ileal loop. No significant difference in bioactivity was observed in isolates from different epidemiological sources. Preliminary characterization data on the NCV LT toxin reveal that it is strikingly similar to cholera toxin.

On-going studies will now concentrate on a detailed taxonomic analysis of the cholera-like vibrios. In addition, genetic studies will be undertaken to determine whether toxigenicity of isolates is plasmid mediated or not.

G. Domestic water use in a rural village.

It is widely believed that the health of people in rural Bangladesh would be greatly improved if these people used increased quantities of water of a higher bacteriological quality for domestic purposes. Rural water supply programs are usually designed on the assumption that if access to an "improved" supply is easy and if the people are educated about the beneficial health effects of abandoning their traditional supplies and using this new supply, then existing water use patterns will change. Experience in many rural areas throughout the world, however, has shown that, in fact, this does not occur.

Recently, a preliminary analysis has been completed based on nine months of in-depth observation on how people in one village in the Matlab area choose water sources for different domestic uses. The study identified three independent variables that were important determinants of use of a water source for drinking. These were the taste of the water, the distance the source was from a family's home, and quarrels (or friendship) generally related to ownership of the water source. With reference to water for all other uses, including cooking, utensil washing, clothes washing, bathing, the most important determinants were quarrels, depth of the water, and distance from the house. Even with the limited data currently available, it is clear that we need a better understanding not only of actual water use patterns, but of the villagers perceptions about important characteristics of water sources if we are to know how people will respond to water supply programs and ultimately how this response will affect health.

III. HOST SUSCEPTIBILITY AND IMMUNITY

The program of the Working Group on Host Susceptibility and Immunity encompasses clinical, laboratory, and field research. One fundamental question is: What are the mechanisms of acquired immunity in enteric infections? As noted in the section on Disease Transmission, epidemiological analysis of hospital cases and family studies suggest that with rotavirus infections a permanent natural immunity is acquired at a very early age, so that rotavirus cases are not seen in older children and adults. This indicates that there is the possibility of developing an effective rotavirus vaccine. In the case of cholera and enterotoxigenic E. coli, the immunological problems seem much more complex. First, because these organism do not invade the tissues, immune mechanisms must work within the intestinal lumen via antibodies in intestinal secretions. Second, there is the unresolved question of how important antitoxic versus antibacterial immune mechanism are in protecting against these diseases. Studies looking at natural infection as well as artificial immunization have been carried out to pursue various aspects of these questions.

In addition to research on acquired resistance, there is a continuous effort to understand the primary defenses in the intestinal tract against infections. A major one currently being investigated is the high acidity in the stomach which is capable of killing most of the enteric pathogens which commonly cause disease.

A. Pre-test of cholera vaccines for a cholera vaccine field trial.

It is well established that the currently available cholera vaccines provide only partial protection for a period of three to six months. Recently, cholera vaccine field trials carried out in India and Indonesia have indicated that the addition of aluminum hydroxide as an adjuvant to the currently available whole cell cholera vaccine can extend the duration of protection for at least two years. The level of protection, however, remains sub-optimal ranging from 50% to 80%. Laboratory investigations in several countries have suggested that the addition of cholera toxoid to the whole cell vaccine can significantly enhance the protective efficacy of cholera vaccine. On the basis of these facts, the U.S.

National Institutes of Health has coordinated an international effort involving the Wellcome Foundation, London, U.K.; the Bangladesh Medical Research Council; and the Cholera Research Laboratory to develop and test the efficacy of whole cell cholera vaccine with the additions of aluminum hydroxide adjuvant and cholera toxoid.

Three new cholera vaccine products were manufactured by the Wellcome Foundation. These were: (1) an aluminum hydroxide adjuvanted formalin treated cholera toxoid; (2) an aluminum hydroxide adjuvanted cholera whole cell vaccine; (3) a combined preparation containing both toxoid and whole cell vaccine. These three products were subjected to extensive safety testing in human volunteers in the U.K. and the U.S.A. prior to being considered for field testing in Bangladesh. In the spring of 1978, these three vaccines along with a tetanus toxoid vaccine were administered to 1,030 volunteers in the Matlab area to determine their reactogenicity and immunogenicity. All volunteers were examined daily by physicians and blood specimens were taken for measuring the antibody response.

An analysis of the results revealed that the vaccines were well tolerated by all of the subjects. There were some local reactions at the site of injection, typical of any cholera vaccine. Eleven subjects were observed to develop skin rashes at various times following injections. These initially caused some concern, however, further analysis reveal that these rashes occurred in subjects in all the vaccine groups, including recipients of a tetanus toxoid control vaccine and therefore were considered only coincidental and unrelated to any of the vaccines. Serological data revealed a good serological response to all of the vaccines which was generally dose related. An unexpected finding was evidence that some of the recipients of the toxoid vaccine developed antibacterial antibodies against cholera as well as antitoxin antibodies. This indicated that the purification process for removing cell wall antigens from the toxoid was incomplete.

Based on the results of this pre-test, a larger scale pre-test involving 2,400 subjects to confirm the freedom from adverse reactions is planned in the spring of 1979. If this proceeds satisfactorily, a large scale field trial will be initiated in late 1979.

B. The local (intestinal) immune response in cholera.

While cholera vaccines which have been developed for human use give only limited protection for a short time, a greater and more sustained protection has been demonstrated in persons who have had a previous episode of the disease. This seems to be related to the local immune system in the intestine, which is largely mediated by a specific antibody called secretory IgA. Detection and quantitation of the local immune response to cholera will be important in the evaluation of new cholera vaccines, especially if they are to be administered orally. Since antitoxic and antibacterial immunity may act synergistically, both types of antibodies must be measured. In the past year assay systems have been developed at CRL to measure immunogobulin specific antitoxin and antibacterial antibodies. These are being applied to detect antibodies in serum, duodenal secretions, and breast milk from cholera patients in the acute and convalescent phase as well as from normal subjects and in subjects receiving various cholera vaccines.

An innovation in this study has been the procedure for obtaining intestinal secretions. Intestinal lavage fluid is obtained by asking the patient to drink a large volume of an isotonic balanced salt solution (250 ml every 10 minutes for a maximum of four hours). Drinking this fluid induces a watery diarrhea. This diarrhea fluid is immediately inactivated, and frozen for the assays.

The initial experience with nine patients with naturally occurring cholera leads to the following conclusions regarding neutralizing antitoxic antibody: (1) The intestinal lavage and milk titers show good correlation and in both there is an early rise in titer followed by rapid fall so that by day 17, antibody titers are minimal or undetectable. (2) Serum antibody, in contrast, has a rapid rise in titer but remains elevated through day 17. (3) Salivary antibody levels remain undetectable throughout. (4) Work on IgA specific antitoxin is continuing but seems to correlate the neutralizing antibody in secretions.

Development of these methods should be important, (1) in quantitating the local immune response in patients, and (2) in evaluating vaccines for their ability to stimulate local antibodies of high titer and long duration.

C. Gastric acid in enteric disease.

Adult patients with cholera, amoebic dysentery, enterotoxigenic E. coli, and shigellosis were studied to determine their ability to produce gastric acid after a fifteen milligram betazole stimulus. These patients were studied on the morning after admission and at seven days, one month and in a few cases, three months after admission. The results reveal that 9 of 32 cholera patients were deficient in gastric acid production in the acute phase of the disease. Among five of these tested after one month, three showed recovery, while two continued to have low gastric acid production.

Sequential studies of gastric acid production in malnourished children have also been performed. Nearly half the children studied showed a deficiency in gastric acid and lack of response to gastric stimulation by histalog. Hypochlorhydria persisted in most of these children well after recovery in weight occurred. These studies confirm other observations that low gastric acid is a risk factor in enteric disease and suggests that this may be aggravated by poor nutritional status.

D. An investigation of the Sereny Test as a model for determining virulence and immunologic protection from invasive enteric organisms.

The Sereny Test has been developed as an indicator to assess the invasive properties of certain enteric bacteria. It depends on the production of inflammation of the conjunctiva of guinea pigs when the eye is innoculated by a test organism. The purpose of this study was to compare the virulence of selected isolates of shigella and of invasive E. coli and in particular to determine if the test could be used as an indicator of cross immunity by observing if challenge by one organism resulted in a cross protection to subsequent challenge by another strain.

The dose response curve to challenge was determined for four invasive strains of shigella and one invasive strain of E. coli. The infectious dose (ED 50) was remarkably similar for all strains, being approximately 10^6 organisms. The incubation period varied with the size of the challenge dose. There was a considerable difference in the duration of infection with different strains of bacteria. In rechallenge experiments with the same organism, reinfection commonly occurred indicating there was little homologous protection produced. Therefore, further experiments on cross protection were not undertaken.

E. An antibody assay for Shiga dysentery.

When the Shigella dysenteriae, Type I epidemic appeared in Bangladesh, there was a need for a sensitive and specific serologic technique to evaluate the immune response to the infection in dysentery cases as well as to assess the extent of the infection in the community. The usual technique of direct bacterial agglutination lacked sensitivity. Attempts were made to set up passive hemagglutination assays based on various published methods, but these ran into numerous technical difficulties and generally were not suitable for small volumes of sera obtained from finger tip specimens in field studies. These technical difficulties were finally solved by developing a new technique using human O Group RH Negative erythrocytes as carrier particles and chromium chloride as a bi-functional coupling reagent for coating shigella lipopolysaccaride antigen on the erythrocytes. This procedure proved especially suitable for the microtitration techniques. In a series of investigations utilizing sera from confirmed cases of Shiga dysentery as well as from non-dysentery diarrheas, the tests proved to be fourfold more efficient in detecting low titers of antibodies than the corresponding direct bacterial agglutination. The sensitivity of detection of infection in confirmed cases was 83% with a high degree of specificity as attested by the fact that in the normal population only about 5% gave a positive reaction. No significant cross reactivity was detected in experiments using seven other non-Shiga strains of shigella bacteria. The reproducability of the assay is compatible with any good quality serologic test.

NUTRITION

Bangladesh, like many other countries in South, and Southeast Asia, has a serious nutrition problem. A recent Bangladesh national nutrition survey indicated that the prevalence of energy protein malnutrition among preschool children (classified according to the system devised by Waterlow) was as follows: 57.9% of the children were moderately or severely stunted, 5.8% wasted and 15.8% both wasted and stunted. Only 20.5% of the children could be classified as normally nourished or mildly malnourished.

In addressing the problem of malnutrition, the scientific program of the Nutrition Working Group has focused on those problems directly linked with diarrheal disease and further has evolved projects taking maximum advantage of the institutional infrastructures already existing at the CRL. Key elements of the program rationale are as follows:

i. Diarrheal disease, because of its frequency, specificity and pathophysiology, is undoubtedly the most important infectious cause of malnutrition globally. The diarrheal diseases compromise nutritional status by reducing food intake and by accelerating wastage of nutrients through malabsorption and metabolic processes.

ii. Nutritional status, conversely, is an important determinate of host defense against diarrheal and other infectious diseases.

iii.. Breastfeeding and weaning practices, which protect against infection, particularly the diarrheal diseases, are also crucial determinates of child and maternal nutritional well-being.

iv. The field, clinical and laboratory infrastructure of the CRL provide unique opportunities for certain types of nutrition research.

A. Energy protein malnutrition and subsequent risk of mortality.

This study was based on a group of 2,019 children in the Matlab area between the ages of 12 to 23 months from 86 villages who were assessed with regard to body weight, length, and arm circumference in the period from November, 1975 through January, 1976. Subsequently, utilizing the Matlab census data and death registration system, it was possible to determine the pattern of mortality over a two-year period by cause of death and relate this to the earlier assessment of nutritional status.

Table 4 summarizes the mortality rates for the first and second year of follow up for these children according to nutritional status as classified by percent weight for age of the Harvard Standard. Noteworthy, 21.2% of these children were classified as severely malnourished. Over the two-year period the mortality rate in the children originally classified as severely malnourished was three times higher than children in the normal range. Impressive is a comparison of the first year and second year mortality. For children in the normal and moderately malnourished class, the mortality rate declined over time as expected. However, for children classified as severely malnourished, the high mortality rate in the first year rose even further in the second year. This observation in conjunction with other data from this study suggests that the children who are identified as severely malnourished at one point in time represent a group who are in a chronic and continuous state of malnutrition and are subjected to a high risk of mortality from year to year.

In looking at specific causes of death, the malnourished children had death rates ranging from 2.3 to 7.0 times higher for disease categories such as diarrhea, measles and other infections. On the other hand, there was, as expected, no difference in mortality by nutritional status for deaths due to accidents.

The risk of death from malnutrition was further aggravated by crowded household conditions. If the better nourished and poorly nourished children were cross-classified as to housing floor space (crowding being less than 242 square feet), the mortality rate of the better nourished children, rose from 19.4 per thousand to 42.8 per thousand in the more crowded houses, while for the poorly nourished

children the mortality rate rose from 76.2 under less crowded conditions to 117.2 per thousand in crowded households. Basically, the mortality rate was six times higher among poorly nourished children in crowded households as compared to better nourished children in less crowded households. This is indicative of the improvement in mortality that may be achieved in this population simply with improvements in nutrition and socio-economic conditions, in the absence of any other health services.

TABLE 4

Mortality rates of 1-2 year old children one and two years following a nutritional survey, by baseline nutritional status (weight for age)

	Degree of Malnutrition (% of Harvard Standard)			
	Normal/Mild (> 75)	Moderate (60-74)	Severe (< 60)	All Children
Number of Children	546	1046	427	2019
Mortality Rate/1000				
First Year	23.8	26.8	46.8	30.2
Second Year	12.8	15.3	65.6	25.3
Both years	36.6	42.1	112.4	55.5

B. Intrafamily food distribution, feeding practices and malnutrition.

This is a longitudinal study on the dynamics and determinants of household food behavior and feeding practices in 120 selected households in the Matlab surveillance area. Its aims are: to delineate intrafamily food distribution; to document maternal and child feeding practices in response to seasonal food shortage and health related conditions such as diarrhea, fever, respiratory illnesses, pregnancy and lactation; to identify the determinants of the behavioral patterns observed; and, to relate nutritional status to food behavior, food availability, nutritional requirements and disease morbidity.

The field procedure has involved, initially, a cross-sectional survey in 1,000 households in four villages to obtain basic socio-economic information as well as a sampling frame to select 120 households for indepth monthly follow-up. Information obtained at monthly follow-up include anthropometry on mothers and preschool age children (adolescents and other adults would be assessed tri-monthly). Dietary intake is measured bi-monthly including how the food is distributed to each family member. Surveillance for morbidity is done every other day. Specialized studies are being undertaken to determine food behavior and practices associated with diarrhea and other infectious illnesses.

Data collection from this longitudinal study is expected to be complete in mid 1979. Analysis will be carried out to relate dietary intake to nutritional requirements estimated from activity records and morbidity. Seasonal variability will also be examined. Particular focus will be on the changes of food distribution during illness and convalescence. The causes of the observed patterns of food distribution in the families will be examined from both an economic and a food belief viewpoint.

A goal of this study is to assess to what degree it may be possible to improve nutritional well-being, particularly among vulnerable children through policies and programs that promote long-term behavioral change, while operating within existing social and economic constraints. Fundamental issues are: how can poor families optimize nutritional well-being within given social and economic limitations; and,why is it that even among families with adequate food resources there are malnourished children? The root of these questions is intrafamily food behavior. The information generated by this study should identify how much latitude for nutritional improvement is available through direct programmatic interventions and how such interventions may be implemented more effectively.

C. Diarrhea, malnutrition and growth.

In this study, a group of 200 children ages three months to four years from two villages in Matlab have been selected for a longitudinal follow-up for one year. These children are visited on alternate days by field workers to

inquire and document all illnesses. Severe illness are treated as appropriate. Rectal swabs are taken from all diarrheal illnesses and examined for vibrio, shigella, salmonella, toxigenic E. coli, rotavirus and parvovirus. Finger-tip blood specimens are obtained at quarterly intervals for immunological studies and a 1 cc. sample of breast milk is obtained monthly from lactating mothers for assays for antibodies against rotavirus and toxigenic E. coli. Dietary studies include assessment of dietary intake in a subgroup of these children during health and during an episode of acute illness. Anthropometric measurements are obtained at monthly intervals. In the treatment of mild diarrheal illness, one sub group of children is receiving the conventional kaolin mixture and another sub group will be provided the oral glucose electrolyte solution.

The objectives of this study are (1) to identify the etiologic agents of diarrheal episodes in the first five years of life; (2) to establish if there is any relationship between serum and breastmilk antibody titers to specific enteric pathogens and the risk of diarrhea caused by these agents; (3) to learn the effect of diarrheal episodes on food intake and growth; and (4) to determine if oral glucose electrolyte solution taken for all cases of diarrhea has a beneficial effect on growth.

Data collection for this study will be completed in mid 1979. It is anticipated that the results of this study will, for the first time, provide definitive information on the relationship between specific causes of diarrhea and states of malnutrition in children in the rural areas. At the same time it will provide some information on the efficacy of oral rehydration in the household setting in proving nutritional status.

D . Breastfeeding and nutrition.

1. Breastfeeding patterns in rural villages.

This study is based on the longitudinal follow-up of nearly 1500 women in the Matlab area who had live births from February through September, 1974. Among these women, the median duration of breastfeeding was observed to be 30 months. Over 75% of the women whose most recently born children were living were breastfeeding at 2 1/2 years post partum. The major reason for discontinuing breastfeeding in the first year was infant death, and in the second year, pregnancy. Insufficient milk was given as a reason for discontinuing breastfeeding by 18% of the women who stopped for reasons other than child death, but among these women almost 60% were pregnant when they stopped. Of breastfeeding women who became pregnant, over 50% continued to breastfeed through the sixth month of pregnancy.

A more intensive follow-up of a sub sample of 200 women with children 17 to 25 months of age revealed a strong seasonal trend in the duration the infant was permitted to suckle. Women reduced suckling during the harvest season (November) when they were most busily engaged with activities related to the rice harvest. This was associated concurrently with an increased frequency of resumption of menstruation among breastfeeding women during the harvest season. Among other factors related to intensity of breastfeeding, suckling time was somewhat lower among women in higher socioeconomic groups and among infants with better nutritional status. Interestingly, no association was found between suckling time and maternal nutritional status, maternal morbidity, infant morbidity or the child's sex.

This study suggests that a trend toward diminishing breastfeeding does not appear to be occurring in rural Bangladesh, unlike the situation in other developing countries. The rural women seem to be taking full advantage of an important natural resource, human milk. Although a large proportion of the women are undernourished, nearly every mother breastfeeds and breastfeeding did not appear to result in a deterioration in the mothers' health as assessed by their ability to maintain body weight. The implications of these findings are that nutritional programs attempting to supplement

breastfeeding women and their infants should be carefully designed to support the current patterns of breastfeeding in Bangladesh. Specifically, feeding programs aimed at infants and children should be designed to supplement breast milk rather than to replace it. The lengthy pattern of breastfeeding also indicates that care must be taken in selecting which contraceptives will be offered to women in the rural area so as not to interfere with this practice.

2. Breastfeeding and food intake among children with acute diarrheal disease.

To determine the role of reduced food intake during diarrhea as a contributor to malnutrition, and to assess the possible means of promoting such intake, the 24-hour food and breast milk intake was measured in a group of children ages 6 to 35 months under three different situations. Thirty of the children were cases admitted to the Matlab treatment center for therapy for acute diarrheal illness. These were divided into two groups. In 15, the children received routine hospital care for diarrheal illness, including oral rehydration. The mothers of a second group of 15 children received, in addition, intensive dietary education and were encouraged to give the children additional food during the acute illness. A third group consisted of 11 healthy children who accompanied their mothers to the Matlab treatment center for surgical family planning services.

Each child was kept with its mother, and the nutrient intake, including measurements of breastmilk consumption by test weighing, were observed over a 24-hour period. For food supplementation, a specially prepared weaning food made of local ingredients was developed. In addition, mothers were permitted to give other foods as they chose. For the 15 children in the intensive nutrition education group, mothers were encouraged by a local worker to feed the child as much as tolerated.

The results indicated the 24 hour energy and protein intake of 15 children hospitalized with acute watery diarrhea averaged 75 Calories/kg and 0.96 grams/kg, respectively. The energy and protein consumption of the 15 children with diarrhea whose mothers received intensive education to promote food intake averaged 60.9 Calories/kg and 0.70 grams/kg, respectively. These

intake levels were significantly lower than 129.9 Calories/kg and 1.89 grams/kg observed among healthy control children. The results indicate that in the sick child, anorexia is an important cause of reduced food intake during diarrhea, and that this cannot be overcome with intensive efforts to promote supplemental feeding. A significant observation was that the intake of breast milk was quite similar in all three groups. The reduced intake was primarily a function of less ingestion of supplemental food by the diarrhea cases. This study emphasizes the importance of breast milk as a nutrient source during diarrhea.

3. Maternal nutrition and lactation performance.

This study has involved 17 women and their infants who were followed at fortnightly intervals for a period of four months post partum. At each visit maternal dietary intakes are recorded and anthropometric examinations of the mothers and infants are performed. Babies are weighed before and after every feed for a 24-hour period in order to determine breast milk consumption. In addition, a milk sample is taken over a 24-hour period for a nutrient analysis. After approximately four months of follow-up the mother and infant were admitted to the nutrition unit of the Save the Children program and provided with special dietary supplements to determine the effect of improved diet on milk volume and composition.

Preliminary analysis of the data indicates that although the study mothers are small by western standards (weighing approximately 40 kg) their percentage expected weights for heights are only slightly below western standards. Nevertheless, milk consumption by infant age are less than reported in western countries. As a result, most infants maintain growth curves parallel to western norms for only the first three months of life.

Milk analyses demonstrate remarkably reduced fat concentrations, slightly reduced nitrogen concentrations and elevated lactose concentrations as compared to previous studies of western mothers. Seven of eleven mothers demonstrated significant increases in the volume of milk production but generally stable concentrations of fat, nitrogen and lactose following maternal dietary supplementation with increased calories and protein. More detailed analysis of the effect on breast milk production of individual supplementation with either protein or carbohydrates is underway. The data available indicate that supplementation of the breastfeeding mother can be one path toward improved infant nutrition, particularly in the early months of life.

E. Nutrient absorption studies.

1. Lactose malabsorption in rural villagers.

The inability to absorb lactose (milk sugar) is common among adults in many parts of the world and relates to the decline in the presence of the enzyme lactase in the intestine which occurs with age. The frequency of lactose malabsorption in infants and young children may, however, be increased with episodes of diarrhea. In late 1977, a village-based study was undertaken in the Matlab area to examine this question.

Anthropometric measurements and diarrhea histories were obtained from approximately 2,000 Matlab villagers. A sample of 200 of these villagers were specifically examined for lactose malabsorption by the breath-hydrogen test. (This test depends on the presence of hydrogen in the breath which is produced when ingested lactose is not absorbed but is broken down by intestinal bacteria.) The results indicate that most of the adult population malabsorbs lactose regardless of the nutritional status or diarrheal history. Children generally absorb lactose normally until about three-years of age when they acquire malabsorption. The acquisition of lactose malabsorption in children could not be specifically related to diarrheal history or nutritional status.

2. Nutritional consequences of milk supplementation in lactose malabsorption.

This study is based on the concern as to whether dietary supplements of whole milk given to lactose malabsorbers will be nutritionally advantageous. Lactose malabsorbing children and normal children of the same age were admitted for a study to the Children's Nutrition Unit at the Save the Children treatment center. Both groups received a vegetable and rice diet either alone or with supplements of lactose-free or lactose containing milk during sequential time periods. In each of these time periods balance studies were performed to measure the absorption and losses of calories, fat and nitrogen.

Preliminary analysis of the data indicates that lactose malabsorbers successfully tolerate a diet which contains milk supplements if the milk is truly a supplement which is given in divided doses and mixed with the regular diet.

POPULATION

Bangladesh is the eighth most populous nation in the world with 80 million people living on 55 thousand square miles of land. Over the past decade rural Bangladesh has experienced high fertility and mortality and,despite aggressive programmatic efforts, these health indicators have not improved. In meeting the health need of this and similar populations four issues are of significance.

i. What are the causes of high mortality and morbidity?

ii. What are the social and biological determinants of human reproduction?

iii. How appropriate, acceptable, effective and safe are modern and traditional health and contraceptive technologies, both theoretically and within any given social, economic and cultural setting?

iv. Within the context of available knowledge and technology how can health and family planning services be delivered efficiently and effectively?

These questions constitute the core of the research program of the Population Working Group. The major research accomplishments within the past year are highlighted below.

A. Demographic surveillance — Matlab and Teknaf.

The Cholera Research Laboratory has maintained large-scale population-based field studies in the Matlab area in Comilla District since 1963 and in the Teknaf area of Chittagong District since 1974. A longitudinal vital registration system has existed in Matlab since 1966 which, since 1968, covers a population of approximately 260,000 persons. In Teknaf, the vital registration project covers approximately 25,000 persons.

In 1978 the CRL completed and published in a 5 volume series a comprehensive description of the 1974 census in Matlab and an analysis of the registered vital

events including migrations and marriages for the years 1974, 1975 and 1976. Annual publications are planned for the vital events registered in 1977 and each successive year. Concurrent with the analysis of these recent data, the CRL has a collaborative project with the Department of Population Dynamics at Johns Hopkins University to undertake a comprehensive analysis of the 1966, 1968 and 1970 censuses in the Matlab area and the vital registration data for the 8 year period 1966 through 1973. In conjunction with this, all the Matlab census and vital registration records will be organized into a common format on computer tape for access by investigators in Bangladesh and throughout the world.

Figure 6 provides a graphic summary of the trends in birth rate, death rate, and crude rate of natural increase (birth rate minus death rate) in the Matlab area over the entire registration period from 1966 through 1977. This clearly illustrates the effects of two major socio-economic disruptions: the war of 1971 and the famine of 1974-75. Both the war and the famine were associated with sharp increases in mortality. The famine in particular was associated with a dramatic decline in fertility, which rapidly rebounded with recovery.

A detailed tabulation of the demographic events during the 1974-75 famine period by 3-month periods revealed that there was a rapidly rising mortality in the latter part of 1974 followed after a 9-month lag, by the rapidly declining fertility in mid-1975. Birth rates fell among women of all age-parity groups indicating that this event affected almost all strata in the population. Also clearly illustrated was dramatic shift in migratory patterns, with a major net out-migration from Matlab which resulted in a net population decline of 2.25% during 1975. It should be noted that in every year there is typically a net out-migration from Matlab ranging from a 0.2% to 0.9% so that the actual growth of population in the Matlab area is less than can be accounted for by the difference in birth and death rates.

In the Teknaf area, the vital registration program indicates that levels of fertility and mortality are both higher than seen in the Matlab area. Comparative data for 1976 and 1977 are summarized in Table 5. Birth rates are 10% and 7% higher and death rates are 7% and 24% higher in Teknaf in each successive year. The

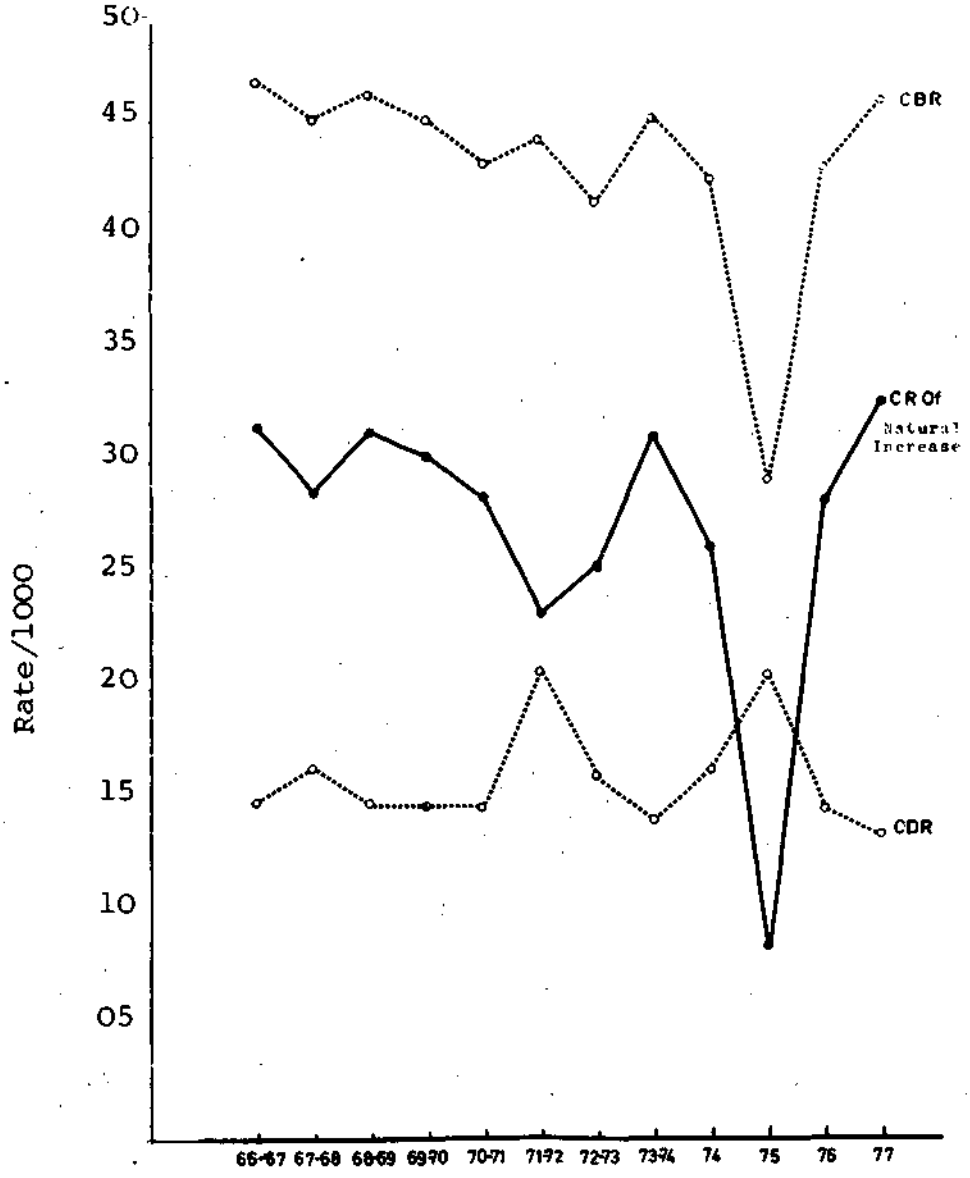


FIGURE 6. Trends in crude birth rate (CBR) crude death rate (CDR) and crude rate of national increase, Matlab 1966-1977.

greatest differences are in infant mortality which is 50% higher in 1977. One factor accounting for this difference is the higher incidence of malaria in Teknaf.

TABLE 5

Population and vital events
Matlab and Teknaf
1976 and 1977

	Matlab		Teknaf	
	1976	1977	1976	1977
Mid year population	260,381	268,894	24,460	25,173
Crude birth rate	43.3	46.4	47.9	49.6
Total fertility rate	6.2	6.7	7.0	7.2
Crude death rate	14.8	13.6	15.9	16.9
Infant mortality rate	112.0	113.7	142.5	171.1

B. Fertility — patterns, determinants, biology and control.

1. Seasonality of fertility.

A critical analysis of the seasonal patterns of fertility by age and parity in Matlab has recently been completed. Figure 7 illustrates the impressive seasonal variation in birth by age group in women for the four year period from May, 1970 through March, 1974. The results of this analysis reveal that seasonality of birth is present for all age and parity groups with seasonal variability ranging between 30% and 50% above and below the mean level. The peak season of births for all ages and parities combined is the beginning of December. There is a clearly defined trend in the seasonal peak for marital fertility by age. For the youngest age group the peak is late October, while for the oldest age group the peak is early January. One possible cause for this shift with age is a decline in fecundability among older women.

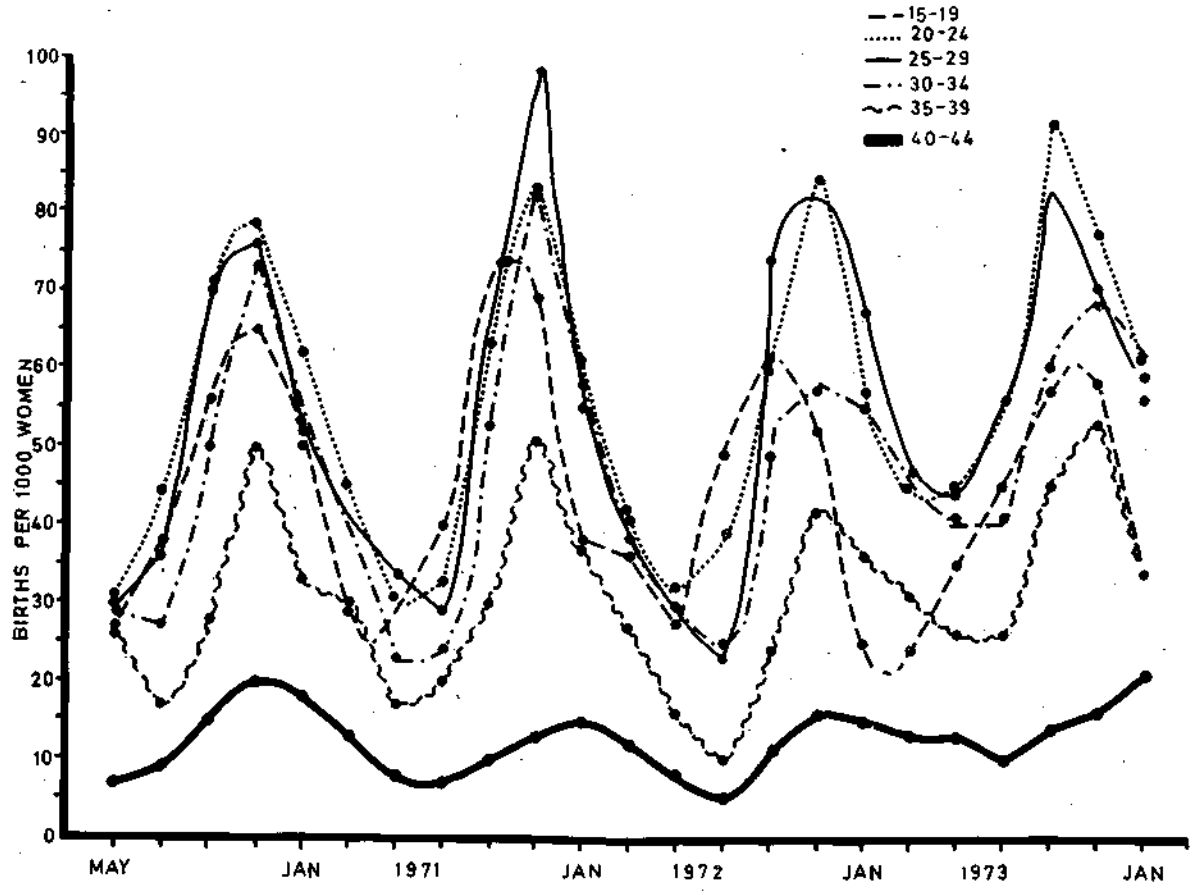


FIGURE 7. Seasonal patterns of births by maternal age, Matlab.

2. Marriage and fertility.

In many traditional societies marriage is universal, and this is the prevailing pattern in rural Bangladesh. According to the 1974 National Census, only 1.1% of males and 0.3% of females had never been married by the age of 45 to 49 years. Almost all marriages are arranged by parents or guardians and are an alliance between kins and lineages rather than individuals.

Analysis of marriage registration data in the Matlab area for 1975-1976 reveal that women married very early with an average age of 16.6 years while grooms had an average age of 24.7 years. From the statistical data in Matlab, it is possible to derive a simple model of the marital life cycle. Out of the potential 40 years of life between the ages of 10 and 50 years, (assuming for the moment no deaths during that life span) an "average woman" would spend 7.0 years as single (6.8 of these years would fall within the age span of 10-19 years) and 29.3 years in marriage (first marriage and re-marriage) which

is the period of marital childbearing. The remaining 3.7 years are accounted for by marital breakdowns, widowhood or divorce. The period of the life span spent as married is also reduced by premature deaths. Taking the 1976 levels of mortality, the losses of the potential childbearing period reach about 2.6 years, or almost 9% of the total effective reproductive life span. In summary, the total effective reproductive life span of the "average woman" is about 26.7 years or 320 months.

How many children may result from such an average marriage pattern? The average interval between live births is in rural Bangladesh 31-34 months. It may thus be expected that a fecund married woman of above average fertility would experience between nine and ten full-term pregnancies in the course of her married life. This purely theoretical result is supported by the empirical findings from Matlab. Currently married women aged 40 years and more who delivered a live birth in 1976 had experienced, on the average, eight previous pregnancies carried to term.

From the life cycle of the "average" rural woman in Bangladesh, it appears that throughout most of her married life she is either pregnant or nursing. Volitional and deliberate regulation of fertility was rare.

The implications of this study are that (1) early marriage is universal in Bangladesh; (2) consequent long duration of marital life contributes to high fertility; (3) fertility regulation within marriage is primarily through non-volitional factors (such as lactational amenorrhea); (4) substantial fertility decline in Bangladesh will require both an increase in the age of marriage and an increase in contraception within marriage.

3. An anthropological approach to sex socialization and philosophies of life in relation to fertility behavior.

In this study, a population consisting of about 200 children between five and thirteen years old and 54 once-married adults in the reproductive age have participated in individual in-depth history interviews. The objective of the study is to generate knowledge on factors in sex socialization from childhood through the reproductive period of life, and the philosophical factors about sexuality and fertility. Sex socialization is defined as the

process by which individuals acquire the knowledge, skills and dispositions that enable them to participate in gender roles and behavior leading to fertility. Since socialization is a life-time process the most important time for socialization is the period of childhood. Therefore, this anthropological study involved interviewing children as well as adults.

The areas of inquiry include learning of gender roles, sources of sex information and its method of communication, the contribution of exposure to sex in the formation of individual philosophies and, in the case of adult respondents, the psychological reasons for making a choice of larger or smaller families. During the past year, the in-depth interviews were completed and the individual responses on various topics are being systematically collated for analysis.

It is anticipated that the results of this investigation will provide basic information on behavior and philosophies about reproduction and family growth. These issues are central to the family and institution of enduring importance in every society. On a more practical side, this investigation is expected to provide basic research data on sex socialization which may be helpful in formulating a suitable sex education program for rural Bangladeshis. Many countries are beginning to promote sex education, not necessarily to reduce fertility, but rather to promote conjugal and parental responsibility,to increase life expectancy of children and in an indirect way to promote national integrity.

4. Traditional contraceptive practice, and abstinence among village women.

In August 1978, a survey on reproductive and sexual behavior and practices was carried out in 22 villages in the Matlab area. A total of 2,340 women participated in the survey and provided detailed information on reproductive behavior particularly regarding sexual practices, breast feeding and contraception. The design and analysis of this project was carried out by CRL investigators in collaboration with the Department of Demography of Australia National University.

Because the survey involved sensitive information, there was careful selection and training of the interviewers and pre-testing of the questionnaire. Further,written

consent was obtained from all women who were willing to participate in the study. The survey could only cover 69% of the total married and eligible women and thus, may not be entirely representative. In particular, it is likely that the more conservative women may have been missed. This limitation notwithstanding, the study was deemed important first, because basic information on sexual behavior is very scanty in general in rural Bangladesh; and second because this survey which was conducted as a part of the comprehensive contraceptive and health services project could provide information that would guide the program effort.

Among questions of particular interest were the practice of abstinence as a traditional means of contraception. This proved to be very infrequent among the 2,340 women.Only 177 (7.6%) stated they refrained from having sexual relations to prevent pregnancy. Among this group however, their efforts could not be expected to be highly successful as 47.2% avoided intercourse during the week before and after a menstrual period. Only 28.6% avoided intercourse at the most effective time - 10 to 15 days after the period.

When asked in general about times to avoid intercourse, the majority of women claimed to avoid sex on more than one occasion in the year. Generally, however, this was related to phases of the moon. Postpartum abstinence was commonly practiced but averaged only about 45 days and would have no effect on fertility since this overlaps with postpartum amenorrhea.

With reference to terminal abstinence, this was rarely practiced to cease childbearing. Ninety-four percent of the women simply indicated that terminal abstinence should occur at old age, 5.8% at menopause, and only 1.26% felt that terminal abstinence should be practiced when a woman becomes a grandmother.

The study indicates that traditional methods of fertility control,particularly abstinence,are very uncommon among rural women. These results should not be equated however, with a lack of desire to terminate childbearing, since among this same population of women more than 30% were found to be using a modern contraceptive method within 12 months after the comprehensive contraceptive and health services program was introduced in the locality.

5. Endocrine factors in relation to reproduction.

As human reproduction is a complex multifactorial process involving physiological and endocrinological factors as well as social and behavioral factors, the CRL has taken the initiative to develop the laboratory capability and basic techniques that will be practical in evaluating the contribution of endocrine factors to reproductive patterns in the population. This line of investigation is being carried out in close collaboration with the Population Division of the Ministry of Health and the Bangladesh Fertility Research Program with the view that the capabilities developed will be utilized to strengthen and augment the national research program in these areas.

The first phase of this research was to establish a laboratory capability in the determination of steroid hormones and related compounds. The hormones of interest initially are estradiol, estriol, progesterone and testosterone. The reagents and instrumentation have been obtained and standard assays have been established. The innovation in this research is to attempt to use saliva rather than blood to study changes in these steroid hormones. The purpose is to circumvent the problems of obtaining blood samples from rural Bangladeshi women for research on these topics. A simple procedure for obtaining whole saliva has been developed by having women chew an inert material. Once the methods are standardized using saliva specimens field investigations will be conducted to determine the normal level of these compounds in saliva of Bangladeshi women throughout the menstrual cycle, and in pregnancy and lactation amenorrhea. Subsequently, the studies will be extended to women on hormonal contraceptives. In conjunction with these investigations, a study is being conducted to assess the reliability of changes in character of the vaginal mucous as an indicator of ovulation in rural Bangladeshi women. The testing of the physical characteristics of the vaginal mucous (slippery at ovulation versus sticky at other times) by the women themselves has been proposed as a means of increasing the reliability of the rhythm method of contraception and in fact is being tested by some private projects in Bangladeshi women.

6. Fertility control services.

a. Simple household distribution of pills and condoms.

In late 1975 the CRL initiated a simplified fertility control project. This involved the free distribution of oral contraceptives and condoms on a house-to-house basis to half the population (130,000) in the Matlab demographic surveillance area by the CRL field staff. The remaining half of the population (which was served by the usual government family planning program) was kept as a control area. In order to evaluate the impact of this project, contraceptive acceptance and prevalence of contraceptive use was assessed by regular cross-sectional sample surveys. In addition, the independently functioning vital registration system monitored changes in fertility.

Figure 8 summarizes the results of this project. This indicates that the house-to-house distribution campaign carried out in October through December, 1975 was effective in recruiting almost 25% of the eligible women as contraceptive acceptors. Subsequent to this, however, in the maintenance phase where supplies were made available by relatively untrained village women serving as depot holders, the new acceptance rate declined to very low levels. The figure also illustrates that this inundation campaign did result (after a nine-month lag) in an immediate measurable decline in the birth rate. This is simply illustrated in the figure by comparing the pattern of births in the distribution with the control area in the 18-month periods prior to and after the program is expected to have an affect. By calculating the difference in births in the distribution versus the control area, it can be estimated that the overall net reduction in fertility in the distribution area over the 18-month period following the program was approximately 10.5%. The figure illustrates, however, that most of the program effect has occurred in the early months; the net effect on fertility seems to be approaching zero after fifteen months. This pattern of effect is consistent with the fact that most of the acceptors were recruited very early in the program and as the program continued very few additional women were added.

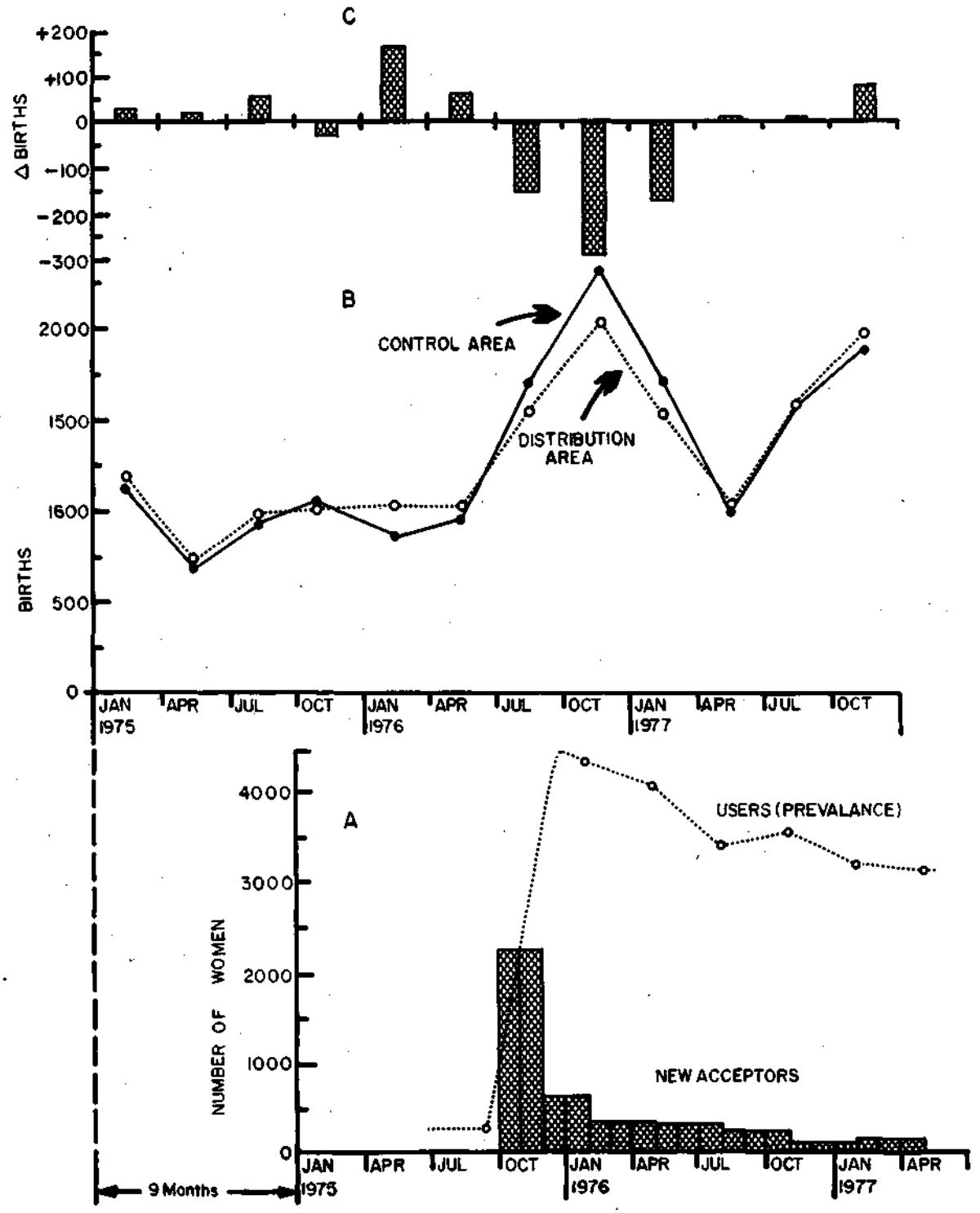


FIGURE 8. Household contraceptive distribution project. A. Pattern of acceptance and use of pills and condoms. B. Trends in births for distribution and control area by 3 month periods. C. Net difference in births (control area - distribution area).

b. The comprehensive family planning and health services project.

As a result of the experience with the simple household contraceptive distribution project, a decision was made in mid 1977 to restructure the programmatic effort to offer a full range of fertility control methods to better meet the individual woman's needs. A sub-project area covering 80,000 population in the Matlab surveillance population was selected and 80 female village workers (FVW) were recruited from this locality to serve as the primary health workers. These FVWs were young married women with a minimum of eight years education. They initially were given one-month training in aspects of human reproduction, maternal and child health and fertility control technology. Subsequently in weekly sessions over the next 18 months they have been given in-service training in maternal and child nutrition, tetanus toxoid immunization and oral rehydration for diarrhea. Beginning in November, 1977, these workers offered the non-clinical contraceptives including injections of Depo Provera to women in their area. Four sub-centers, staffed by more qualified lady family planning visitors (LFPV) were set up to provide treatment for side effects, IUD insertions and menstrual regulations. At the central Matlab rural health center, staff were trained for provision for male and female sterilization.

Table 6 summarizes the level of contraceptive practice reached with this revised programmatic effort after fifteen months. Overall, 32% of the eligible women were using a contraceptive method, with the trend continuing to rise. This may be compared with a 13.4% prevalence at 15 months in the original project which was steadily declining. Not only is there a more sustained recruitment of new acceptors in the comprehensive program, but also there is a much higher rate of continued practice among those who accept the contraceptive method. As the table indicates, the provision of long acting injections and sterilization are clearly important aspects of this program. Also important, however, is the provision of a variety of services, as other data indicate that many women switch methods from time to time before determining which method best fits their individual need.

Preliminary analysis of the birth and death rates from this project area in comparison with the remaining Matlab population indicate that this effort is having a significant impact on fertility and also on neonatal

mortality from the maternal tetanus toxoid immunization program which was initiated in mid 1978. A long-term follow-up will be required to fully assess the impact of this effort.

TABLE 6

Matlab Health Services Project

Prevelance of contraceptive use by method as of January, 1979

Method	Number of users	Percent of eligible couples
Injectable	2121	16.0
Oral	550	4.1
Condom	200	1.5
IUD	136	1.0
Vaginal	102	0.8
Tubectomy	853	6.4
Vasectomy	126	0.9
Other	200	1.5
TOTAL	4288	32.2

C. Mortality.

1. Causes of death among children.

From the longitudinal demographic surveillance program in Matlab the causes of death of children under five in the period 1975 to 1977 were analyzed. The most significant causes of death were diarrheal diseases, tetanus, measles, fever and respiratory diseases. Table 7 summarizes the death rate by specific causes among infants, and children age one to four. The overall infant mortality rate was 146.3 per thousand live births, with neonatal tetanus (37.4), diarrhea (23.4), and respiratory disease (10.4), as the most significant identifiable causes. The one to four year mortality averaged 35.1 per thousand, with diarrhea (15.9), measles (4.5), fevers (2.9), and respiratory disease (1.6), accounting for most one to four year deaths.

TABLE 7

Cause specific mortality for infants under 1 year and for children ages 1-4 years

Matlab, 1975-77

Cause	Mortality rate/1000/year	
	Infants (under 1)	Children (1-4)
Diarrhea	23.4	15.9
Tetanus	37.4	0.6
Measles	3.1	4.5
Fever	7.3	2.9
Respiratory	10.4	1.6
Drowning	0.6	2.2
Skin	1.9	0.4
Other	62.2	7.0
TOTAL	146.3	35.1

Mortality trends over the past ten years show sharp temporary rises in response to the war of 1971 and the famine conditions of 1974-75, but no definitive long-term trend. Most striking was the differential mortality by sex, which is illustrated in Figure 9. This reveals that after the first month of life, female deaths exceed male deaths by 10% to 20% throughout childhood.

Given the specific identifiable causes of death, the data suggests that the delivery of a few basic immunizations (tetanus, measles, BCG and DPT vaccines) and oral hydration for diarrhea could result in a 41% reduction of infant mortality and a 33% reduction of the one to four year mortality.

2. Effects of tetanus toxoid on neonatal mortality.

The data from the Matlab vital registration program has revealed that approximately half of all infant deaths occur in the neonatal period (first month of life) with the remaining occurring over the next 11 months. Based on the villagers reports of the symptoms leading

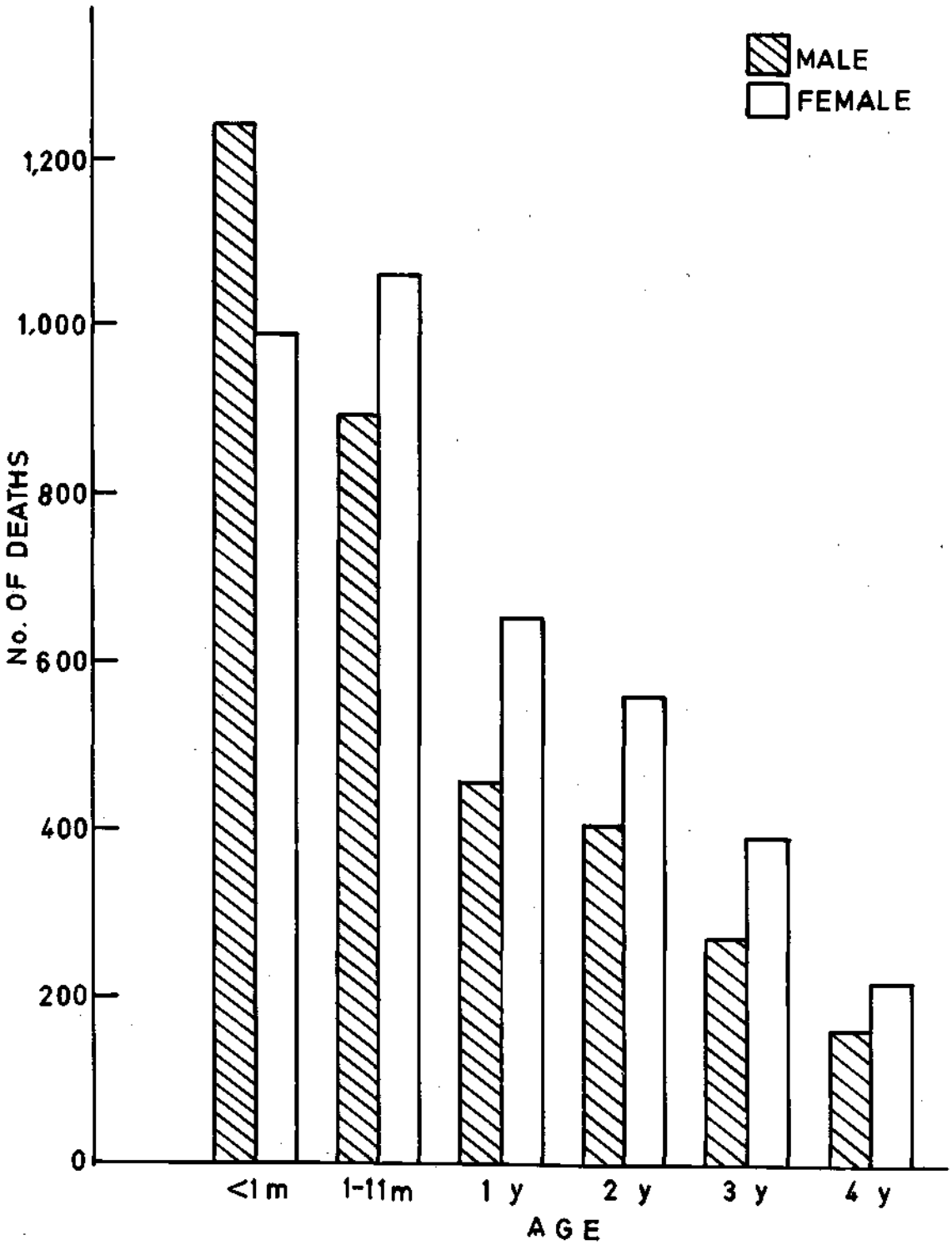


FIGURE 9. Pattern of mortality by sex in children ages 0-4 years, Matlab, 1975-77.

to death the data have indicated that approximately 40% of these neonatal deaths are probably related to neonatal tetanus. This infection is acquired by contamination of the umbilical cord of the infant at the time of delivery and usually results in death between the fifth and twenty-fifth day of life.

Studies in many parts of the world have shown that this disease can be prevented by immunizing women with tetanus toxoid during the course of pregnancy. Protection to the infant occurs through the passive transfer of maternal antibodies to the infant through the placenta.

In the 1974 cholera vaccine field trial conducted by the CRL in the Matlab area, the control vaccine was tetanus toxoid. Since participants in the trial included women and children, approximately half of the women in the Matlab population received one, or two injections of tetanus toxoid during July-August, 1974.

Because of the vital registration system in the Matlab area, it has been possible to analyze the effects of the tetanus toxoid immunization on neonatal mortality rates to determine if it provided against neonatal tetanus. This is of some special interest because in the vaccine field trial pregnant women were specifically excluded as participants to avoid the possibility of any untoward reaction on the fetus by the new cholera vaccine. This selection of participants for the tetanus toxoid injection was therefore quite different than what is ordinarily recommended to prevent neonatal tetanus in a population.

Table 8 summarizes the neonatal mortality experience in women having received cholera vaccine as compared to those receiving one or two injections of tetanus toxoid. Data is shown for two time periods: one year and two years following the vaccine program. In both years there is a significant reduction in neonatal mortality among mothers receiving two injections of tetanus toxoid. The average reduction in neonatal mortality rate is about 34%. One injection of tetanus toxoid seems to have an affect in the first year, which seems to have disappeared in the second year.

These data are consistent with the clinical assumption that a high proportion of neonatal deaths in this population are in fact due to neonatal tetanus. Further, the data confirm the major beneficial effects that can be expected from a national maternal immunization program with tetanus toxoid.

TABLE 8

Neonatal mortality rate by vaccine status of Mothers who participated in the 1974 Cholera vaccine field trial[a]

	Cholera Toxoid	Tetanus Toxoid	
		One injection	Two injections
Birth Cohort	Rate/1000	Rate/1000	Rate/1000
April 1975-March 1976	68.4 (1652)[b]	35.6 (534)	44.1 (1044)
April 1976-March 1977	54.5 (2734)	49.4 (729)	37.5 (1946)
TOTAL	59.7 (4386)	43.5(1263)	39.8 (2990)

a Injections given in July-August 1974
b Number of births given in parentheses

TRAINING AND EXTENSION

I. RESEARCH TRAINING

A. International Trainee.

Mr. Richard R. Daniel was awarded a three year pre-doctoral research training scholarship by the Wellcome Trust. The award provided for Mr. Daniel to study at the University of Surrey in the United Kingdom and the Cholera Research Laboratory in Bangladesh, the second year of his study being undertaken in Bangladesh. Mr. Daniel was at the Cholera Research Laboratory from January to December, 1978 undertaking studies on "A taxonomic and environmental study of pathogenic non-cholera vibrios in Dacca and Guildford" and was working in the Microbiology Laboratory. Mr. Richard R. Daniel has completed his research at the Cholera Research Laboratory and is now back in England writing-up his thesis.

B. National Trainees.

1. National Council of Science and Technology Fellow.

CRL provided a one-year research training for National Council of Science and Technology Fellow, Mrs. Khaleda Begum, in the area of Microbiology. The following is a summary of Mrs. Begun's studies: "The total bacterial flora was enumerated in different age groups of people reporting to our hospital with moderate to severe dehydration. This group was compared with bacterial flora present in the comparable group of normal population and the difference enumerated. The pathogenic strains have been characterized and the E. coli tested for ST and/or LT and sensitivity of these to different antibiotics tested."

2. CRL Training Fellowships.

The Training Working Group decided, in February, 1978, that six CRL fellowships should be advertised in the following areas:

Nutrition	-	2 Fellowships
Clinical Epidemiology	-	2 Fellowships
Clinical Research	-	1 Fellowship
Microbiology	-	1 Fellowship

As at December, 1978, three of the above fellowships had been filled and the fellows had commenced working. The other three fellowships are expected to be filled early in 1979. Several of these fellows are expected to work towards M.Phil. degrees at the Dacca University. Details of those fellowships already taken-up are as follows:

a. Mr. Zahid Muzaffar joined CRL in October, 1978 to take up his fellowship in Nutrition. Mr. Muzaffar is working in the laboratory setting up different biochemical tests and also developing the protocol for his M. Phil degree: His work is being supervised by Dr. Ayesha Molla.

b. The second Nutrition fellowship was taken up by Dr. Md. Shafiqul Alam Sarkar in November, 1978. Dr. Sarkar is working under the supervision of Dr. A.M. Molla and is involved in research protocol on Food Absorption in Diarrheal Diseases.

c. Dr. Md. Momtaz Hossain joined in October, 1978 to take up his fellowship in Clinical Research. Dr. Hossain is working under the supervision of Dr. A.M. Molla and is involved in the research protocol on Rice Starch-Electrolyte Oral Solution.

II. TECHNICAL AND APPLIED TRAINING.

The CRL conducted a number of special courses on technical topics. Generally these courses involved practical experience with clinical or laboratory procedures. A summary of these courses is given below:

A. International Trainees.

1. Post Doctoral Trainees.

a. WHO sponsored Dr. Ahmed Imam Taha, Under-Secretary of State, Government of the Arab Republic of Egypt, on a four-week training course at the Cholera Research Laboratory. The course was from 5 February to 4 March, 1978. Dr. Taha also visited other medical institutions in Dacca as well as visiting Matlab and Chandpur.

b. Dr. Ilyas and Dr. Krisnomurti, Physician Microbiologists from the University of Gadjah Mada, Yogyakarta, Indonesia visited the Laboratory for training in different microbiological aspects of diarrheal diseases from 21 November to 15 December, 1978. The training included collection of clinical samples both from hospital and field, identification and characterization of known pathogens like salmonella, shigella, V. Cholerae, identification of enteropathogenic and enterotoxigenic E. coli, production of toxin and assay of stable toxin by infant mouse assay and labile toxin of CHO cell assay, detection of rotavirus antigen by ELISA assay from stool or rectal swab collected from patients and also microtitre assay method for vibriocidal titre in blood. They also worked on the determination of antibiotic levels in the blood in antibiotic treated patients. During this period they also took field trips to the villages under study at Matlab and visited some hospitals at Dacca.

2. Predoctoral Trainees.

a. Two medical students came to CRL at the beginning of 1978 as part of their medical electives. Both students stayed eight weeks. Mr. William MacAlpine was from the University of Dundee, Scotland and during his time at CRL he helped with the cholera vaccine trial. Mr. R.P. Cochran arrived on 30 January, 1978 from Georgia, U.S.A. While he was here, Mr. Cochran spent his time learning how to treat diarrhea and worked in clinical studies and on data analysis.

b. The Presbyterian Fellowship in Bangladesh sent two of their medical students for training at CRL. Dr. Wayne Thorpe spent four weeks here in April, 1978 and Mr. Murray Lumpkin, from Bowman Gray School of Medicine, U.S.A. was here for two weeks in November, 1978. During their time here, the students had general training in nutrition, diarrheal management and other infectious diseases.

c. Mr. Bruce Duncan from Johns Hopkins Medical School, Baltimore, U.S.A. underwent a ten-week study tour at CRL, beginning 11 June, 1978. Mr. Duncan worked on a project, arranged for him by CRL, involving an epidemiologic study related to family planning in Bangladesh Ministry of Health.

d. Dr. S. Shrimodori and two medical students from Kyushu University, Japan trained at CRL from 18 to 27 August, 1978. They cameby aid of the International Medical Foundation of Japan. During their stay here they studied the bacteriological and clinical diagnosis of diarrhea, including cholera. They were also interested in other tropical diseases and visited the Institute of Post-Graduate Medicine & Research, the Infectious Diseases Hospital and Shishu Hospital.

e. In September, 1978 Mr. Hoyle, a medical student from U.S.A. spent two days in the Dacca Treatment Centre and then went to Matlab to gain experience and assist in clinical management of cholera patients during an epidemic.

B. National Trainees.

1. Rural Health Center Medical Officers.

In collaboration with the Government of the People's Republic of Bangladesh Directorate of Health Services (Preventive), a systematic training program was started in late 1978 for the Rural Health Centre doctors in Bangladesh. Each week about 10 doctors are delegated by the Government to come to the CRL Dacca for a 5-day course. The physicians are given lectures on causative agents for diarrheal diseases, diarrheal disease pathophysiology, the method of training of paramedics at the Thana level, bacteriology of cholera, E. coli, and other diarrheas, clinical aspects, management and complications of diarrheal diseases, principles of IV and oral therapy, salmonellosis and shigellosis, paediatric diarrhea, oral rehydration, epidemiology, parasitology, and protozoal diseases. Case presentations are given in the Treatment Centre. About half the time is spent in the practical aspects of diarrheal disease management. Over a one-year period 500 doctors will be trained. They will subsequently be participating in the National Oral Rehydration Program and they shall serve as trainers in the Thana level training of the paramedics and other health workers in the Thana.

2. Short term training courses.

Aside from the training of the physicians, training has been provided, usually for shorter duration, in

quite a number of areas, on request from other organizations in Bangladesh. The following is a list of the areas of training, the number of trainees, the requesting institutions and duration of the courses.

a. Paramedical Training in Treatment of Cholera

Radda Barnen	- 41 Trainees	5 Courses	½ day each	
School of Nursing	- 46 "	1 "	1 "	"
Presbyterian Church U.S. - Tongi Clinic	- 2 "	2 "	2 "	"
Aeromedical Inst. & Central Med. Board (Stds. & Instructors)	- 34 "	2 "	1 "	"
Family Plng. Trng. Inst. Fmly. Welfare Vstors. Azimpur & Comilla	- 94 "	8 "	1 "	"
Para-Med. Inst. Sanitary Insp. Trnees.	- 22 "	1 "	2 "	"

b. Laboratory Technicians Course

Para-Medical Institute	- 26 Trainees	3 Courses	15 days each
Para-Medical Institute	- 24 "	6 "	10 " "
Para-Medical Institute	- 24 "	6 "	20 " "

c. Clinical Pathology

Para-Medical Institute	- 1 Trainee	1 Course	2 months on
Children's Unit	- 1 "	1 "	4 days only

d. Electro Medical Equipment Maintenance Repair

UNICEF/TEMO	- 22 Trainees	2 Courses	4 wks.each

e. Library Administration & Organization

BRAC - 1 Trainee 1 Course 8 days only

f. Microbiological Analysis of Water

Pfizer Laboratories - 1 Trainee 1 Course 5 days only

g. Applied Nutrition & Dietetics

Institute of Nutrition & Food Science - 8 Trainees 1 Course 1 day only

h. Clinical Aspects of Diarrheal Diseases at Matlab

IPGM - 6 Trainees 1 Course 1 day only

i. Field Visit to Teknaf

IPGM - 5 Trainees 1 Course 1 day only

III. CRL STAFF DEVELOPMENT

The following CRL employees received special training under CRL sponsorship:

A. International training.

1. Mr. A.K.M.A. Chowdhury, Head, Statistics Branch was sent to Johns Hopkins University, U.S.A. to study for a Doctor of Science in Demography for twelve months. He left in April, 1978. Mr. Chowdhury is expected to complete the requirements for his Ph.D. degree before the end of 1979.

2. Susan Fuller Alamgir, Head Librarian CRL was supported in the U.S.A. in January, 1978 for courses on Library System Analysis and Contemporary Management Theory for six weeks.

3. Dr. Abu Taher, Physician, CRL was sent to the United Kingdom for a twelve months course on Gastroenterology in April, 1978.

4. In September, 1978, Mrs. Saleha Begum, Coding Assistant, went to the United States and is taking some courses on programming.

5. Dr. Malik Mehdi Kabir, Physician, went to the United States in September, 1978 and attended courses, for one quarter, at the Johns Hopkins University.

6. In October, 1978, Dr. Tapan Kumar Chakraborty, Physician, went to the United Kingdom for one year. He is planning to complete a D.C.H. course.

7. Mr. Akbar Ali, Branch Head, Biochemistry went to the United Kingdom in October, 1978 to commence training under a British Technical Cooperation Training Program. The training is for one year.

B. National Training.

1. Rajshahi University - CRL Collaborative Training: Mr. K.M.A. Aziz, Investigator, is continuing research work on "Sex Socialization and Philosophies of Life to Fertility Behaviour - An anthropological approach" for submitting a thesis to the Institute of Bangladesh Studies, Rajshahi University leading to a Ph.D. degree. Mr. Aziz is expected to complete his requirement for Ph.D. degree by June 1980.

2. Mr. M.A. Kashem Sahikh, Senior Statistical Assistant, Mr. Md. Shafiqul Islam, Senior Community Studies Assistant, and Mr. Mizanur Rahman, Statistical Assistant, attended a course on "Population Research & Evaluation" in ISRT, Dacca University. The course was held during May, June and November, 1978.

3. Mr. Md. Abdul Jabbar, Special Assistant attended a six-month English language course at the YMCA, Dacca from July, 1978.

4. From July, 1978, Mr. Md. Shamsul Islam Khan, Acting Head Librarian, attended a nine-month course for a Diploma in Personnel Management at BMDC, Dacca.

5. A one-day orientation course on Logistic & Supply System for Voluntary Organizations, held by the Directorate of Population Control and Family Planning, Dacca in September, 1978 was attended by Mr. Aurangzeb Md. Alamgir, Special Assistant.

6. From October, 1978, Mr. Mahbubur Rahman, Administrative Assistant, attended a six-week training course on accounting organized by RAPPORT Bangladesh Ltd.

7. A ten months secretarial science course, which began in December, 1978, is being attended by Mr. Meer Md. Ramzan Ali.

8. A two weeks course entitled FORTRAN programming language was attended by Mr. M. A. Kashem Sahikh, Senior Statistical Assistant in May/June, 1978.

C. Inservice Training

1. A group of nine CRL staff attended a training program entitled "Multiple Regression Analysis" in December, 1977. The course was for five days.

2. Miss Sajida Begum received two-months' training in the CRL Clinical Pathology Laboratory beginning September, 1978.

IV. EXTENSION ACTIVITIES

A. National

1. Epidemic Aid, Chandpur

During the outbreak of a cholera epidemic in Chandpur Sub-Division in September-October, 1977, and subsequently in several other places in Bangladesh, 41 physicians and 55 advanced medical students were given 14 courses, of 3 days' each, in the establishment of rehydration centers and the treatment of cholera. Immediately after the training these physicians and students were all involved in handling of the epidemics on their own in several Bangladesh rural areas.

2. Medical Aid, Burmese Refugees

In May, 1978, the CRL at the request of the Government of Bangladesh provided medical assistance to the Burmese refugees located in camps in the Teknaf area. The program involved establishing of a diarrhea treatment center in the Leda camp where approximately 20,000 refugees were located. Initially, the treatment facility

was operated by CRL staff but within a few weeks refugees were trained to provide part of the management under the direct supervision of a CRL para-medical worker. Within the first two months of operation, 14,000 cases were treated by the treatment center. In addition to therapy the CRL maintained bacteriological surveillance of the cases and the environment and provided guidance to the Government on environmental sanitation and epidemic control.

B. International

Epidemic Aid, Maldives

Cholera struck Maldive in April, 1978. At the request of the Government of Maldive, a medical team consisting of two physicians, a nurse and microbiologist went to the islands. Members of the team remained in the Maldives approximately 4 weeks. The medical team assisted in streamlining the treatment of cholera and other diarrheal diseases in the newly organized diarrhea ward that had been established. Additionally they provided training to the local staff on various aspects of the clinical diagnosis and management of cholera and other diarrheas. The microbiologist provided guidance and assistance in the laboratory diagnosis of cholera in support of the epidemiological control programs.

INTERNATIONAL SCIENTIFIC REVIEW MEETING

An International Scientific Review Meeting was held in Dacca, Bangladesh, from February 6 through 14 to review the scientific activities and competence of the Cholera Research Laboratory and make recommendations for the future. The names of the twenty-six scientists who participated at this meeting are listed below:

Dr. D. Barua,
Medical Officer, Bacterial & Venereal Infections, WHO, Geneva, Switzerland.

Dr. Philip S. Brachman,
Director, Bureau of Epidemiology, Centre for Disease Control, Atlanta, Georgia, USA.

Dr. David Bradley,
Director, Ross Institute of Tropical Hygiene, London, UK.

Dr. Charles Carpenter,
Professor, Department of Medicine, School of Medicine, Case Western Reserve University, Cleveland, Ohio, USA.

Dr. Philip Corfman,
Director, Centre for Population Research, National Institute of Child Health & Human Development, NIH, Bethesda, Maryland, USA.

Dr. A.T. Shafiq Ahmed Chowdhury,
Companiganj Health Project, Noakhali, Bangladesh.

Dr. H.M. El Bermawy,
Deputy Director General, Research & Development, Department of Health Services, Ministry of Health, Cairo, Egypt.

Dr. Sultan Hashmi,
Director, Pakistan Institute of Development Economics, Islamabad, Pakistan.

Dr. Jan Holmgren,
Associate Professor, Department of Medical Microbiology, University of Göteborg, Gulhedsgaten, Sweden.

Dr. Monowar Hossain,
Chairman, Bangladesh Institute of Development Studies, Dacca, Bangladesh.

Dr. A.M. Mostaqul Huq,
Director of Health Services (Preventive), Government of Bangladesh, Dacca, Bangladesh.

Dr. Zakir Hussain,
Chief, Health & Population Control, Planning Commission, Government of Bangladesh, Dacca, Bangladesh.

Dr. George Immerwahr,
Consultant, Demographic Institute of the University of Sri Lanka, Colombo, Sri Lanka.

Professor Nurul Islam,
Director, Institute of Post-Graduate Medicine, Dacca, Bangladesh.

Dr. Atiqur Rahman Khan,
Director, Bangladesh Fertility Research Program, Dacca, Bangladesh.

Dr. Harding Le Riche,
Professor of Epidemiology, Department of Preventive Medicine, University of Toronto, Ontario, Canada.

Dr. F. James Levinson,
Chief, Food & Nutrition Division, U.S. Agency for International Development, Dacca, Bangladesh.

Dr. Donald Mackay,
Deputy Director, Ross Institute of Tropical Hygiene, London, UK.

Dr. L.J. Mata,
Director, Institutio de Investigaciones en Salud (INISA), University of Costa Rica, San Jose, Costa Rica.

Dr. Peter M. Moodie,
Deputy Director, Department of Tropical Medicine, School of Public Health & Tropical Medicine, University of Sydney, Australia.

Dr. Aung Myat,
Epidemiologist, WHO, Dacca, Bangladesh.

Dr. O. Ogunbi,
Professor, Department of Microbiology, Lagos University, Lagos, Nigeria.

Dr. Vinodini Reddy,
Director, Clinical Research, National Institute of Nutrition, Hyderabad, India.

Dr. L.T. Ruzicka,
Senior Fellow, Department of Demography, Research School of Social Sciences, Australian National University, ACT, Australia.

Dr. Julie Sulianti Saroso,
Head, National Institute of Health Research & Development, Ministry of Health, Jakarta, Indonesia. (Chairman)

Dr. A. Zahra,
Director, Division of Communicable Diseases, WHO, Geneva, Switzerland.

The following is a summary of the major recommendations:

1. The meeting recommends the internationalization of the CRL and the new institution be called the International Center for Diarrheal Disease Research (ICDDR). This recommendation is made in recognition of the fact that diarrheal diseases constitute a major world health problem and there is a need for an international institution which addresses this problem.

2. The principal objective of the International Center would be governed by a concern for improving health of the community. The preoccupation with diarrheal disease prevention and control implies the necessity to identify determinants of diarrheal disease distribution in the community, besides undertaking clinical and laboratory research, and should also include the development of appropriate technologies of intervention for prevention and control and their testing in community situations.

3. Another important objective of the Center would be to provide training to Bangladeshi and other nationals in the areas of its activities and competence in collaboration with national, regional and international organizations.

4. It is important that the Center's research agenda be problem-orientated and address problems of priority and does so in a manner that is most likely to develop applicable interventions with reasonable prospect of success. This could be achieved by designing studies with the involvement of health service implementors. Furthermore, to ensure this orientation on a continuing basis, the meeting advises that individuals known for their social responsibilities and concerns be included on the scientific review committees and co-ordinating committees.

5. The meeting agreed that research in diarrheal diseases, in the broadest sense, should be of paramount importance in the proposed International Center. Past and current work in this area has been outstanding in regard to scientific quality and applicability to health problems in Bangladesh and other developing countries. Current and proposed research programs in this area offer the prospect of defining the etiology, pathophysiology and treatment of virtually all acute diarrheal illnesses. The results of such research will be directly applicable to a major health problem in Bangladesh and in other developing countries.

6. The meeting favours biological and demographic population studies at the Center provided they are relevant to diarrheal diseases and related health problems. The meeting recognizes the demographic data now available and yet to be collected are unique. A great deal of information of both practical and theoretical importance is available from this source and the meeting endorses continuation of this activity. It recommends that more social data be gathered and that the data be made available to other institutions in Bangladesh and in other countries, to permit full utilization of this unique resource.

7. The meeting recommends that the International Center address itself to the study of diarrheal diseases as they relate to food and nutrition. Relevant factors include food availability and food consumption at the household level, food utilization and the nutritional status. Studies should also examine the reduction of nutrient energy intake associated with diarrhea and, for instance, the economic and/or productivity effects of temporary disability due to diarrheal disease. Also, the effect of diarrhea on food utilization, nutrient loss, nutrient diversion, or nutrient wastage deserves investigation.

8. The meeting generally agreed that the results of scientific research should be developed to the point that they could be used by health professionals and by the public. At the point where interventions become practical and applicable, a strong effort should be made to help local agencies to use such information effectively. The Center should aim to produce effective interventions together with a methodology for their introduction, evaluation, and incorporation into the local health care service.

9. In establishing the Center there are several special considerations such as the possibility of the Center drawing away local talent from national centers. This may be guarded against by the development of positive and mutually collaborative partnerships between the Center and local institutions so that a spirit of complementarity prevails and local initiatives and capabilities are facilitated by the Center's presence. There are several ways by which these complementary relationships may be established, some of these are: full exchange of information, secondment of research and teaching staff, joint research undertakings, contractual research by national institutions, sharing of equipment, facilities and personnel. In addition, a joint committee representing the Center and local institutions for program co-ordination in Bangladesh could continuously monitor the program and projects and recommend necessary adjustments and suggest specific collaborative arrangements.

INTERNATIONALIZATION OF THE CHOLERA RESEARCH LABORATORY

The process of transforming the Cholera Research Laboratory into the International Centre for Diarrhoeal Disease Research, Bangladesh, began in 1976 with initiatives taken by the Directing Council and Dr. Willard Verwey, Director of CRL. These were followed by formal considerations by the governments of Bangladesh and the United States of America, which ultimately led to the two governments signing an amendment to the CRL Project Agreement on July 15, 1977 which authorized the CRL to "take appropriate actions....pertaining to the conversion of the laboratory from its present status to an independent international non-profit institution within Bangladesh governed by an international Board of Trustees." Concurrent with this action, the Ministry of Health and Population Control of the Government of Bangladesh established a Sub-committee on Internationalization which began work on a draft Charter for the new institution.

During Fiscal Year 1978 the following steps were taken:

October 1977—A "Draft Prospectus" for the proposed International Centre was prepared by the CRL and circulated to the international community.

December 6-8, 1977—An Informal Meeting relating to the development of an International Centre for health research from the Cholera Research Laboratory was organized by the External Resources Division, Ministry of Planning, Government of Bangladesh, at the request of the Sub-committee on Internationalization. Participating in this meeting were representatives from the following governments and agencies: Australia, Bangladesh, Netherlands, Norway, United Kingdom, United States of America, Sweden, Ford Foundation, International Development Research Center (Canada), National Institutes of Health (U.S.A.), United Nations Development Programme, United Nations Fund for Population Activities, UNICEF, World Health Organization and World Bank. The major recommendation of the meeting was that an Interim International Committee (IIC) be established which would be convened and chaired by the United Nations Development Programme to coordinate the final steps leading to the establishment of the International Centre.

February 6-14, 1978—An International Scientific Review Meeting was convened in Dacca, Bangladesh to review the scientific activities and competence of the Cholera Research Laboratory and make recommendations for the future. (The list of participants and Summary Report of this committee are given elsewhere.)

February 17 - September 22, 1978—Eleven meetings of the Interim International Committee were convened in Dacca under the chairmanship of Mr. Bernard Zagorin, Resident Representative, UNDP, Dacca, Participating in these meetings were representatives from the following governments and organizations: Australia, Bangladesh, United Kingdom, United States of America, World Health Organization, United Nations Fund for Population Activities, UNICEF, World Bank, International Development Research Centre, Ford Foundation. The IIC developed the final draft Ordinance relating to the ICDDR,B and also defined the terms of reference for a plenary IIC meeting to be held in Geneva.

The following steps were taken in the transition period at the close of FY 1978:

October 1978—A "Five-Year Program Proposal" for the International Centre for Diarrhoeal Disease Research, Bangladesh was prepared by the CRL on the basis of the recommendations of the International Scientific Review meeting and the Interim International Committee. This was circulated to the international community in preparation for the plenary IIC meeting.

December 6, 1978—The President of the People's Republic of Bangladesh signed the Ordinance establishing the International Centre for Diarrhoeal Disease Research, Bangladesh.

February 13-14, 1979—The plenary meeting of the Interim International Committee was convened in Geneva at the Headquarters of the World Health Organization under the Chairmanship of Mr. William T. Mashler, Senior Director, Division of Global and Interregional Projects, UNDP. Representatives from twenty-five countries and international organizations participated in this meeting. The committee accepted a Memorandum of Understanding which was signed by sixteen countries and organizations and elected eleven at-large members to the first Board of Trustees.

The Memorandum of Understanding and new Trustees follow:

I. TEXT OF MEMORANDUM OF UNDERSTANDING RELATING TO INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH.

Preamble

The acute diarrhoeal diseases are one of the leading causes of sickness and death in less developed countries. In many regions they are, in fact, the leading cause of sickness and death. In rural areas they may account for as many as half the deaths of children in the first five years of life and may be the cause of as much as one-third of all deaths in the general population. In the developing countries they are a major cause of human suffering and economic loss.

Experience has repeatedly shown that major health problems cannot be solved by a narrowly focused effort or in institutions remote from the setting where the problems exist. The diarrhoeal diseases have close biological and socio-economic links to the problems of malnutrition and high fertility which also are of major importance to less developed countries. Further, these entities share many of the same social and economic causal factors and interact to reinforce each other. This being the case, the solutions to the problem of diarrhoeal diseases require consideration of nutrition and reproduction, and an integrated research effort should be carried out in locations where the problems can be explored in their full context.

The Centre

In consultation with other interested governments and organizations, the Government of Bangladesh has taken an initiative toward approaching these problems on an international scale: it has promulgated the International Centre for Diarrhoeal Disease Research, Bangladesh Ordinance 1978 for the establishment of said Centre. The purpose of the Centre will be:

a) To undertake and promote study, research and dissemination of knowledge in diarrhoeal diseases and directly related subjects of nutrition and fertility with a view to developing improved methods of health care

and means for the prevention and control of diarrhoeal diseases and for the improvement of public health programs with special relevance to developing countries.

b) To provide training to Bangladeshi and other nationals in areas of the Centre's competence in collaboration with national and international institutions.

The Centre will succeed to the assets, liabilities and staff of the Cholera Research Laboratory of Dacca. Among other things, it will continue work originated by the laboratory.

Organization

The Centre will be an autonomous, philanthropic, non-profit organization. An Interim International Committee has been constituted to assist in the establishment of the Centre: The Committee helped the Bangladesh Government in the formulation of the Ordinance for the establishment of the Centre; and the Committee will select some of the members of the initial Board of Trustees of the Centre. The Chairman of the Committee is the United Nations Development Programme; the initial members of the Committee were the World Health Organization (WHO) and the following governments and organizations providing resources for the work of the Cholera Research Laboratory: Australia, Bangladesh, the Ford Foundation, International Development Research Centre, United Nations Fund for Population Activities, United Nations Children's Fund, United Kingdom, and the United States of America. Under the authority provided in the Ordinance the Chairman has added to the Committee the following governments and organizations:

Colombia, Denmark, Ecuador, Egypt, Federal Republic of Germany, Indonesia, India, Kuwait, Netherlands, Philippines, Sweden, Thailand, Union of Soviet Socialist Republics, Population Council, Rockefeller Foundation.

The Board of Trustees will appoint the Director of the Centre, approve the research and other programs of

the Centre, set administrative policies and practices, authorize the annual budget and approve an annual report of activities. It will appoint and have the advice, at least once every two years, of an independent scientific review committee.

The Board is to be composed of sixteen Trustees. They shall serve in their individual capacity, and shall be persons qualified to serve by reason of scientific, research, administrative or other appropriate experience. Three will be designated by the Government of Bangladesh, one will be named by the Director-General of WHO, and the Director of the Centre will be a Trustee. The remainder of the Trustees of the initial Board will be selected by the Interim International Committee, and are to be chosen in such a way as to be broadly representative of the countries cooperating in the work of the Centre. Apart from the designee of WHO, a majority of the Trustees shall be from developing countries and not less than one-third from developed countries.

Financing

The total expenditure budget of the Centre for the first five (5) years of its operations, estimated to begin on July 1, 1979, is estimated at an amount equivalent to U.S. $27,212,000. Towards these expenditures of the Centre, certain governments and organizations, subject in some cases to legislative or other approvals intend, for the present, to provide support in the amount and manner indicated in Annex A, which is incorporated herein and made a part hereof. Other signatories hereto shall provide to the Centre such amounts as may be agreed upon with the Centre. It is envisaged that initial and later donors will provide additional sums from time to time in the light of the continuing needs of the Centre.

Participation in the Centre

With a view to embodying this common idea of ours as set forth above for the purpose of promoting the health and welfare of peoples of developing countries,

we the undersigned hereby acknowledge the establishment of the Centre as described in the Ordinance and, by signing this Memorandum of Understanding on behalf of our Governments and organizations, respectively, in the City of Geneva on the 14th day of February 1979, signify our intention to support and to cooperate in the work of the Centre.

Signed in Geneva by:

Bangladesh	Thailand
Colombia	United States of America
Ecuador	Ford Foundation
Egypt	Population Council
India	Rockefeller Foundation
Indonesia	UNDP
Kuwait	UNFPA
Philippines	WHO

II. LIST OF TRUSTEES FOR THE ICDDR,B.

Dr. A. R. A. Al-Awadi, Minister of Public Health, Kuwait

Dr. D. J. Bradley, Professor of Tropical Hygiene and Director of Institute, Ross Institute of Tropical Hygiene, London School of Hygiene and Tropical Medicine, London

Dr. C. C. J. Carpenter, Director, Department of Medicine, University Hospital of Cleveland, Cleveland, Ohio,U.S.A.

Dr. J. Holmgren, University of Göteborg, Institute of Medical Microbiology, Göteborg, Sweden

Dr. G. W. Jones, Department of Demography at Australian National University, Canberra, Australia

Professor J. Kostrzewski, Chief, Department of Epidemiology, State Institute of Hygiene, Chocimska 24, Warsaw, Poland

Professor L. J. Mata, Director, Instituto de Investigaciones en Salud (INISA) Universidad de Costa Rica, Ciudad Universitaria "Rodrigo Facio" San Pedro, Costa Rica

Dr. V. Ramalingaswami, Director, All India Institute of Medical Sciences, New Delhi, India

Dr. J. Sulianti Saroso, Advisor to Minister of Health, Jakarta, Indonesia

Dr. O. M. Solandt, Chairman, Science Council of Committee on Population and Technology, Ottawa, Canada

Dr. M. K. Were, Senior Lecturer, Department of Community Medicine, University of Nairobi, Kenya

Professor Badruddoza Chowdhury, Minister for Health and Population Control, Government of Bangladesh

Professor M. A. Matin, State Minister for Health and Population Control, Government of Bangladesh

Mr. M. K. Anwar, Secretary, Health Division, Ministry for Health and Population Control, Government of Bangladesh

Dr. Albert Zahra, Director, Division of Communicable Diseases, WHO, Geneva

STAFF OF THE CHOLERA RESEARCH LABORATORY

FY 1978

W. Henry Mosley, M.D., M.P.H.	Director
M. Mujibur Rahaman, M.B.B.S., Ph.D.	Deputy Director
K.M.S. Aziz, Ph.D.	Scientific Director
Lincoln C. Chen, M.D., M.P.H.	Scientific Director
William B. Greenough III, M.D.	Scientific Director
Mr. Md. Shahabuddin	Controller & Acting Administrator
Mr. Philip O. Weeks	Administrator
Mr. Mark P. Tucker	Physical Plant Manager

Investigators	Research Area
Brian Seaton, Ph.D.	Biochemistry
David A. Sack, M.D.	Clinical-Immunology
Trinidad S. Osteria, Sc.D.	Demography
Robert E. Black, M.D.	Epidemiology
Shushum Bhatia, M.B.B.S., M.P.H.	Maternal Child Health
Stanley R. Becker, Ph.D.	Demography
K.M.A. Aziz, M.A., M.Phil.	Anthropology
Abdul Majid Molla, M.B.B.S. Ph.D.,D.H.C.	Pediatrics-Gastroenterology
Ayesha Molla, M.Sc., Ph.D.	Biochemistry
A.S.M. Mizanur Rahman, M.B.B.S.	Health Services
A.K.M. Alauddin Chowdhury, M.Sc.	Demography
John Briscoe, Ph.D.	Sanitary Engineering
L.T. Ruzicka, Ph.D.	Demography
William M. Spira, Ph.D.	Microbiology
A.K.M. Jamiul Alam, M.B.B.S.	Clinical
Kenneth H. Brown, M.D.	Nutrition
Michael H. Merson, M.D.	Epidemiology
Colin W. McCord, M.D.	Health Services
Robert H. Gilman, M.D.	Clinical-Parasitology

Scientific Branch Heads/Program-Coordinator	
Abdullah Al-Mahmud, M.Sc.(Vet)	Animal Resources Branch
Akbar Ali, B.Sc.	Biochemistry Branch
Aporn Samad, B.Com., M.E.S.	Statistics Branch (Acting)
Md. Rafiqul Islam, M.B.B.S.	Physicians Branch (Acting)
Ansaruddin Ahmed, M.B.B.S.	Immunology Branch
Md. Imdadul Huq, M.Sc	Microbiology Branch
M.H. Munshi, M.B.B.S.	Teknaf Project (Branch)
Moslemuddin Khan, M.B.B.S., D.P.H.	Community Studies Branch
Md.Shamsul Islam Khan, M.A.	Library & Publications Branch (Acting)

(continued) Scientific Branch Heads/Program-Coordinator

Mrs. Pankajini Biswas	Dacca Hospital Branch
Mrs. Beatrice B. Shaw, M.Sc.	Health Services Coordinator

Matlab Field Station Supervisors (Scientific)

Md. Younus, M.B.B.S.	Health Services
Mr. Jyotsnamoy Chakraborty	Health Services
Mr. A. Mazid Sarder	Demographic Surveillance
Mr. M.R. Khan	Special Studies (Acting)

Matlab Field Station Supervisor (Administration)

Mr. Bejoy R. Saha, B. Com, M.B.A.	Administration

Administrative Branch Heads

Abul Kalam Azad, M.A., LL.B.	Personnel Management Br.
Mr. Rabindra Nath Majumder	Supply Management Br.
Mr. Noor Mohammad Mermalat	Transport Management Br.
Mr. M. Mujibur Rahman	General Services Br.
Mr. A. H. Chowdhury	Maintenance (Superintendent)
Mr. A. Razzak	Vehicles Maintenance Br.
Mr. M. Sobhani	Electro-Mechanical Br.
Mr. Md. Siddique	Instrument-Fabrication Br.

Consultant

Mr. M.R. Bashir	Consultant-Development
Mr. Nuran Nabi	Management Consultant

Personnel Summary

On September 30, 1978, CRL had 719 fulltime employees, including 110 temporary Female Village Workers. Of the total CRL staff, 402 are working in research areas. They may be classified as follows:

1.	Scientists (Investigators)	23
2.	Physicians	14
3.	Technicians	124
4.	Scientific Support	241
		402

The rest of the staff are Administrative and Maintenance personnel for the support of the research work. They are classified as follows:

1.	Officers	17
2.	Mid-level	75
3.	Lower-level	225
		317

CHANGES IN SENIOR STAFF IN FY 1978

Name	Position	Effective Month/Year
(1) Promotion and Redesignation		
Dr. M. Mujibur Rahaman	Deputy Director	Oct 77
Mr. A.K.M. Alauddin Chowdhury	Investigator	Jan 78
Dr. Abdullah Al-Mahmud	Chief Veterinarian & Head, Animal Resources Br.	Jan 78
Mr. Akbar Ali	Head, Biochemistry Br.	Jan 78
Dr. A.K.M. Jamiul Alam (Late)	Chief Physician	Jan 78
Dr. Md. Younus	Physician In-Charge	April 78
Mr. Makhlisur Rahman	Research Associate	April 78
Mr. A.K.M. Abdul Matin	Special Duty Officer	April 78
Mr. Bejoy R. Saha	Supervisor, Administration, MFS	April 78
Mr. Jyotsnamoy Chakraborty	Supervisor, Health Services, MFS	April 78
Mr. A. Mazid Sarder	Supervisor, Demographic Surveillance, MFS	April 78
Mr. M.R. Khan	Supervisor (Acting), Special Studies, MFS	April 78
(2) New Appointments		
Dr. Stanley R. Becker	Post-Doctoral Fellow	Jan 78
Mr. M.R. Bashir	Consultant	May 78
Mr. Nuran Nabi	Management Consultant	May 78
Dr. Abdul Majid Molla	Senior Investigator	July 78
Dr. Ayesha Molla	Investigator	July 78
Mrs. Beatrice B. Shaw	Health Services Program-Coordinator	Aug 78
(3) Departures		
Dr. John Briscoe	Sanitary Engineer	Dec 77
Dr. L.T. Ruzicka	Demographer	March 78
Dr. William M. Spira	Microbiologist	June 78
Dr. A.K.M. Jamiul Alam	Chief Physician	Expired June 78
Mr. Nuran Nabi	Management Consultant	July 78
Dr. Kenneth H. Brown	Guest Investigator (JHU)	July 78
Dr. Michael H. Merson	Epidemiologist	Aug 78
Dr. Colin W. McCord	Senior Scientist	Aug 78
Dr. Robert H. Gilman	Guest Investigator (JHU)	Aug 78
Mr. Philip O. Weeks	Special Assistant to the Director	Aug 78
(4) Leave of Absence		
Mrs. Susan Fuller Alamgir	Head, Library & Publications Br.	June 77
Mr. A.K.M. Alauddin Chowdhury	Investigator	August 78

COLLABORATING RESEARCHERS

The following are scientists who participated in collaborative research with CRL:

Scientist and Institutions	Nature of Work
Dr. Frits and Ida Orskov, WHO International Escherichia Center, Copenhaven	Serotyping strains of E. Coli
Dr. Dolores Evans, Health Science Center, Houston, Texas, U.S.A.	Antibodies to E. Coli in breast milk of Bangladeshi mothers.
Dr. Nate Pierce, Johns Hopkins University, Baltimore, Maryland	Evaluation of flourescent antibody test for antitoxin containing lymphocytes in breast milk.
Dr. Jan Holmgren, University of Gotteborg, Sweden	Participating in the protocols: "Local Immunity in Cholera"; "Clinical Trial of Chlorpromazine as a therapeutic antisecretory agent in Cholera": "Clinical Trial of Charcoal GM_1 Ganglioside in Cholera and E. Coli Enterotoxin Diarrhea".
Ann Mari Swennerholm, University of Göteborg, Sweden	Participating in the protocol: "Local Immunity in Cholera".
Dr. Robert Yolken, National Institutes of Health, Bethesda, Maryland, U.S.A.	ELISA assay for rotavirus.
Dr. A.Z. Kapkiain National Institutes of Health, Bethesda, Maryland, U.S.A.	CF assays for rotavirus in a seroepidemiology of rotavirus infection in Matlab.
Dr. Sandra Huffman, Johns Hopkins University, Baltimore, Maryland, U.S.A.	Determinants of post partum amenorrhea and menarche.

Scientist and Institution	Nature of Work
Dr. John Kantner and Dr. Zenas Sykes Johns Hopkins University, Baltimore, Maryland, U.S.A.	Computer work with DSS data involving large scale matching of files which cannot be done easily at CRL.
Dr. Bernard Rowe, Central Public Health Laboratory, Colindale, London, U.K.	Serotyping E. Coli.
Dr. John Mellor Wellcome Research Laboratories, Kent, U.K.	Cholera vaccine development
Dr. John P. Craig Downstate Medical Center, U.S.A.	Cholera vaccine development
Dr. H. Greenberg Laboratory of Infectious Diseases, National Institutes of Health, Bethesda, Maryland, U.S.A.	Parvovirus detection in rural villagers.
Dr. G. K. Morris Epidemiologic Investigations Laboratory Branch, Bureau of Epidemiology, Center for Disease Control, Atlanta, Georgia, U.S.A.	Evaluation of culture medium for V. cholera.
Dr. P. Taylor Bureau of Epidemiology, Center for Disease Control, Atlanta, Georgia, U.S.A.	Field research on E. Coli and rotaviruses.
Dr. John Caldwell and Dr. Patricia Caldwell Department of Demography, Australia National University Canberra, Australia	Studies of traditional fertility methods in Matlab.
Dr. Rita Colwell Department of Microbiology, University of Maryland Baltimore, Maryland, U.S.A.	Genetic analysis of vibrio isolates.

Scientist and Institution	Nature of Work
Dr. Atiqur Rahman Khan Population Division, Ministry of Health, Dacca, Bangladesh	Family planning research project
Dr. Kamaluddin Ahmed Professor and Director, National Nutrition Institute Dacca Univeristy, Dacca, Bangladesh	Nutrition field studies
Dr. Habibur Rahman Director, National Institute of Public Health Nutrition, Dacca, Bangladesh	Oral therapy field projects
Dr. Bradley Sack Department of Medicine Johns Hopkins University Baltimore, Maryland, U.S.A.	Cholera and E. Coli - microbiological and immunological studies.

REVIEW BOARD ON PROTECTION OF HUMAN SUBJECTS

The Cholera Research Laboratory is required by Bangladesh law to have all research and programs involving the use of humans reviewed and approved by the Bangladesh Medical Research Council. As an additional assurance that the interests of all human subjects are adequately protected, the CRL has established a Review Board on Use of Human Subjects.

The Board members individually bring special competence into the biomedical and social science fields as well as law, religion, and other areas so that they are collectively able to judge the risks and consequences of proposed projects, and ensure adequate protection of the rights and welfare of human subjects.

The Board is responsible for reviewing all research and other related activities carried on by the CRL which involves human subjects.

The Board members are listed below:

Dr. K.M.S. Aziz, B.Sc. (Honors), M.Sc., Ph.D (Duke), Scientific Director, Cholera Research Laboratory, Dacca. Laboratory, Research, Microbiology and Ecology. Contribution as basic Scientist.

Dr. M. Mujibur Rahaman, M.B.B.S., M.Sc., Ph.D (Glasgow), Scientific Director, Cholera Research Laboratory, Dacca. Clinical Research and Nutrition. Registered Medical Practitioner in Bangladesh. Contribution as a Clinician.

Dr. William B. Greenough, M.D. (Harvard), Scientific Director, Cholera Research Laboratory, Dacca. Certified by National Board of Medical Examiners, U.S.A., 1958, and American Board of Internal Medicine, 1969. State of Maryland license. Clinical Research. Contribution as a Clinician.

Dr. Kamaluddin Ahmed, M.B.B.S., Ph.D. (Glasgow), F.C.P.S., Professor of Pharmacology, Institute of Post-Graduate Medicine & Research, Dacca. Licensed to use radioactive materials on human beings. Registered Medical Practitioner in Bangladesh. Clinical Pharmacology. Contribution as a Clinician.

Mr. Mustafa Kamal, M.A. (London), Barrister-at-law. Advocate General, Bangladesn. Lawyer. Contribution as a member of the legal profession.

Mr. Maulana Md. Emdadullah, M.A., Momtazul Mohaddeseen (Madrasah Education Board), completed courses in Islamic Studies and language in Syria. Cultural Officer, Islamic Foundation, Dacca. Religion. Contribution as a religious leader.

Dr. Sufia Ahmad, M.A., Ph.D. (London), Associate Professor, Department of Islamic Hisotry & Culture, Dacca University. Lay person. Contribution as a woman and non-scientific person.

Dr. Brian Seaton, M.A., Ph.D. (Oxford), A.I.M.L.S. (Associate of the Institute of Medical Laboratory Sciences). Special Investigator, Cholera Research Laboratory, Dacca. Certified Medical Laboratory Technologist in the United Kingdom. Biochemistry, Clinical Chemistry and Reproductive Endocrinology. Contribution in the field of laboratory sciences.

DIRECTING COUNCIL

The Outline of Operations under the Project Agreement provides that the Cholera Research Laboratory shall be governed by a Directing Council appointed by the participating governments. The persons who have served on the Directing Council during FY 1978 are shown below:

	Tenure	
Government of Bangladesh	From	To
Dr. Mostaqul Huq, Director of Health Services (Preventive)	June 1974	-
Dr. Zakir Hossain, Chief, Health & Population Control	Mar. 1976	-
Dr. Abdul Quader Khan, Director, Institute of Epidemiology, Disease Control & Research (Malaria Institute)	Aug. 1975	Jan. 1978
Dr. Md. Shamsuzzoha, Director, Bangladesh Medical Research Council	Jan. 1978	-
Dr. Yousuf Ali, Professor of Medicine, Dacca Medical College	Oct. 1976	-
United States Government		
Mr. Charles R. Gurney, Chief, Health & Population Division USAID	Sept. 1977	-
Dr. F. James Levinson, Chief, Food & Nutrition Division USAID	Oct. 1977	-
British Government		
Mr. Michael C. McCulloch, First Secretary (AID), British High Commission	Mar. 1976	Aug. 1978
Mr. G.A. Williams, First Secretary (AID), British High Commission	Aug. 1978	-

FINANCIAL SUMMARY FY 1978

During the period October 1, 1977 through September 30, 1978 the CRL received cash contributions totaling U.S. $2,513,278. Including the previous years cumulative carry-over, a total fund amounting to U.S. $2,858,268 was available for FY 1978 of which U.S. $2,539,186 was expended. A breakdown of funds received by source and the amount expended is provided below:

Sources	Contribution (including carryover) U.S.$	Expenditure U.S.$	Balance U.S.$
1. United States of America:			
a) Taka fund	1,281,859	1,139,631	142,228
b) PASA account	952,740	794,589	158,151
c) CDP contract	160,278	160,278	---
2. Government of Bangladesh	56,000	54,093	1,907
3. Government of U.K.	166,000	166,000	---
4. Government of Australia	114,918	108,323	6,595
5. Ford Foundation	90,000	79,799	10,201
6. IDRC of Canada	36,473	36,473	---
	2,858,268	2,539,186	319,082

In addition to this cash contribution, the CRL received in kind support (logistics, facilities, personnel) from the Government of Bangladesh and the U.S.A., and the Ford Foundation which are estimated as follows:

	U.S.$
1. Government of Bangladesh	311,000
2. U.S.A.	144,617
3. Ford Foundation	50,000
	505,617

Including these amounts, the total operation cost for FY 1978 was U.S.$3,044,803.

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Aziz, K.M.A.: Present Trends in Medical Consultation Prior to Death in Rural Bangladesh. Bangladesh Medical Journal. Vol. 6, No. 11, October 1977, pp.53-58.

Chowdhury, A.K.M.A. Huffman, S.L. and Curlin, G.T.: Malnutrition, Menarche and Marriage in Rural Bangladesh. Social Biology. Vol. 24, No. 4, 1977, pp. 316-325.

Chowdhury, A.K.M.A. and Chen, L.C.: The Interaction of Nutrition, Infection and Mortality During Recent Food Crisis in Bangladesh. Food Research Institute Studies. Vol. 16, No. 2, 1977.

Greenough, W. B., III: Chapter on Cholera in "Current Therapy 1978". Edited by Conn. W.B. Saunders Co., Philadelphia, pp. 13-18.

Hughes, J.M., Boyce, J.M., Aleen, A.R.M.A., Wells, J.G., Rahman, A.S.M.M. and Curlin, G.T.: Vibrio Parahaemolyticus Enterocolitis in Bangladesh: Report of an Outbreak. Am. J. of Trop. Med. and Hygiene. Vol. 27, No. 1, January 1978, pp. 106-112.

Huffman, S.L., Chowdhury, A.K.M.A. and Mosley, W.H.: Postpartum Amenorrhea: How is it affected by Maternal Nutritional Status? Science. Vol. 200, June 9, 1978, pp. 1155-1157.

Huffman, S.L., Chowdhury, A.K.M.A., Chakroborty, J. and Mosley, W.H.: Nutrition and postpartum amenorrhea in rural Bangladesh. Population Studies. Vol. 32, No. 2, July 1978, pp. 251-260.

Koster, F.T., Levine, J., Walker, L., Tung, K.S.K., Gilman, R.H., Rahaman, M.M., Majid, M.A., Islam, S. and Williams, R.C.: Hemolytic-uremic Syndrome after Shigellosis Relation to Endotoxemia and Circulating Immune Complex. New England J. of Medicine. April 27, 1978, pp. 927-933.

Mosley, W.H., Osteria, T. and Huffman,S.L.: Interactions of Contraception and Breastfeedings in Developing Countries. Journal of Biosocial Sciences. Vol. 4, Supplement, 1977, pp. 93-111.

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Rahaman, M.M., and Alam, A.K.M.J.: Rose spots in Shigellosis caused by Shigella Dysenteriae Type I Infection. British Medical Journal. Vol. 2, 1977, pp. 1123-1124.

Rahaman, M.M.: The Causes and Effects of Famine in the Rural Population: A Report from Bangladesh. Ecology of Food and Nutrition. Vol. 9, 1978, p. 99-102.

Ruzicka, L.T. and Chowdhury, A.K.M.A.: Marriage and Fertility in Rural Bangladesh. International Planned Parenthood Federation Medical Bulletin. Vol. 12, No. 4, 1978, pp. 3-4.

Sack, David A., Eusof, A., Merson, M.H., Black, R.E., Chowdhury, A.K.M.A., Ali, A., Islam, S. and Brown,K.H.: Oral Hydration in Rotavirus Diarrhoea: A Double Blind Comparison of Sucrose with Glucose Electrolyte Solution. Lancet. August 5, 1978, pp. 281-282.

ABSTRACTS AND LETTERS PUBLISHED

Ahmed, Ansaruddin, Gilman, R., Aziz, K.M.S. and Rahaman,M.M.: Characterisation of Humoral Antibody in Shiga Dysentery by Immunoglobulin Class. Proceedings of the Third Bangladesh Science Conference. January 8-12, 1978, p. 167.

Ali, Akbar, Rahaman, M.M., Aziz, K.M.S. and Alam, A.K.M.J: Low Serum Protein Concentration in Hospitalized Patients. Proceedings of the Third Bangladesh Science Conference, January 8-12, 1978, p. 167.

Ali, S., Hoque, A.S.M.M. and Aziz, K.M.S.: Abundance and Biomass of Freshwater Snails in the three Ponds of Dacca. Proceedings of the Third Bangladesh Science Conference, January 8-12, 1978, p. 93.

Aziz, K.M.S. and Alam, K.: Studies on Toxins obtained from Shigella Dysenteriae Type I. Proceedings of the Third Bangladesh Science Conference, January 8-12, 1978, p. 164.

Aziz, K.M.S., Huq, A. and Oppenheimer, J.R.: Seasonal Distribution and Comparative abundance of Phytoplankton in three Ponds in Dacca, Bangladesh. Proceedings of the Third Bangladesh Science Conference, January 8-12, 1978, p. 71.

Hoque, A.S.M. Motaharul, Aziz, K.M.S.: Distribution of Ligochaetes in RamnaLake with special reference to the level of pollution at different stations. Proceedings of the Third Bangladesh Science Conference, January 8-12, 1978, p. 64.

Islam, M.S. and Aziz, K.M.S.: Association of Vibrios with some hydrophytic plants. Proceedings of the Third Bangladesh Science Conference, January 8-12, 1978, p. 52.

Khan, M.U., Chakraborty, J., Sarder, A.M. and Khan, M.R.: Water source and the incidence of Cholera in Rural Bangladesh. Proceedings of the Bangladesh Science Conference, January 8-12, 1978, p. 148.

Mosley, W.H.: Health,Nutrition and Postpartum Amenorrhea in Rural Bangladesh. International Family Planning Digest

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Mosley, W.H., Rahaman, M.M., Chen, L.C., Aziz, K.M.S. and Greenough, W.B., III: International Research Laboratory in Bangladesh. (Letter to editor), Lancet. March 18, 1978, pp. 602-603.

Mosley, W.H.: Cholera Research in Bangladesh. (Letter to editor), Lancet. May 6, 1978, pp. 991-992.

Oppenheimer, J.R., Aziz, K.M.S. and Huq, A.: Biological and Physiochemical studies in three Ponds in Dacca, Bangladesh. Proceedings of the Third Bangladesh Science Conference, January 8-12, 1978, p. 99.

Rahaman, M.M. and Greenough, W.B., III: Shigellosis and Haemolyticuremic Syndrome. (Letter to editor), Lancet. May 13, 1978, pp. 1051.

Rahman, M., Ahmed, F. and Islam, A.: Foliar diagnosis of Mineral deficiencies in Mango. Proceedings of the Third Bangladesh Science Conference, January 8-12, 1978, p. 148.

Wahed, M.A., Aziz, K.M.S., Chowdhury, A.K.M.A. and Rahaman, M.M.: Occurrence of two electrophoretically distinct Albumins in Human Serum. Proceedings of the Third Bangladesh Science Conference. January 8-12, 1978, p. 148.

CRL PUBLICATION SERIES

Author	Title	Date
CRL	Annual Report 1977	November, 1977
Working Papers		
J.M. Hughes J.M. Boyce R.J. Levine Moslemuddin Khan G.T. Curlin	Water and the Transmission of El Tor Cholera in Rural Bangladesh.	December, 1977
A.K.M. Alauddin Chowdhury G.T. Curlin	Recent Trends in Fertility and Mortality in Rural Bangladesh 1966-1975.	January, 1978
T. Osteria Makhlisur Rahman R. Langsten Atiqur Rahman Khan D.H. Huber W.H. Mosley	Assessment of the Matlab Contraceptive Distribution Project—Implications for Program Strategy.	April, 1978
Makhlisur Rahman T. Osteria J.Chakraborty D.H. Huber W.H. Mosley	A Study of the Field Worker Performance in the Matlab Contraceptive Distribution Project.	July, 1978
R.Langsten J.Chakraborty	Constraints on Use and Impact of Contraceptives in Rural Bangladesh.	August, 1978
T. Osteria W.H. Mosley A.I. Chowdhury	The Demographic Impact of the Contraceptive Distribution Project.	September, 1978
Moslemuddin Khan G.T. Curlin	Development of Milk Teeth in Rural Meheran Children of Bangladesh.	September, 1978

Author	Title	Date
Scientific Papers		
Moslemuddin Khan G.T. Curlin	Urban Cholera Study 1974 and 1975, Dacca.	December, 1977
George T.Curlin R.J. Levine A. Ahmed K.M.A. Aziz A.S.M. Mizanur Rahman W.F. Verwey	Immunological Aspects of a Cholera Toxoid Field Trial in Bangladesh.	March 1978
L.T. Ruzicka A.K.M. Alauddin Chowdhury	Demographic Surveillance System - Matlab. V.1. Methods and Procedures.	March 1978
L.T. Ruzicka A.K.M. Alauddin Chowdhury	Demographic Surveillance System - Matlab. V.2. Census 1974.	March, 1978
L.T. Ruzicka A.K.M. Alauddin Chowdhury	Demographic Surveillance System - Matlab. V.3. Vital Events and Migration 1974.	March, 1978
L.T. Ruzicka A.K.M. Alauddin Chowdhury	Demographic Surveillance System - Matlab. V.4. Vital Events and Migration 1975.	March, 1978
L.T. Ruzicka A.K.M. Alauddin Chowdhury	Demographic Surveillance System - Matlab. V.5. Vital Events, Migration and Marriages 1976.	March, 1978
Moslemuddin Khan A.K.M.J.Alam A.S.M. Mizanur Rahman	Ten Years Review of the Age and Sex of Cholera Patients.	May, 1978
M.I. Huq G. Kibriya	A Study of Selected Intestinal Bacteria from Adult Pilgrims.	August, 1978

Author	Title	Date
Special Publication		
Susan Fuller Alamgir M. Shamsul Islam Khan H.A. Spira	Index to CRL Publications and Scientific Presentations, 1960-1976.	August, 1978

PAPERS SUBMITTED FOR PUBLICATION

Becker, S.B.: Seasonal Patterns of Fertility Measures. Journal of American Statistical Association, 1978.

Brown, K.H., Parry, L., Khatun, M. and Ahmed, Md. G.: Lactose Malabsorption in Bangladeshi Village Children: Relation with age, History of Recent Diarrhea, Nutrition Status and Breastfeeding. American Journal of Clinical Nutrition, 1978.

Brown, K.H., Rajan, M.M., Chakraborty, J., and Aziz, K.M.A.: Failure of a Large Dose of Vitamin A to enhance the Antibody Response to Tetanus Toxoid in Children. Journal of Pediatrics, 1978.

Chen, L.C.: Interaction of Agriculture, Dietary Practices, and Infection of Seasonal Dimensions of Energy Malnutrition. Journal of Food and Ecology, September 1978.

Chen, L.C.: Morbidity and Mortality Control of Diarrheal Disease: Some Strategic Issues. American Journal of Clinical Nutrition, 1978.

Gilman, R.: String Capsule Culture of S. Typhi. Lancet.

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Huffman, S.L.: Nutrition and Human Reproduction: Research Needs. American Journal of Clinical Nutrition.

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Islam, M.R., Greenough, W.B., III, Choudhury, A.K. Azad, Sack, D.A. and Rahaman, M.M.: Labon-Gur (Common Salt and Brown Sugar) Oral Rehydration Solution in the Diarrhoea of Adults. Lancet.

Khan, M.U., Curlin, G.T. and Chakraborty, J.: Growth and Development Studies: Meheran. Bangladesh Medical Journal. August 1978.

Khan, M.U., Curlin, G.T. and Huq, I.: Epidemiology of Shigella Dysenteriae Type I Infections in Dacca Urban Area. Tropical and Geographic Medicine.

Merson, M.H., Sack, R.B., Kibriya, A.K.M.G., Mahmood, A. Ali, Ahmed, K.S. and Huq, I.: Efficacy of pooling strains for laboratory diagnosis on Enterotoxigenic E. Coli (ETEC) Diarrhea. Journal of Clinical Microbiology.

Mosley, W.H.: Health, Nutrition and Mortality in Bangladesh. Research in Human Capital and Development.

Morris, G.K., Merson, M.H., Huq, I., Kibriya, A.K.M.G., Black, R.E.: Comparison of Plating Media for Isolating Vibrio Cholerae. Journal of Clinical Microbiology.

Rahaman, M.M., Alam, A.K.M.J. and Islam, R.: S. Dysenteriae I Bacteremia in Children. Journal of Pediatrics.

Rahaman, M.M., Majid, M.A. and Monsur, K.A.: Intravenous Rehydration in Cholera and non-Cholera Diarrhoea: A Comparative Evaluation of Two Solutions. Bulletin W.H.O.

Sack, D.A., Islam, S., Brown, K.H., Islam, A., Kabir, A.K.M.I., Chowdhury, A.M.A.K. and Ali, Akbar: Oral Therapy in Children with Cholerae: A Double Blind Comparison of Sucrose with Glucose Electrolyte Oral Solution. Pediatrics.

Sack, D.A., Islam, Sirajul, Rabbani, H. and Islam, Asma: Single Dose Doxycycline for Cholera. Antimicrobial Agents and Chemotherapy.

PAPERS PRESENTED AT MEETINGS

Bangladesh Association for the Advancement of Science Conference, January 10-12, 1978, Chittagong, Bangladesh.

Aziz, K.M.A.: Changing Patterns of Marriage in Rural Bangladesh.

Rahaman, M.M. and Islam, M.R.: Labon-Gur-Salt and Sugar as a Home Based Treatment for Diarrhoeal Illness.

Fifth International Conference on Global Impact of Applied Microbiology, Bangkok, November, 1977.

Aziz, K.M.S., Huq, M.I. and Ahmed, Ansaruddin: Studies on the Toxin Elaborated by a Vibrio-like Organism Isolated from an Epidemic of Diarrhea.

Huq, M.I. and Ahmed, M.U.: Development of a Broad Base Culture Collection Centre in Bangkok.

Huq, M.I., Aziz, K.M.S., Khan, M.U., Alam, A.K.M.J and Ahmed, A.: Studies on an unusual Diarrhea Epidemic caused by a Vibrio-like Organism.

Conference on Seasonal Dimension to Rural Poverty, Institute of Development Studies, University of Sussex, Brighton, July 3-6, 1978.

Becker, S. and Sarder, A.M.: Seasonal Patterns of Vital Events and Migration in Matlab, Bangladesh: Review of Basic Patterns and Detailed Analysis of Mortality.

Chen, L.C., Chowdhury, A.K.M.A. and Huffman, S.L.: Interactions of Agriculture, Dietary Practices and Infection on Seasonal Dimensions of Energy Protein Malnutrition.

U.S.-Japan Joint Cholera Conference, Karatsu City, Japan, September, 27-29, 1978.

Black, R.E., Merson, M.H., Rowe, B., Taylor, P.R., Rahman, A.S.M.M., Huq, M.A., Alim, P.R.M.A., Sack, D.A. and Curlin, G.T.: Epidemiology of Enterotoxigenic Escherichia Coli in Rural Bangladesh.

Daniel, R.R.: Experimental Pathogenicity of O Group I Non-Agglutinating Vibrio Cholerae.

Khan, M.U. and Shahidullah, M.: Pattern of Intra-familial Spread of Cholera.

Spira, W.M., Daniel, R.R., Ahmed, S., Huq, A. and Eusof, A.: Clinical Features of Infection with O Group I Non-Agglutinating Vibrio Cholerae, Isolated from Diarrhoeal Patients in Dacca, Bangladesh.

Conference of the Population Council, New York, August 15,1978.

Chen, L.C.: Intervention Study on Reproductive Behavior and Contraceptive Technology in Rural Bangladesh.

The Asian Pacific Pediatric Gastroenterology Workshop, Institute of Public Health, Dacca, Bangladesh, October 28-November 1, 1977.

Greenough, W.B., III: Lecture delivered on Field Studies in Paediatric Gastroenterology.

Mosley, W.H.: Lecture delivered on Cholera Research Laboratory as a Regional Resource.

Rahaman, M.M.: Lecture delivered on Clinical Research in Gastroenterology.

XV International Congress of Pediatrics, October 23-29, 1977, New Delhi, India.

Rahman, M.M., Khan, M.U. and Wahed, M.A.: Oral Rehydration in Acute Non-cholera Diarrhoea: Role of Tetracycline in Shortening the Duration.

Symposium on Diarrhea at the XVth International Congress of Pediatrics, New Delhi, October 23-29, 1978.

Greenough, W.B., III: Pathogenic Mechanisms Involved in Toxigenic and Invasive Bacterial Diarrheas.

Symposium on Malnutrition During Pregnancy and Lactation: Perinatal Nutrition Problems. XI International Congress of Nutrition, August 27-31, 1978, Rio de Janero, Brazil.

Huffman, S.L., Chowdhury, A.K.M.A. and Sykes, Z.M.: Breastfeedings Patterns in Relation to Maternal Nutrition Status and Fertility: A Longitudinal Study in Bangladesh.

Huffman, S.L., Breastfeedings Patterns in Rural Bangladesh.

Population Association of America Annual Meeting, April, 1978.

Huffman, S. L., Chowdhury, A.K.M.A. and Sykes, Z.M.: Lactation and Fertility in Bangladesh.

First Annual Veterinary Conference of the Bangladesh Veterinary Association, Mymensingh, September, 1978.

Huq, M.I.: Researches on Medical Microbiology and its Relationship to Veterinary Microbiology.

Rahman, A.S.M. Hamidur and Gilman, R.H.: Studies on the Fresh Water Molluscan Fauna of Veterinary and Public Health Important Prevalent in Bangladesh.

First National Seminar on Zoonooses organized by Ministries of Fisheries and Livestock, WHO and UNICEF, Dacca, December 20-22, 1977.

Huq, M.I.: Study on the Bacterial Zoonoses with reference to Salmonellosis and Coli Bacillosis.

Eighth International Epidemiological Association, September-October, 1977, San Juan, Puerto Rico.

Rahman, M.M., Verwey, W.F. and Majid, M.A.: Evaluation of Hydration with Oral Electrolyte Solution in Moderate Hydration caused by Acute Diarrhoea.

43rd Nobel Symposium, Stockholm, Sweden, August 6-11, 1978.

Greenough, W.B., III: Current Principles in the Treatment of Cholera and Related Dehydrating Diseases.

Merson, M.H.: Epidemiology of Cholera and Enterotoxigenic E. Coli Diarrhea.

78th Annual Meeting of the American Society of Microbiology, Los Vergas, May 14-19, 1978.

Huq, M.I., David, B.R., Weaver, R.E., Hollis, D.G., Martin, W.T. and Brenner, D.J.: EF6: A Newly Recognized Organism.

Symposium of Parasitic Diseases, sponsored by Pfizer Bangladesh Laboratories, Ltd., July 1, 1978, Hotel Intercon, Dacca.

Rahaman, M.M. and Islam, S.: Comparative Clinical Trial of Tinidazole and Metronidazole in Amoebic Dysentery.

Second National Conference on Voluntary Sterilization of Bangladesh Association for Voluntary Sterilization, Dacca, Bangladesh, January 21-22, 1978.

Huber, Douglas H., Rahman, Makhlesur and Chakraborty, J.: Sterilization Clients in the National Campaign - A Follow-up in Matlab Thana.

CRL SEMINAR PROGRAM

Speaker & Affiliate	Topic	Date
Tieng Pardthaisong, Research Demographer, McCormack Family Planning Program, Chiang Mai.	Analysis of the Recent Fertility Decline in the Chiang Mai Region of Thailand.	28 October, 1977
Dr Nate Pierce, Johns Hopkins Univ., Baltimore.	The Immune System of the Gut.	3 November, 1977
Dr Robert Yolken, National Institute of Health, Bethesda.	ELISA Assay	15 November, 1977
Dr George Morris, C.D.C., Atlanta.	Primary Isolation Procedures for some common Pathogenic Bacteria.	18 November, 1977
Dr Nobuya Ohtomo, The Chemo-Sero-Therapeutic Research Inst., Japan.	Sub-Units of Cholera Toxin	2 December, 1977
Dr Nizam Uddin Ahmed	Conjugal Role Segregation and Developmental Cycle of the Domestic Group in Rural Bangladesh.	30 December, 1977
Dr Ahmed Imam Taha, Under-Secretary of State, Arab Republic of Egypt.	Health Services Delivery in Egypt.	24 February, 1978
Dr Yutaka Zinnake, National Defence College, Japan.	Biological Effects of Cholera Toxin on Melanoma Cells.	24 March, 1978
Dr J.C. Caldwell, Australian National University, Canberra.	Measuring the Impact of Sexual Abstinence on Fertility.	7 April, 1978
Dr A.T.M. Faizur Rahman, Irradiation & Pest Control Inst., Bang. Atomic Energy Comsn., Dacca.	A Self Reliant Strategy to Freedom from Hunger & Energy Crisis in a Developing Country - Bangladesh.	14 April, 1978

Dr Obaidullah, Population Program Officer	Population Education	14 July, 1978
Dr M.H. Merson, Investigator, CRL.	Review of Research on Epidemiology of Diarrheal Diseases.	31 August, 1978
Dr S. Becker, Investigator, CRL.	Seasonality of Vital Events in Matlab with Specific Reference to Deaths & Socio-economic Status.	15 September, 1978
Mr G.M. Quereshi, Bangladesh Management Development Centre	Making Work More Human	22 September, 1978
Dr Cato Aall, Food & Nutrition Adviser, FAO/UNDP.	Nutrition Situation of Burmese Refugees	6 October, 1978
Dr L. Poudayl, Chief Officer, Central Health Lab., Bir Hospital, Kathmandu, Nepal.	Laboratory Services in Nepal	3 November, 1978

LIST OF VISITORS TO THE CHOLERA RESEARCH LABORATORY OCTOBER 1977 - SEPTEMBER 1978

OCTOBER 1977

Joseph van den Boomen,
Chief, Population and Development Section,
Population Division, United Nations, New York, USA.

Moni Nag,
UNFPA Consultant, Population Council, New York, USA.

George Cernada,
Associate Professor, Department of Public Health,
School of Health Sciences, University of Massachusetts, USA.

Dr. A.O. Lucas,
Director of the Special Program for Research & Training
in Tropical Diseases, WHO, Geneva, Switzerland.

Dr. Inger Inadomi,
Head, Division of Health, Population, Nutrition & Education,
Norwegian Agency for International Development, Oslo, Norway.

Dr. Hoivik,
Surgeon Consultant, Norwegian Agency for International
Development, Oslo, Norway.

Mr. McGeorge Bundy,
President, Ford Foundation, New York, USA

Dr. John Beale,
Head, Biology Division, The Wellcome Research Laboratories,
Kent, England.

Dr. Marvin Sears,
Head, Department of Ophthalmology, School of Medicine,
Yale University, USA

Mr. Tieng Pardthaisong,
Research Demographer, McCormack Family Planning Program,
Chiang Mai University, Chiang Mai, Thailand.

Professor S. Bergstrom,
Chairman, Global (HQ) Advisory Committee on Medical Research,
WHO, Geneva, Switzerland.

Dr. Goran Sterky,
Research Officer, Health Sciences, Swedish Agency for
Research Co-operation with Developing Countries (SAREC),
Stockholm, Sweden.

Dr. R. Bradley Sack,
Director, Johns Hopkins University ICMR, Baltimore, Maryland, USA.

Dr. Nathaniel F. Pierce,
Associate Professor of Medicine, Johns Hopkins University, Baltimore, Maryland, USA

Robert Lawrence,
Bangladesh Desk Officer, CIDA, Ottawa, Canada.

Participants of the First Annual Meeting of the Asian Pacific Society for Pediatric Gastroenterology:

Dr. Michael Gracey,
Pediatric Gastroenterologist, Princess Margaret Children's Medical Research Foundation, Perth, Western Australia.

Dr. John Mitchell,
Pediatrician, Sydney, Australia.

Dr. John Mckim,
Pediatrician, Ontario, Canada.

Dr. Hentyantno Hendardji,
Head, Department of Child Health, General Hospital, Jambi, Indonesia.

Dr. Djauhar Ismail,
Pediatrician, Social Pediatric Sub-division, Department of Child Health, Faculty of Medicine, Gadjah Mada University, Yogyakarta, Indonesia.

Dr. Sunoto,
Sub-division of Gastroenterology, Department of Child Health, Medical School, University of Indonesia, Jakarta, Indonesia.

Dr. Suharjono,
Head, Sub-division of Gastroenterology, Department of Child Health, Medical School University of Indonesia, Jakarta, Indonesia.

Dr. A.F.J. Willem Tumbelaka,
Head, Department of Child Health, Medical School, University of Indonesia, Jakarta, Indonesia.

Dr. S. Wiradisuria,
Pediatrician, Indonesia.

Dr. K.N. Jalan,
Chief Co-ordinator, Kothari Centre of Gastroenterology & Visiting Physician, Calcutta Medical Research Institute, Calcutta, India.

Dr. Dilip Mahalnabis,
Scientist, Kothari Centre of Gastroenterology & Research Director, Calcutta Medical Research Institute, Calcutta, India.

Dr. S.C. Paul,
Director, Cholera Research Centre, Calcutta, India.

Dr. P. Udani,
Director/Professor, Institute of Child Health, J.J. Group of Hospitals & Grant Medical College, Bombay, India.

Dr. John Biddulph,
Professor of Child Health & Chairman of the Department of Clinical Sciences, Medical Faculty, University of Papua New Guinea, Boroko, Papua New Guinea.

Dr. A.C. Ludan,
Pediatrician: Fellow of Philippines Pediatric Society, Quezon City, Philippines.

Dr. Peria D. Santos-Ocampo,
Pediatrician (Secretary-General, Association of Pediatric Societies of South-East Asian Region), Medical Centre, Manila, Philippines.

Dr. Hamid Ali Khan,
Professor of Pediatrics (Retired), Jinnah Post-Graduate Medical Centre, Karachi, Pakistan. Also, Executive Vice-President, Pakistan College of Physicians & Surgeons, Karachi, Pakistan.

Dr. Sombodhi Bukkavesa,
Professor of Pediatrics, Faculty of Medicine, Sriraj Hospital, Mohidol University, Bangkok, Thailand.

Dr. Maurice Dusai,
Pediatrician, Los Angeles, California, USA.

Dr. Jon Rohde,
Pediatrician, the Rockefeller Foundation, Yogyakarta, Indonesia.

NOVEMBER 1977

Dr. C.W.L. Jeanes,
Special Adviser, Health & Population, Canadian International Development Agency (CIDA), Ottawa, Canada.

R.H. Lawrence,
Planning Officer, Asia Division, CIDA, Ottawa, Canada.

Mr. Oscar Harkavy,
Program Officer-in-Charge, Ford Foundation, New York, USA.

Ms. Sheila Sharpley,
Deputy High Commissioner, New Zealand High Commission, New Delhi, India.

Dr. Nobuya Ohtomo,
Director, Research & Training, The Chemo-Sero-Therapeutic Research Institute, Kumamoto, Japan.

Dr. Robert Yolken,
PHS Officer, Laboratory of Infectious Diseases, NIAID, National Institutes of Health, Bethesda, Maryland, USA.

Dr. Manual Carballo
World Health Organization, Geneva, Switzerland.

Dr. Y.C. Yu,
United Nations Population Division, New York, USA.

Mr. W. Seltzer,
United Nations Statistical Office, New York, USA.

Michael Lackner,
United Nations Statistical Office, New York, USA.

Dr. Gebre-Medhin,
Institute of Nutrition, Uppsala University, Uppsala, Sweden.

Dr. Yngve Hofvander,
Professor of Pediatrics, University Hospital, Uppsala, Sweden.

Dr. A.C. Almanzor,
Asian Regional International School of Social Work, Manila, Philippines.

DECEMBER 1977

Ms. Margaret Goodman,
Member, Congressional Team, House of International Relations Committee, USA.

Dr. David Burman,
Department of Child Health Care, Bristol University, Bristol, UK. (Consultant to WHO.)

Dr. L. Poudayl,
Medical Superintendent (Chief), Central Health Laboratory, Bir Hospital, Kathmandu.

Mr. Harold Graves,
Consultant, USA.

Dr. Robert S. Gordon,
Special Assistant to the Director, National Institutes of Health, Bethesda, Maryland, USA.

Dr. Marjorie A. Koblinsky,
Program Officer, Health Sciences, IDRC, Asia Regional Office, Singapore.

Dr. Clifford A. Pease,
Deputy Director, Office of Health, Technical Assistance Bureau, USAID, Washington, USA.

Ms. Farida Shah,
Research Associate, Department of Population Dynamics, The Johns Hopkins University, School of Hygiene & Public Health, Baltimore, USA.

Dr. Allan Rosenfield,
Director, College of Physicians & Surgeons of Columbia University, Centre for Population & Family Health, New York, USA.

Dr. H.T. Mahler,
Director-General, World Health Organization, Geneva, Switzerland.

Dr. V.T.H. Gunaratne,
Regional Director, WHO South-East Asia Regional Office, New Delhi, India.

Ms. Anne R. Devancey,
University of California, School of Medicine, California, USA.

Professor Thomas P. Roswell,
Ministry of Education (Agricultural Division), Stockholm, Sweden.

Dr. Robert S. Anderson,
Department of Communication Studies, Simon Fraser University, Burnaby, B.C., Canada.

Members of Smallpox Commission:

Dr. P.N. Shrestha,
Chief, Smallpox Eradication Project, Department of Health Services, Kathmandu, Nepal.

Dr. U. Thein Nyuint,
Director, Disease Control, Department of Health,
Rangoon, Burma.

Dr. I.F. Setiady,
Director, Epidemiology & Quarantine, Ministry of Health,
Jakarta, Indonesia.

Dr. S. Jatanasen,
Director, Division of Epidemiology, Ministry of Public
Health, Bangkok, Thailand.

Dr. J.C. Lerche,
Director, National Institute of Health, Oslo, Norway.

Dr. Alexander D. Langmuir,
Professor, Harvard University Medical School, Department
of Preventive Medicine, Boston, USA.

JANUARY 1978

Dr. R.T. Ravenholt,
Director, Office of Population, AID Washington, USA.

Dr. Susan T. Pettiss,
Director, Blindness Prevention, Helen Keller International,
New York, USA.

Dr. R. Bradley Sack,
Director, Johns Hopkins University ICMR, Baltimore,
Maryland, USA.

Dr. R. Para Rata Segaram,
Ophthalmologist - Short-term Consultant for WHO.

FEBRUARY 1978

Mr. David E. Bell,
Vice-President, Ford Foundation, New York, USA.

Mr. John Bresnan,
Head, Asia & Pacific Office, Ford Foundation, USA.

Dr. Duff Gillespie,
AID Project Officer, USAID, Washington, USA.

Dr. W.K. Journey,
Rural Water Supply, Health Sciences Division, IDRC, Canada.

Dr. Barry Gaberman,
Ford Foundation, New York, USA.

Mr. Harold Graves,
Consultant, USA.

Professor J.C. Caldwell,
Head, Demographic Department, Australian National University, Canberra, ACT, Australia.

Dr. J.A.B. Nicholson,
Medical Adviser, Ministry of Overseas Development, London, UK.

Members of International Scientific Review Committee:

(See page 75.)

MARCH 1978

Dr. John Lindenbaum,
Professor of Medicine, Columbia University, New York, USA.

Mrs. Shirley Lindenbaum,
Professor of Anthropology, New College, New York, USA.

Dr. Yutaka Zinnaka,
Department of Bacteriology, National Development Medical College, Saitama, Japan.

Dr. Marjorie Koblinsky,
Program Officer, Health Sciences, IDRC, Asia Regional Office, Tanglin, Singapore.

Dr. Susan Koscielecki,
Program Officer, Population & Health Sciences, IDRC, Ottawa, Canada.

Professor K.N. Seneviratne,
Director, Institute of Post-Graduate Medicine, Colombo, Sri Lanka.

Members of the International Islamic Seminar:

Dr. Soufi Abu Talib,
President, Cairo University, Cairo, Egypt.

Professor Urgku Abdel Aziz,
Vice-Chancellor, University of Malaysia, Kuala Lumpur, Malaysia.

Dr. Ali Artiq,
Secretary General, Organization of Arab Petrol Exporting Countries (OAPEC), Kuwait.

Professor Khurshid Ahmed,
Director, Islamic Foundation, Leicester, UK.

Dr. Mahmud Sakr,
Dean of Economics, University of Jordon, Amman, Jordon.

Dr. Najmuddin Bamat,
UNESCO, Paris, France.

Dr. Khairi Issa,
Dean, Faculty of Economics, Cairo University, Egypt.

Dr. Maqsood Siddiqi,
Energy Consultant, UNILEVER, Middlesex, UK.

Mr. Mahmood Safwat,
Director, Abu Dhabi Development Bank, Abu Dhabi.

Dr. Mustafa Bilge,
Institute of Islamic Studies, Istanbul, Turkey.

Dr. Ali Abdullah Al-Daffa,
University of Petroleum & Minerals, Dahran, Saudi Arabia.

Dr. Hasan Abu Rukba,
Dean, Faculty of Economics, King Abdel Aziz University, Jeddah, Saudi Arabia.

Dr. M. Ghiyasuddin,
The Muslim Institute, Slough, UK.

Dr. Hashim Al-Mallah,
Dean, College of Arts, University of Mosul, Mosul, Iraq.

Dr. Rif'at Al-Mahjoub,
Professor of Economics, Cairo University, Cairo, Egypt.

Mr. Burhan Al-Dajjani,
Secretary-General, Association of Arab Chambers of Commerce, Industry, and Agriculture, Beirut, Lebanon.

Hakim Mohammed Said,
President, Hamdard Foundation, Nazimbad, Karachi, Pakistan.

Dr. Ezzeddin Ibrahim,
Cultural Adviser to H.H. the President of the United Arab Emirates, the Palace, Abu Dhabi.

Dr. Ahmed Al-Sabbah,
Director, Research & Development Centre, King Abdel Aziz University, Jeddah, Saudi Arabia.

H.E. Dr. Ahmed Abu Ismail,
Chairman, Planning Committee, People's Assembly, Cairo, Egypt.

Dr. Malik Al Badri,
Professor of Psychology, Faculty of Education, University of Riyadh, Riyadh, Saudi Arabia.

H.E. Dr. Mehdi Ben Abboud,
Professor, Mohammed V University, Rabat, Morocco.

Dr. Rawane M'Baye,
Director, Islamic Institute, Dakar, Senegal.

Dr. Hassan Gwarzo,
Professor, Ahmadou Ballo University, Zaria, Nigeria.

Dr. Mohamoud Zouber,
Director, Centre Ahmed Baba, Timuktu, Mali.

Dr. Abdul Hamid Abu Suleiman,
Secretary-General, World Assembly of Muslim Youth, Riyadh, Saudi Arabia.

Mr. Zafrul Islam,
Assistant Secretary-General, General Secretariat, Organization of the Islamic Conference, Jeddah, Saudi Arabia.

Dr. Garib M. Gamal,
Director, Technical Affairs, General Secretariat, Organization of the Islamic Conference, Jeddah, Saudi Arabia.

Dr. Ashrafuz Zaman,
Director, Economic Affairs, General Secretariat, Organization of the Islamic Conference, Jeddah, Saudi Arabia.

Mr. Bakare Drame,
General Secretariat, Organization of the Islamic Conference, Jeddah, Saudi Arabia.

Mr. Mustafizur Rahman Khan,
General Secretariat, Organization of the Islamic Conference, Jeddah, Saudi Arabia.

Dr. Sayed Ali Ashraf,
King Abdel Aziz University, Jeddah, Saudi Arabia.

APRIL 1978

Dr. David Seel,
Director, Presbyterian Medical Centre, Hwasandong, Chunju, Colla Pukdo, South Korea.

Dr. Lee,
Staff Physician, Presbyterian Medical Centre, Hwasandong, Chunju, Cholla Pukdo, South Korea.

Dr. John Clemens,
Case Western Reserve University, Cleveland, Ohio, USA.

Dr. N.K. Shah,
Regional Adviser, WHO, New Delhi, India.

Ms. Belen H. Abreu,
Executive Trustee, Ramon Magsaysay Award Foundation, Manila, Philippines.

Dr. Ulf Thornaborg & Mrs Thornaborg,
Swedish Save the Children Fund, Stockholm, Sweden.

MAY 1978

Dr. J. Jarrett Clinton,
Senior Representative, East & South Asia, the Population Council, New York, USA.

Mr. Martin Greeley,
Research Associate, Institute of Development Studies, Brighton, England.

Dr. Robert Chambers,
Fellow, Institute of Development Studies, Brighton, England.

Dr. K.A. Khaleque,
Research Fellow, Imperial College, London, England.

Mr. S. Raghavachari,
Regional Adviser in Vital Statistics, ESCAP, Bangkok, Thailand.

Dr. Marwi Soerohardjo,
Department of Obstetrics & Gynaecology, Faculty of Medicine, Gadjah Mada University, Indonesia.

Dr. Viqar Zaman,
Professor of Microbiology, Faculty of Medicine, University of Singapore, Singapore.

JULY 1978

Ms. Lisa Hilder,
Medical Student, University of Sydney Medical School, Sydney, Australia.

Dr. Andrew Dean,
Centre for Geographic Disease Research, Honolulu, Hawaii, USA

Dr. Jean F. Rogier,
Cholera Task Force, Department of State, Washington, USA

AUGUST 1978

Dr. S. Shimodori,
Department of Microbiology, School of Medicine, Kyushu University, Fukuoka, Japan

Mr. K. Matsuda,
Medical Student, School of Medicine, Kyushu University, Fukuoka, Japan

Mr. J. Takamatsu,
Medical Student, School of Medicine, Kyushu University, Fukuoka, Japan

SEPTEMBER 1978

Dr. Robert S. Northrup,
The Rockefeller Foundation, Yogjakarta, Indonesia.

Dr. Marjorie A. Koblinsky,
Program Officer, Health Sciences, IDRC, Asia Regional Office, Singapore

ICDDR,B (CRL) publications can be obtained from Publications Unit, International Centre for Diarrhoeal Disease Research, Bangladesh, G.P.O. Box 128, Dacca - 2, Bangladesh.

List of current publications available:

A. CRL Annual Report 1976.

CRL Annual Report 1977.

B. Working Paper:

No. 1. The influence of drinking tubewell water on diarrhea rates in Matlab Thana, Bangladesh by George T. Curlin, K.M.A. Aziz and M.R. Khan. June 1977 (Rep. Sept 1978). 21 p.

No. 2. Water and the transmission of El Tor cholera in rural Bangladesh by James M. Hughes, John M. Boyce, Richard J. Levine, Moslemuddin Khan, George T. Curlin. Dec 1977. 27 p.

No. 3. Recent trends in fertility and mortality in rural Bangladesh 1966-1975 by A.K.M. Alauddin Chowdhury, George T. Curlin. Jan 1978. 14 p.

No. 4. Assessment of the Matlab Contraceptive Distribution Project - implications for program strategy by T. Osteria, Makhlisur Rahman, R. Langsten, Atiqur R. Khan, Douglas H. Huber and W. Henry Mosley. Apr 1978. 25 p.

No. 5. A study of the field worker performance in the Matlab contraceptive distribution project by Makhlisur Rahman, T. Osteria, J. Chakraborty, Douglas H. Huber and W. Henry Mosley. Jul 1978. 17 p.

No. 6. Constraints on use and impact of contraceptives in rural Bangladesh: Some preliminary speculations by R. Langsten, J. Chakraborty. Aug 1978. 23 p.

No. 7. The demographic impact of the contraceptive distribution project by T. Osteria, W.H. Mosley and A.I. Chowdhury. Sept 1978. 17 p.

No. 8. Development of milk teeth in rural Meheran children of Bangladesh by Moslemuddin Khan and George T. Curlin. Sept 1978. 23 p.

No. 9. A follow-up survey of sterilization acceptors in Matlab, Bangladesh by Makhlisur Rahman, Douglas Huber and J. Chakraborty. Oct 1978. 31 p.

No. 10. The Demographic Impact of Sterilization in the Matlab Village-Based MCH-FP Program by T. Osteria, S. Bhatia, J. Chakraborty and A.I. Chowdhury. Nov 1978. 23 p.

No. 11. Parental dependency on children in Matlab, Bangladesh by Makhlisur Rahman. Dec 1978. 28 p.

No. 12. An areal analysis of family planning program performance in rural Bangladesh by T. Osteria, S. Bhatia, A.S.G. Faruque, J. Chakraborty. May 1979. 19 p.

C. Scientific Report:

No. 1. Double round survey on pregnancy and estimate of traditional fertility rates by A.K.M. Alauddin Chowdhury. Jul 1977. 28 p.

No. 2. Pattern of medical care for diarrheal patients in Dacca urban area by Moslemuddin Khan, George T. Curlin and Md. Shahidullah. Aug 1977. (Rep. Jun 1978). 20 p.

No. 3. The effects of nutrition on natural fertility by W. Henry Mosley. Aug 1977. (Rep. Aug 1978). 25 p.

No. 4. Early childhood survivorship related to the subsequent inter-pregnancy interval and outcome of the subsequent pregnancy by Ingrid Swenson. Aug 1977. (Rep. Apr 1979). 18 p.

No. 5. Household distribution of contraceptives in Bangladesh - the rural experience by Atiqur R. Khan, Douglas H. Huber and Makhlisur Rahman. Sept 1977. 19 p.

No. 6. The role of water supply in improving health in poor countries (with special reference to Bangladesh) by John Briscoe. Sept 1977. (Rep. Feb 1979). 37 p.

No. 7. Urban cholera study, 1974 and 1975, Dacca by Moslemuddin Khan and George T. Curlin. Dec 1977. 24 p.

No. 8. Immunological aspects of a cholera toxoid field trial in Bangladesh by George T. Curlin, Richard J. Levine, Ansaruddin Ahmed, K.M.A. Aziz, A.S.M. Mizanur Rahman and Willard F. Verwey. Mar 1978. 16 p.

No. 9. Demographic Surveillance System - Matlab. Volume One. Methods and procedures. Mar 1978. 28 p.

No. 10. Demographic Surveillance System - Matlab. Volume Two. Census 1974 by Lado T. Ruzicka, A.K.M. Alauddin Chowdhury. Mar 1978. 48 p.

No. 11. Demographic Surveillance System - Matlab. Volume Three. Vital events and migration, 1975 by Lado T. Ruzicka, A.K.M. Alauddin Chowdhury. Mar 1978. 45 p.

No. 12. Demographic surveillance system - Matlab. Volume Four. Vital events and migration, 1975 by Lado T. Ruzicka, A.K.M. Alauddin Chowdhury. March 1978. 48 p.

No. 13. Demographic surveillance system - Matlab. Volume Five. Vital events, migration, and marriages - 1976 by Lado T. Ruzicka, A.K.M. Alauddin Chowdhury. March 1978. 55 p.

No. 14. Ten years review of the age and sex of cholera patients by Moslemuddin Khan, A.K.M. Jamiul Alam and A.S.M. Mizanur Rahman. May 1978. 18 p.

No. 15. A study of selected intestinal bacteria from adult pilgrims by M.I. Huq, G. Kibryia. Aug 1978. 15 p.

No. 16. Water sources and the incidence of cholera in rural Bangladesh Moslemuddin Khan, W. Henry Mosley, J. Chakraborty, A. Majid Sardar and M.R. Khan. Dec 1978. 19 p.

No. 17. Principles and prospects in the treatment of cholera and related dehydrating diarrheas by William B. Greenough, III. Jan 1979. 20 p.

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