

CHOLERA RESEARCH LABORATORY

ANNUAL REPORT

1977

Cholera Research Laboratory

G.P.O. Box 128

Dacca 2 - Bangladesh

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PREFACE

This Annual Report provides a broad overview of the research program of the Cholera Research Laboratory (CRL) for the period October 1, 1976 to September 30, 1977 with comments of specific findings and trends which are considered important. Persons interested in obtaining full technical details of any of the research are invited to communicate directly with the Director, CRL.

The Cholera Research Laboratory (CRL) operates 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 (IDRC) of Canada, UNICEF, and the Ford Foundation.

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INTRODUCTION

The 1977 fiscal year can be considered as a year of transition for the Cholera Research Laboratory. The CRL experienced not only a change in the scientific leadership during the course of the year, but, more importantly, has undergone major structural changes in the scientific program as preliminary steps for the proposed transformation to an International Center for Health Research.

Dr. Willard Verwey the Director since 1974 was forced by illness to retire in December 1976 and was replaced by Dr. W.H. Mosley who joined the CRL in March 1977. In the interim Dr. M. Mujibur Rahaman provided the leadership that sustained the development of the research program of the CRL which had been initiated under Dr. Verwey's guidance.

During the course of the summer of 1977 there was major expansion in the international scientific staff with senior scientists joining the Laboratory from Britain, the Philippines, India, and Australia as well as the United States. (see page 70) The CRL has also been fortunate enough to attract Bangladeshi senior scientists from international positions abroad who will be joining the research program in the next fiscal year.

Special efforts have been undertaken to strengthen the quality of the scientific program. Most important to the CRL is the protection of human subjects involved in its research program. Although all research carried out by the CRL is reviewed by the Bangladesh Medical Research Council, the CRL in FY77 established as an additional safe-guard a Review Board on Use of Human Subjects. This Review Board is comprised of Bangladeshi and international members and follows a defined set of policies and procedures to ensure adequate protection of the rights and welfare of human subjects. (see page 66) This review mechanism has been accepted by the United States Department of Health, Education and Welfare as fully meeting its standards for the protection of human subjects. The World Health Organization is the only other international institution outside the United States that has a review process meeting this high international standard.

The CRL has also revised the policies and procedures for development and critical review of all scientific protocols. A major innovation has been inviting as consultants to the review process scientists working in related areas in teaching and research institutions in Bangladesh.

Coupled with these structural changes has been a re-organization of the scientific staff into Research Working Groups. These Working Groups are focused on the five major problem areas that the CRL has determined as priorities for its research efforts. These areas are:

1. Therapy for diarrheal diseases.
2. Host resistance.
3. Disease Transmission.
4. Malnutrition.
5. High fertility.

This problem-orientated approach permits the CRL to establish a more coherent linkage between the laboratory, clinical and field research efforts that are directed towards solving each of these problems. Further, it facilitates the development of a multidisciplinary team approach because of the recognition that each of these problems has both bio-medical and socio-cultural dimensions. The summaries of the research presented in this report are organized according to the programmatic efforts of the various research working groups.

A new activity initiated late in FY 1977 is the development of training programs. Over the years the CRL has always provided a substantial amount of training for local institutions and some international groups on an ad hoc basis (see page 42). This year, in anticipation of its transformation to an International Center, the CRL has designated a Scientific Director responsible for training and is initiating plans for a co-ordinated training effort. Training programs will range from individualized research training to courses and seminars on technical and applied topics. These will be co-ordinated with institutions both in Bangladesh and in other developing countries, and will concentrate on technical and professional needs in the region.

Institutionally, actions have been taken by the Government of Bangladesh and the United States Government resulting formal approvals in principle of the transformation of the CRL into an International Center for Health Research governed by an International Board of Directors. The CRL, in conjunction with the Government of Bangladesh, has established a Sub-committee on Internationalization which has prepared a draft charter, developed a prospectus for the new Center and initiated contact with potential donors. FY 78 will be the year when definitive discussions and presumably actions will be taken which will transform the CRL into an International Center for Health Research.

DIARRHEAL DISEASE RESEARCH

In Bangladesh and other parts of the world with similar socioeconomic problems, diarrhea is a principal cause of death and a major cause of illness and loss of time from work. The studies done by the scientific staff of CRL this year have addressed this problem in a variety of ways. Because of the immediate needs of large numbers of patients, therapy has been placed first in order of discussion. This does not imply that it is the highest priority. Research on improving the resistance of people and populations to causative agents of diarrhea, while less evident now, seems to hold exciting prospects for effective preventive measures in the near future and will be increased. Studies on the transmission of disease-producing agents in nature ultimately hold the best prospect for the discovery of simple applicable ways to intercept vicious cycles, but much research is required to develop a sufficiently complete picture to know where the most accessible points for intervention may be.

1. THERAPY

In 1968 there was a great simplification in the treatment of cholera with the advent of oral rehydration. Effective treatment in simple surroundings became a feasible alternative to hospital based care. Recently, an additional dimension to oral glucose-electrolyte treatment of diarrhea has been suggested. A child's nutritional state may be improved if oral rehydration is used regularly to treat recurrent episodes of diarrhea. This opens a broad area of research to determine what actually is the impact of oral rehydration in populations affected by diarrhea, and to define optimal means for wide-spread application.

a. Household delivery of oral therapy: This year a study was carried out in four villages in the Matlab area to evaluate the effect of oral therapy in reducing diarrhea morbidity. In two villages glucose-electrolyte solution was provided and in

two comparable villages Kaolin mixtures. Field Assistants visited diarrhea patients on the first and third day and measured serum sodium. In the two months of study, too few severe cases were seen to adequately judge effectiveness of oral therapy in such cases. There was, however, a significantly lower serum specific gravity in the patients treated with glucose-electrolyte solutions indicating better hydration.

Other important observations were a great variability in the sodium concentrations of home mixed solutions (90-230 mEq/liter). Also there was a consistent pattern of behaviour in that all mixing errors tended to be in the direction of too much salts in relation to water. These observations indicate a need for more research on how best to instruct families to mix the replacement solution if serious complications of the therapy itself are to be avoided.

b. Simplified treatment centers and home therapy: In Dacca during the time from 1971 until 1976, the total number of diarrhea patients visiting CRL increased from 9,463 to 62,637, a rise of 662% or 132% each year. Over this time the CRL has moved from intravenous to oral therapy. The switch has permitted the staff to effectively meet this increase with only a limited increase in cost.

In 1977 a total of 78,605 patients were treated. A restricted program with a Treatment Center concept has been applied that has eliminated all laboratory work, including bacteriology, and sophisticated bedside measurements without any increase in mortality. This innovative approach has been designed to maximize the use of family members and less trained health workers in the care of patients. Since this has just recently been fully implemented, a detailed analysis of its results is not yet available. A future study along this line will focus on the minimum necessary observations by the least trained people that can still yield on outcome of care in diarrhea equivalent to that established with trained

physicians and nurses and a higher technology in the CRL hospital ward.

One study addressing this point was carried out during this year. Patients presenting with moderately severe dehydration due to diarrhea (defined by a plasma specific gravity of 1.029 or more) were rehydrated in the out-patient tents then sent home with instructions on how to give glucose electrolyte solution by mouth. Of the 277 patients meeting these criteria and put on this regimen, 230 were successfully rehydrated in the clinic and at home. The remaining 47 patients required supplementary intravenous fluids. Of 174 milder cases, 12 were ultimately considered to be failures of oral rehydration. Thus, oral rehydration alone was effective in 83% of moderately severe cases and 93% of mildly dehydrated patients in the simple setting of a tent clinic or home.

c. Composition of oral therapy solution: Controversies exist about composition of oral glucose electrolyte diarrhea replacement solution. The concentration of sodium is still considered too high by many pediatricians, although there has been a general consensus among experts in diarrhea treatment that 90 mEq/liter is safe for adults and children. The issue of whether sucrose may be substituted for glucose is still not fully resolved, yet it is of great practical concern since sucrose is more available and less costly. The question of a more palatable and stable base than bicarbonate and a lower concentration has not been sufficiently explored and a number of instances of tetany have been observed. Flavourings may enhance the acceptance of the solution and could be useful adjuncts. During this year several questions related to the composition of oral replacement solution have been studied.

A series of children less than three years of age were treated with oral glucose-electrolyte solutions with three different concentrations of sodium 120, 90 and 60 mEq/liter. There were two

instances of serious hypernatremia in the group receiving oral rehydration with a sodium concentration of 120 mEq/liter. This suggests that concentration is too high. No clustering of hyponatremia in the patients receiving the lower concentrations of sodium was seen.

A study on adults and children has been initiated with a double blind design to define the relative failure rates of glucose as compared to sucrose diarrhea replacement solutions. The design is such that the question will be answered with respect to the several different major causes of diarrhea in Bangladesh. These include V. cholerae, E. coli and Rotavirus.

A small study comparing bicarbonate with citrate has been made. This showed no significant difference in the correction of acidosis as measured by the plasma bicarbonate after four hours of treatment.

Another comparison was made between unflavoured oral rehydration solution and an orange flavoured mixture. When no choice was given, there was an equal intake by patients. When a choice was provided, there was a clear preference for the flavoured mixture.

d. Future studies of oral therapy: These experiences provide direction for future research. The highest priority is to analyze the variables that will allow the most effective application of oral therapy to the widest possible number of people who experience diarrhea. Factors affecting acceptance and ability to administer the fluid in sufficient quantity in proportion to losses are all unknowns.

Although we know that family members can give effective oral rehydration in a simple treatment center setting, we do not know whether oral diarrhea treatment solutions can be safely mixed at home and given as a home care measure. An intermediate step will be the provision of oral diarrhea treatment solution by a village health worker who lives in the community. A

community treatment center is a third possible way to provide care. Each of these and other possibilities will be considered carefully and studies designed to answer specific aspects.

Residual questions about the composition and safety margins of oral rehydration mixtures will also be approached. The need for base and potassium, and the safest sodium concentration will be further studied with emphasis on what compromises are safe and effective if only materials from a village bazar are available.

e. Antibiotic trials: This year an antibiotic trial with Doxycycline in cholera has been completed. This antibiotic, although more expensive than tetracycline, has a longer duration of action so that a single daily dose for 3 days was as effective as four daily doses of tetracycline. Thus the total expense is about equal, but it has an advantage of convenience. In addition, this antibiotic is excreted from the body by the intestinal tract rather than depending on the kidney and so is safe in patients who are at risk of renal shutdown. In the future, further antibiotic trials in cholera do not seem indicated since no important resistance has occurred to the currently effective agents.

A practical test of the effect of tetracycline in shortening the duration of diarrhea in an out-patient setting was done by selecting 190 patients of all ages on the basis of presenting with moderately severe, dehydrating diarrhea. Oral hydration with glucose electrolyte solution was given to all, but on alternate days tetracycline was prescribed for home use for a total of four days. Follow-up home visits were made to 135 cases to determine the benefit, if any, of tetracycline. It was found that in 62% of the control cases and 76% of the tetracycline cases, diarrhea stopped in one day or less. Overall, tetracycline did not have any important effect on the course of the diarrhea. Although the issue of whether or not all patients actually took the medicine

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1968-11	1991-17
1969-6	1992-42
1970-7	1993-71
1971-4	1994-32
1972-3	1995-24
1973-6	1996-9
1974-N	1997-6
1975-1	
1976-N	
1977-N	
1978-11	
1979-4	
1980-N	
1981-N	
1982-N	
1983-N	
1984-1	
1985-12	
1986-76	
1987-2	
1988-20	
1989-25	
1990-27	

can be raised, the results still stand, since in a typical setting of out-patient care there was no benefit gained with the extra cost of the antibiotic.

Two other trials of antibiotics in diarrhea have been done this year. One in a series of patients with enterotoxigenic E. coli disease demonstrated that tetracycline could shorten the course of patients with the most severe diarrhea; the other, in patients with Shigella dysentery, is a trial of a single dose of ampicillin. This study is not yet complete, but is important since the main barrier to treatment of dysentery is the high cost of the treatment with expensive antibiotics such as ampicillin.

f. Future studies in diarrhea inhibitors: The main problem which defeats oral rehydration in patients with severe dehydration is inability to keep up with a very high rate of intestinal secretion. Since it is known that cholera and E. coli toxins act through cyclic nucleotide systems, a series of inhibitory drugs are becoming available for clinical trials. An agent that could reduce diarrhea from 1,000 to 700 milliliters per hour (30%) might well make the difference between success and failure in the oral treatment of cholera.

Antibiotics will shorten diarrhea, but have no impact on the early hours when fluid losses and the risk of shock and sudden death are greatest. No antisecretory agents have been studied as yet in patients. High on the priority list for the coming year will be carefully monitored balance studies in the Clinical Research Center for such drugs. Possible candidates include indomethacin, and nicotinic acid. Two folk remedies may also deserve attention: bel fruit and nutmeg. In less than five carefully studied patients it can be found whether or not there is an important effect on rate of secretion.

2. HOST RESISTANCE

a. Intestinal immunity: During 1977 a major new research effort was initiated that may provide the basis for novel approaches to vaccines directed against enteric pathogens. Evidence in experimental animals and human volunteers, indicates that local immunity exerts a far stronger protective influence against infection than do circulating antibodies. Local immune mechanisms of the gut are little understood, and the only sure way to measure the local response at present is by intestinal biopsy or a direct graded challenge with the infecting agent. A simply proxy measure of intestinal immunity to specific antigens is needed to study the nature of this protective mechanism to disease or to define the local gut response to artificial immunization with vaccines.

The CRL has developed a collaborative program with other laboratories which are developing new methods applicable for the assessment of intestinal immune responses to antigens important in the pathogenesis of diarrheal diseases. As a result both a hemolytic plaque assay and a fluorescent antibody system has been set-up to detect lymphocytes committed to cholera toxin. This will be used in studies of cholera cases to determine whether intestinal lymphocytes committed to make antibodies to cholera toxin can be detected in the circulating blood or breast milk. This approach will begin to lay a rational foundation for the development of oral vaccines that can stimulate the intestinal immune system.

b. Enterotoxin assays: Since studies of immunity are contingent on the identification of specific antigens which are of crucial importance in pathogenesis, there will be a continued interest in maintaining a very advanced capacity for the measurements of such mediators of diarrheal disease. This year the assays for the family of enterotoxins which act upon adenylate cyclase have been established or maintained at a high level. These include the chinese hamster ovary cell (CHO) tissue culture assay, which

has been the main "work horse" for detection of cholera toxins or heat labile E. coli toxin and the Y mouse adrenal tumor cell assay. The rabbit skin permeability assay and the rabbit loop assay continue to be available. For detection of E. coli stable toxin, the infant mouse gastric assay is standardized and in heavy use. The means for serologic recognition of different O and K antigens of E. coli are also available. This year capacity in this area has been much enhanced by collaboration with the Collindale Laboratories in the United Kingdom.

c. Enterotoxigenic E. coli diarrhea: Several important studies employing specific tests for toxins or other antigens have been done. Of 176 males over ten years of age admitted to CRL who did not have cholera or dysentery, 62% were positive for E. coli which produced either heat labile toxin (LT), heat stable toxin (ST), or both toxins. LT-ST disease was more severe and prolonged than ST only disease. Although this study indicates a major role for toxigenic E. coli in the non-cholera diarrheas in Bangladesh, the fact that 17% of adult patients did not have a recognized pathogen suggests that we are still ignorant of some important causes of diarrhea here.

In January and February of 1976, CRL scientists studied the etiology of watery diarrhea in children less than ten years attending the out-patient clinic at the Cholera Hospital in Dacca. Laboratory techniques included the CHO cell assay for LT and the infant mouse assay for ST. Cultures from 115 children negative for the classical bacterial pathogens were studied for E. coli toxin using both five individual picks of E. coli and pools of ten organisms. Seventeen (15%) children had ST only E. coli isolated and ten (9%) had ST/LT organisms. Rotavirus accounted for about 30% of the remaining cases.

d. Amebic dysentery: Studies on amebic dysentery were done which have better defined the clinical

presentation and correlates of severe necrotic amebic colitis. Delayed hypersensitivity reactions were decreased in patients with severe disease, but not in milder forms. Since severe disease is present in older people with limited cellular immunity, the question is raised as to whether reduced host defenses may precede and lead to fulminant disease.

e. Shigella Shiga dysentery and the hemolytic - uremic syndrome: Observations were completed on the hemolytic-uremic syndrome and leukemoid response in children with Shiga dysentery. This work indicated that the presence of circulating endotoxin on admission correlated with subsequent evolution of the hemolytic-uremic picture. There was not, however, correlation with the leukemoid response. Immune complexes were no more common in patients with these complications than in others.

The question remains whether endotoxin itself or another bacterial substance, for which endotoxin is a marker, may be directly responsible for the clinical syndromes observed. An additional new observation, that rose spots (usually characteristic of typhoid fever) occur in Shigella dysenteriae type 1 disease has also been reported.

f. Pineapple gastroenteritis: A clinical curiosity has been observed in the past year. A syndrome of hypersensitivity to pineapple resulting in vomiting and diarrhea has been observed with considerable frequency at the CRL hospital. This has seasonal aspects and leads to vascular collapse that can be confused with cholera. The clinical picture in this group of patients indicates that a local allergic response in the gut can lead to a syndrome that shows many of the characteristics of bacterial diarrheas. How such responses are triggered by allergens may aid in further understanding of the pathogenesis of watery diarrhea.

g. Gastric acid and host resistance: An important host defense that has been studied this year that is

not dependent on immunity is the secretion of gastric acid. Base-line and stimulated levels of acid secretion have been studied in cholera, E. coli diarrheas and dysentery cases. Since acid secretion can be altered by foods and drugs, studies which show a correlation of changes in acid secretion which are associated with different diarrheas may be helpful in identifying high risk populations and could lead to innovative preventive measures which operate through this protective mechanism.

3. DIARRHEAL DISEASE TRANSMISSION

a. The incidence and causes of acute diarrhea: One of the major barriers to the development of effective interventions to break the cycle of diarrheal disease transmission in populations has been the limited ability to detect a causal agent in the majority of the cases. A recent analysis of the hospitalized cases seen at the Matlab Rural Treatment Center in 1975 illustrates the problem. During the course of that year 1,964 persons (0.7%) out of a population of 263,000 in the field surveillance area required hospitalization for an acute diarrheal illness. Routine bacteriological studies revealed that 28% of these cases were cholera, 2.7% were shigella, 0.2% were due to salmonella and 6.7% were associated with non-cholera Vibrios. In the vast majority of the cases (62%) a specific causal agent was not detected.

In recent years there have been two major scientific break-throughs which have vastly extended the possibilities of detecting a causal agent for most diarrheal diseases. The first was the discovery that some strains of the ubiquitous E. coli, which were considered normal inhabitants of the human intestinal tract, are capable of producing at least two enterotoxins (one of which is similar to cholera toxin) and thus are causal agents of acute diarrheal disease. The second advance was the discovery by electron-microscopy that many acute diarrheas in children were associated with a virus particle now called Rotavirus.

A preliminary investigation of 48 hospitalized diarrhea cases in the Matlab hospital in December 1974 through January 1975 revealed that Rotavirus was associated with 50% of the diarrhea cases under the age of two years, while enterotoxigenic E. coli were associated with 40% of the diarrhea cases over the age of 10. Thus the results from this limited study suggests that these agents could account for a major proportion of the previously undiagnosed diarrhea cases. The CRL has been taking steps to initiate more detailed field studies of the incidence and routes of transmission of these organisms through the population.

A hospital surveillance for enterotoxigenic E. coli was initiated in the Matlab hospital in February, 1977. Preliminary results indicate that these organisms are associated with 50% of the severe diarrhea cases in adults and about 20% of hospitalized diarrheas in children. Characteristically the organisms causing the diarrhea produced both the heat stable (ST) and heat labile (LT) toxins or only ST. Diarrheas associated with only LT producing organisms are infrequent. Detailed family and community studies are being initiated to trace the epidemiological pattern of spread of these organisms within the community.

More detailed studies of Rotavirus epidemiology at CRL have been limited by the lack of readily available diagnostic techniques. One community has been followed with serial serological surveys over a 12 month period to establish the pattern of acquisition of Rotavirus antibodies. Recently the CRL has made arrangements in collaboration with the National Institutes of Health to establish the ELISA technique for detecting Rotavirus antigen in the stools. This technique, which will be functioning in the fall of 1977, will then permit the first definitive studies of Rotavirus transmission in Bangladesh.

b. An epidemic of acute diarrhea associated with vibrio-like organisms: The close association of non-agglutinable (NAG) Vibrios with diarrheal disease

has been well established since 1964. Choleraic diarrhea due to Aeromonas shigelloides and Aeromonas hydrophilia has also been reported by several authors. In the CRL experience over the past several years organisms in this general group have only been associated with 20-40 cases of diarrhea annually. Beginning in 1975, however, acute diarrheas associated with vibrio-like organisms began to appear with increasing frequency. In Dacca, there were 167 cases in 1975, 207 cases in 1976 and 413 cases in the first seven months of 1977. This increase in incidence, particularly in the Spring of 1977, prompted more intensive microbiological, clinical and epidemiological studies which will be briefly summarized below.

Extensive microbiological studies, which are continuing, reveal that these organisms had some cultural, morphological and biochemical characteristics near the genus Vibrio. In sugar fermentations they belonged to a variety of Heiberg Groups. More than half were Group III, with smaller numbers in Groups I, II, V and VII. Other findings, however, such as the guanine-cytosine ratio, increased salt tolerance, failure to produce indole, a negative lysine decarboxylase test, and a positive Kanagawa test put them in a different category than the well recognized Vibrio parahemolyticus, other vibrios and the genus Aeromonas.

Studies for enterotoxin revealed that culture filtrates did contain a heat labile toxin that produced fluid in the ligated small intestine of rabbits. The organism also produced a partially heat stable mouse lethal toxin which killed mice within three hours when given intraperitoneally. Preliminary studies suggest that both the fluid accumulating toxin and the mouse lethal toxin are non-antigenic.

Detailed clinical studies of 34 cases of acute diarrhea associated with these organisms revealed that all patients had diarrhea, 97% had vomiting, 35% had fever and 75% had a history of abdominal pains. 67% presented with moderate to severe dehydration. In 75% of the cases, the stool on microscopic examination revealed a large number of pus cells and red blood cells. In particular, patients infected with the

Heiberg Group VII organisms had bloody or red stools, fever, and a leucocytosis.

Because of the possibility that these vibrio-like organisms were only coincidentally associated with a diarrhea produced by another agent, isolations of E. coli were obtained from the stools of 41 cases and tested for heat stable (ST) and heat labile (LT) enterotoxin. Eleven cases proved positive for both ST and LT, three cases were ST positive and one was LT positive. In a concurrent study of similar cases at the Matlab hospital paired acute and convalescent sera were obtained from fourteen patients. Surprisingly, none showed a rise in antibody titers against the organism found in their stool over the course of their illness.

Epidemiological studies to determine the association of these organisms with illness in family contacts and with environmental contamination were undertaken in both the urban and rural areas by following up families of hospitalized cases with rectal swab and environmental cultures of a period of ten consecutive days. Primary attention was focused on the Group III organisms which accounted for more than 50% of the hospitalized cases.

The results were strikingly unrevealing. In the urban studies among 159 family contacts of 29 index cases infected with the Group III organisms only one had a positive rectal swab culture with the same organism. Similarly, in family studies undertaken in the rural areas none of 1,175 rectal swabs taken from household contacts of hospitalized cases yielded Group III organisms. Food and water jars within the house were routinely negative and only five of 325 surface water samples had low numbers of Group III organisms.

The results of these studies, particularly with the Group III organism leave uncertain the question of whether or not these organisms were actually the cause of the diarrheal episodes seen in the hospitalized cases. It is clear that the Group III organism found in the stools of acute diarrhea patients

were not a common inhabitant of the local environment of the case or of the stools of healthy family contacts. Because of the association of enterotoxigenic E. coli with a significant number of these cases, it is possible that these cholera-like vibrios were only coincidentally associated with the diarrheal episode. Studies on this problem are continuing.

c. Studies of cholera transmission in rural households: The transmission cycle of cholera in endemic areas is unarguably associated with contaminated water, but the actual path of the organism from one infected host to other susceptibles has not been studied definitively. Interest in this subject has been sharpened recently by studies at the CRL which show that simply providing safe water for drinking, for example by drilled wells, has not been sufficient to reduce the incidence of cholera when contaminated surface waters in canals and tanks is available for other uses.

Because surface waters, such as canals and rivers, have such large volumes, permitting substantial dilution of fecal contamination, the question has arisen as to whether such low doses of Vibrio cholerae, as may be detected in these waters, can actually cause disease or whether or not there is a bacterial multiplication step, for example, in contaminated food. Knowledge of these details of cholera transmission dynamics is important in understanding both the level of host susceptibility to infection as well as in devising methods to interrupt its spread.

A study design to look at these questions was undertaken in the Matlab area during the 1976/77 cholera season. When a cholera case was admitted to the hospital, the Bari (neighbourhood) was immediately visited and the water sources in contact with the patient were subjected to intensive epidemiological, environmental and microbiological surveillance. The infection status of all persons in the study area and contamination of all potential environmental vectors (surface water, tube-well water, cooking and drinking jars, pots and utensils, food, food pre-

paration surfaces and hands) were monitored daily or at more frequent intervals for at least eight days.

Thirteen Baris involving 695 individuals in 118 families were studied. Field follow-up revealed that 47 of these persons ultimately were infected with V. cholerae. Virtually all cases of infection could be linked to the use of demonstrably contaminated surface water for bathing and/or for cooking. Detailed analysis suggested that exposure to contaminated cooking water was a much greater risk factor than bathing. Actual food contamination was detected only twice in 1,500 samples and in neither case could it be linked with human infection.

The study clearly suggested that the cooking water was contaminated before being brought into the house and that water contamination within the house was rare. For example, drinking water jars filled from tube-wells were not contaminated even though they were kept side by side with cooking jars and dipped into in identical fashion. Further, over 1,400 finger and utensil washes taken during the study were uniformly negative. Under these circumstances it is difficult to support the view that in-house transmission occurred.

In terms of infectious dose, the study suggested that the dose which most people receive rarely exceeded 1,000 organisms per exposure. It thus appeared that frequent exposure to relatively low levels of V. cholerae was the normal means of transmission in this environmental situation. The infection rate with these doses was 8.8% with a ratio of asymptomatic excretors to clinical cholera at about 25 to 1, while the ratio of mild diarrhea cases to clinical cholera was 10 to 1.

d. The relationship between water consumption and dysentery: In contrast to cholera which is typically considered to be a water borne disease, shigella dysentery has been classified as a water washed disease. This is based on studies in some areas which have suggested that the incidence of dysentery is less dependent on the quality of water than on the quantity of water that

may be available; that is, it seems more directly related to the level of cleanliness and hygienic practices of the families in the community.

Field studies were undertaken in Teknaf at the southern tip of Chittagong to establish the relationship between the quantity of water used and the incidence of dysentery and shigellosis. This area was selected because of a high frequency of dysentery and because the locality has a problem with limited water supply.

The study covered a population of approximately 4,000 and the study design involved a questionnaire survey to obtain information from each family on the quantity of water carried for both drinking and washing from the communal wells. The quantity was estimated based on the number of water pitchers carried, since essentially all water pitchers in the area were manufactured locally with a standard design. Regular household surveillance of diarrhea was carried out over a twelve month period with rectal swab cultures collected for specific diagnosis of shigella.

The results indicated a strong association between the amount of water used and incidence of diarrhea. Among families where the water used was less than 20 liters, per capita, per day, the annual attack rate for clinical dysentery was 31% and for confirmed shigellosis was 5.4%. For families using more than 30 liters, per capita, per day, the rates were 19% and 2.8%. These data indicate that the quantity of water available may be associated with the incidence of dysentery, presumably through its association with better hygienic practices, such as washing hands, food utensils, etc. Confirmation of these observations will require expanding the study to a variety of ecological areas where there is greater variability in availability of water. This will determine how much effect increasing the volume of water available can have in reducing the problem of dysentery in these rural areas.

e. Ecological studies of vibrio species in canal and tank environments: Because of the strong association of V. cholerae with water borne transmission,

systematic observations were undertaken to better define the behaviour of *Vibrio* species in natural waters in localities that had a history of high cholera incidence. The study focused on detecting variations in the concentration of *Vibrio* species associated with different micro-environments (water, sediment, plants, phyto $\bar{7}$, and zooplankton) as a function of season. One closed tank and one tidal canal were selected for study in village Meharon in Matlab.

Distinctive differences were found between the physico-chemical characteristics of the study tank and canal areas. The non-mixed tank, for example, developed strong oxygen and pH gradients throughout the day during periods of intense sunlight. The complete mixing of water by tidal flow in the canal prevented this almost completely.

V. cholerae was not detected at the sampling sites during the year; however, non-agglutinable strains of *Vibrios* were frequent. These *Vibrios* were isolated from many places in both the tank and the canal and the organisms could not be associated with sediment, phyto $\bar{7}$, or zooplankton unlike some other *Vibrio* species.

A highly significant association between NAG *Vibrios* and water hyacinths was observed. This observation was extended to V. cholerae, El Tor through laboratory tests in model tanks. These studies confirmed that El Tor *Vibrios* adhere strongly to all surfaces of the water hyacinths within minutes of exposure. Plants placed in contaminated water concentrate El Tor *Vibrio* at a level 10 to 50 times over the surrounding water. Further, organisms attached to the plants appear to maintain their viability better than those free in the water. Further studies on the range of this phenomenon in natural waters are being undertaken. It is possible that the adherence of these pathogens to plants such as water hyacinths which move great distances with tidal flow could play an important role in cholera transmission in the low-lying riverine areas.

f. Water use practices and perceptions: Because the incidence of diarrheal diseases and cholera in particular is so strongly linked to the quality and quantity of water that a village family uses, it is important to document actual water use practices. More important is an understanding of the attitudes and perceptions of the villagers about suitability of different sources of water for different purposes. Only through this means can a rational foundation be laid for intervention programs which could improve the situation.

An indepth study on water use practices and perceptions of a group of 180 families in one village in Matlab has been initiated. Data are being collected through interviews obtained once every three months. Families are questioned about the source and quantities of water used for different purposes by different family members. Open ended questions are asked about the suitability of different sources of water and a series of questions are asked about factors that may effect the attractiveness of a water source such as ownership, quality of the water and distance. These data will be incorporated into a formal analytical model to assess the strength of the various potential determinants of water use choices.

Based on the results of this localized indepth study, there are plans for extension of this investigation to a variety of ecological sites throughout Bangladesh by more limited cross-sectional surveys.

g. Use of organic waste materials: The improper disposal of fecal waste is obviously another important link in the chain of events facilitating diarrheal disease transmission. Typically, efforts to introduce sanitary latrines into the village setting have been totally unsuccessful; often because the villagers do not perceive directly the benefits that might be derived from their use. A technological advance that has been recently proposed as a solution to this problem is the introduction of bio-gas generators. Both human fecal waste and other organic waste are

collected in these containers and through bacterial action produce gas which can be used for cooking and ultimately residual product is left which is free of harmful organisms and suitable for fertilizing the land.

There are unfortunately some potential drawbacks to this technology in terms of the village economy. Successful introduction of bio-gas generators assumes that in addition to human feces, other organic waste, such as cow dung and rice straw, which are required for its operation, are not otherwise being put to practical use in the village. This, in fact, is generally not the case. Typically there may be a well-established pattern of use of these materials that is intimately linked to the social and economic structure of the community. Thus, the introduction of a new technology may not simply have a health benefit, but could have an undesirable social impact.

A study has been initiated in one village in Matlab to elucidate the relationship between the patterns of use of organic material and the social structure. A census, including income, land use patterns and work habits, was taken covering all the families in the village. Fifty families were then selected for intensive, fortnightly surveys. Data are collected on work activities by the people and animals, on the production and distribution of food, on the use of organic materials for feed, fertilizers and fuel and on agricultural inputs. Measurements are taken of organic materials which are used. This work is currently in progress and analysis of the results are not yet available.

h. Health consciousness in rural populations: Fundamental to the control of diarrheal diseases in the rural setting are personal and household hygienic practices. These in turn are dependent on the awareness that individuals have about the causes and prevention of disease. In order to devise rational health education programs or to achieve acceptance of safe water supplies or latrines, it is important to determine what is the level of knowledge about disease transmission among village populations.

Two hundred families in the Teknaf area were selected for an interview survey with questions covering hygienic practices, knowledge of enteric diseases, parasitic infestations and nutrition. Some of the findings were as follows:

Only twenty percent were aware that indiscriminate defecation might spread disease. Almost 50% felt it caused no harm. Interestingly, 98% were willing to make a latrine near their home, though only 35% indicated a willingness to pay the expense of installation.

With reference to the acquisition of intestinal worms in children, only 3.5% were aware that walking bare-foot could result in hook worm and there was essentially no knowledge as to how other parasites were acquired. Similarly, only 3-5% felt the spread of diarrhea and dysentery was related to polluted water or bad food, though 10% felt it might be acquired on contact with a patient.

When questioned about infant malnutrition, 45% indicated no knowledge of its causes. The majority of villagers did believe that breast feeding should be continued beyond two years. Coupled with this view (which intrinsically may benefit the infant) was the view by 80% of the respondents that the feeding of boiled rice to infants before the age of one year would be harmful by causing intestinal disease. With reference to other foods, only 1% believed children could digest rice, meat and fish before the age of one year, while the majority felt a child had to be over 2½ years old to take these foods.

The results of this survey provide a crude indication of how the level of health knowledge in the village relates to patterns of disease transmission and also indicates the very basic levels of health education that must accompany any environmental intervention program.

i. Studies of Fasciolopsis buski transmission: In recent years a number of villages in the Dacca area

have been discovered to be endemic for *Faciolopsis buski*, an intestinal fluke. This large parasite inhabits the small intestine and releases eggs which pass with the stool. If the eggs enter water, they hatch into a miracidium which infects a snail host. After about a month, cercariae are released which swim to a water plant where they encyst. These metacysts are then ingested directly when water plants, such as water chestnuts, or water caltrop, are eaten, or the skin peeled with the teeth.

This parasite has been described in many areas throughout Asia, but there is very limited information about its prevalence in Bangladesh. It is possible that it has been introduced relatively recently since Partition by immigrants from Assam or other areas of India.

Limited epidemiological surveys are being carried out in affected villages to define the exact routes of transmission of this organism and its impact on health. Studies are also being carried out in unaffected villages to determine if environmental factors and snail hosts are present which would be conducive to transmission of the parasite. *Fasciolopsis buski* is not a serious problem in Bangladesh at this time, however, these studies will seek to determine if there is the potential for more extensive spread of this parasite in the coming years.

j. Baby homes and antibiotic resistant diarrheas: The problem of epidemics of severe infections with antibiotic resistant organisms in new born nurseries is well recognized in the Western world. This has not been a problem in most developing countries such as Bangladesh, because all deliveries were done at home and nurseries and orphanages were non-existent. This situation changed in Bangladesh following the 1971 war. Since then several baby homes have been established to take care of war orphans and other abandoned children.

In May 1977 several babies under the age of two months from one baby home were admitted with gastroenteritis. Shigella flexneri was isolated from one

case and found to be resistant to the six antibiotics, tetracycline, ampicillin, chloramphenicol, kanamycin, streptomycin and septrin. Prior to this case the laboratory had never detected a strain resistant to all six antibiotics among over 700 tested. Follow-up cultures of 75 babies at the baby home identified two more Shigella flexneri having the same antibiotic resistance pattern.

Antibiotic sensitivity studies were also carried out on the "normal" E. coli found in these 75 children. Ten strains were found to be resistant to six antibiotics and an additional 32 strains were resistant to five antibiotics. These results in the baby home can be contrasted with a survey of E. coli from the general Dacca population which revealed that only 2 of 28 strains were resistant to 5 or more antibiotics. A similar survey of 18 E. coli from Matlab showed two-thirds of the strains sensitive to all antibiotics and none resistant to more than 3 antibiotics.

In June 1977 babies were admitted from another baby home with fever and diarrhea and found to have Salmonella paratyphosa B which were resistant to ampicillin. Again, a survey of 41 babies in this home revealed that five had E. coli resistant to five or more antibiotics.

The acquisition of antibiotic resistance in bacteria which are pathogenic only for individuals with defective host defenses has become a major problem in developed countries, particularly in hospitals where such susceptibles are crowded together and antibiotic usage is high. These studies indicate that with the establishment of similar facilities such as nurseries, coupled with intensive antibiotic usage, the same problems of antibiotic resistance are appearing. This issue is of much more concern in a developing country situation like Bangladesh than in the Western world, primarily because not only may relatively non-pathogenic bacteria be involved but serious pathogens as well. These are not limited to hospital environments, but circulate freely throughout the community because of the poor environmental living conditions of the population.

NUTRITION

Malnutrition is one of the many manifestations of poverty. As such, its causes and consequences are multi-dimensional. Consequently, CRL scientific activities aimed at improving nutritional well-being draw upon a variety of disciplinary skills and, because of its institutional comparative advantages, are targeted primarily toward those aspects of malnutrition most intimately related to the diarrheal diseases and gastrointestinal function. The scientific work of the past year that reflects these considerations may be categorized into three broad headings: infection and nutrition; growth and development of children; and breast-feeding.

1. INFECTION AND NUTRITION

It is well established that infection worsens nutritional status and, conversely, that malnutrition compromises host resistance against infection. The interlocked problems of infection and malnutrition are particularly significant with diarrheal illnesses, since these diseases are highly prevalent in poor countries often accounting for over one-third of deaths among pre-school children. Diarrheal diseases affect nutritional status by (1) reducing food intake (through loss of appetite, interruption of breast-feeding, and/or culturally reinforced changes of feeding practices in response to illness); (2) interfering with the absorption of nutrients (malabsorption); and (3) causing wastage of nutrient utilization by the body. The relative importance and mechanisms of these nutrient-loss pathways and the potential beneficial impact of infection control on nutritional status are considered high research priority by CRL scientists. Several exploratory studies were conducted on the role of infections in compromising nutritional status and, conversely, on the significance of malnutrition in reducing host defence against infection. In these studies, infection included not only bacterial and viral etiologic agents but also parasitic infestations, such as ascariasis, hookworm, giardia and Fasciolopsis Buski.

a. Measles, malnutrition and dysentery: One example of infection-nutrition research is the field study in Teknaf in 1975-76 during an epidemic of measles. In addition to documenting the considerable weight loss, morbidity, and mortality impact of the epidemic, the study noted that the attack rate from shigellosis was significantly higher among children recovering from measles as compared to non-measles children. The findings suggest that reduced host resistance, possibly due to compromised nutritional status, consequent upon one infection may enhance vulnerability to another infection. Thus, immunization against measles will not only prevent measles but may also secondarily interrupt the vicious spiral of infection, reduced host resistance, and reinfection.

b. Nutrition and diarrhea morbidity and mortality: The importance of nutritional status on diarrheal disease morbidity was documented in a study of hospitalized cholera patients. Ninety-seven cholera cases were classified according to nutritional status and the course of hospitalization was followed. Malnourished patients were found to experience a significantly longer duration (30-70%) of cholera diarrhea than normally nourished counterparts. The increased stool loss was unrelated to antibiotic usage, to the presence of parasites, or to the diet given. These findings are consistent with the hypothesis of increased debilitation and morbidity among malnourished cholera victims.

In another study, the mortality experience of 945 children hospitalized for diarrheal diseases was examined according to nutrition status at admission. Despite advanced therapeutic intervention, the mortality rate among malnourished children was over three-fold that of the normally-nourished children. The results indicate that malnourished diarrheal patients presenting to health care facilities receive greater-than-normal medical attention, and even under the best of circumstances, may do poorly.

c. Malabsorption: Previous studies at the CRL have documented a high prevalence of sub-clinical mal-

absorption of nutrients among otherwise normal residents of Bangladesh and other poor tropical countries. When stressed by acute diarrhea, these individuals may experience a further deterioration of gastrointestinal absorptive capacity due to reduction of mucosal enzymatic activity and/or decreased transient time of food through the gastrointestinal tract.

Two studies are in progress to assess the potential nutritional significance of the sub-clinical absorption defect. One metabolic study is attempting to measure the impairment of nutrient absorption among otherwise normal Bangladeshi children. Another study is focusing on the impairment in the absorption of lactose (a constituent of milk), utilizing the "hydrogen breath test" as a simple field procedure.

Gastrointestinal nutrient losses during episodes of acute episodes of acute diarrhea are being examined in two other studies. One is attempting to measure the loss in absorption of food (local diet) during the active purging phase of diarrhea. Another study attempting to measure the active protein losses through the gastrointestinal tract which occur during dysentery. These studies should contribute to a better assessment of the relative importance of malabsorption and diarrheal illness as contributing factors to malnutrition in Bangladesh.

d. Analytical studies: In efforts to identify the role of public health interventions in improving nutrition, two analytical studies were undertaken. In the first a conceptual framework was developed to scrutinize the potential importance of various nutrient-loss pathways related to infectious diseases, particularly the enteric diseases. Research lacunae were identified and the potential consequences of three public health interventions - immunoprophylaxis, antibiotic feedings, and environmental sanitation (water supply, and personal hygiene) - were assessed. Preliminary results suggest that although overall loss of nutrients from infection may be small in magnitude, these losses, when confined to specific population sub-groups, may be significant in contributing to acute malnutrition.

A second study examined the pattern of diarrheal disease morbidity and mortality in the Matlab study area and concluded that: (1) diarrheal morbidity remains largely hidden from centralized service facilities- (2) diarrheal morbidity is associated with poor nutrition status; and (3) morbidity control needs to be considered, along with mortality control, in the selection of appropriate intervention strategies.

2. GROWTH AND DEVELOPMENT

Over the past several years the CRL has been conducting two longitudinal studies on the growth and development of pre-school children in rural Bangladesh. These studies, located in Matlab and Teknaf, have obtained detailed data on anthropometry, illnesses (particularly diarrheal diseases), and selected dietary information to study the effects of health and nutrition on growth and development. The Matlab study consists of bi-weekly visits and health care services since 1974 for 400 children under age ten in the village of Meheran; the Teknaf study began in 1975 and involves weekly visits and health care for 300 children under age three years.

a. Meheran growth study: Preliminary analysis of the longitudinal Meheran data has generated useful growth and development anthropometric standards (weight, and height, head, chest, and arm circumference, and cranio-coccyx and leg length) for rural Bangladeshi children. In addition to documenting the lower-than-Western growth patterns, the analysis has identified low birth weight, failing growth after the first six months of life, inadequate and tardy food supplementation, and repeated episodes of infectious diseases as important variables retarding normal growth. In-depth analyses are underway to pin-point with more precision the relative importance of these factors.

b. Teknaf growth study: With nearly two years of prospective observation (including weight, height, illnesses, and dietary intake among a small subsample), the Teknaf study data are now in the

process of preliminary analysis. One striking relationship thus far documented is the close association between dysentery and growth and development. A parallel, but distinctly lower, growth curve was noted among the dysentery victims. It is not yet known whether this association reflects the consequences of dysentery on nutrition or the increased susceptibility of the malnourished to dysentery infections.

3. BREAST-FEEDING

No other sociobiological practice is as important as breast-feeding in determining the nutritional well-being of mothers and children. Breast milk is acceptable, inexpensive, readily available, and possesses unparalleled nutritive and anti-infectious properties. Furthermore, breast-feeding has contraceptive effects, protecting the health of mother and child against the deleterious consequences of short birth-spacing. Because of its crucial role in infection prevention, nutrition, and birth-spacing, breast-feeding has received much scientific attention from CRL researchers over recent years. These investigations have attempted to identify the pattern of breast-feeding and supplementation, particularly in rural Bangladesh and to examine the role of breast milk in maternal-child nutrition.

a. Breast-feeding patterns: Earlier longitudinal studies at CRL reported that the median duration of full breast-feeding in Bangladesh is about ten months. Full weaning does not customarily take place until the on-set of the next pregnancy, making rural Bangladesh one of the most intensive and extended breast-feeding societies worldwide. Two prospective field investigations on growth and development in Matlab and Teknaf discussed earlier, when analyzed, will provide more indepth information on patterns of breast-feeding and supplementation. During 1975-77, however, another specially-designed longitudinal study of 200 women was completed in Matlab on the pattern, intensity and duration of breast-feeding.

At fortnightly intervals closely supervised observations on actual breast-feeding practices were observed over an entire day combined with detailed information on dietary practices, supplementation, and women's work. These data are currently being processed and when completed, will provide additional information on means to promote adequate nutrition for children via breast milk, to foster earlier and more food supplementation of children, and to extend the protection afforded by breast-feeding against infection and short birth-spacing.

b. Lactation and nutrition: One central question related to breast-feeding is the adequacy of breast milk for infant well-being, particularly among malnourished mothers. A prospective study is underway among a series of poor, primiparous urban mothers in Dacca to define the volume and composition of breast milk, to relate these findings to maternal and infant nutrition status, and to identify appropriate means of nutrient supplementation to mothers to improve breast milk production.

A battery of nutritional measurements are being obtained from mothers and infants and the 24 hour volume and composition (solids, protein, fat, lactose, carotene, and vitamin A) of breast milk are determined fortnightly. At 16 weeks post-partum, the mothers and children are admitted to a metabolic ward for six weeks to study the effects of dietary supplementation on milk production. Preliminary results suggest that maternal food supplementation can improve lactation performance but the significance and optimal type and timing of such an intervention have not yet been defined.

POPULATION

During 1976-77, the Population group operated three major field programs in an effort to identify the patterns, determinants, and consequences of high fertility and high mortality in Bangladesh, with an aim of meeting basic needs in fertility regulation and improved health and welfare. The three programs are: a demographic surveillance project; a contraceptive distribution project; and a field study of the determinants of natural fertility.

1. DEMOGRAPHIC SURVEILLANCE

The CRL has maintained continuous vital registration systems in Matlab thana, in central Bangladesh since 1966 and in Teknaf thana on the southern coast since 1974. The Matlab program covers a population of 264,000 residing in 233 villages and the Teknaf system encompasses a population of about 40,000. These two field surveillance areas have become increasingly valuable resources of the CRL. Accurate vital rates and the capacity to maintain ongoing surveillance of specific parameters provide an essential back-bone for field research in diarrheal diseases, population and nutrition. Accurate vital rates are particularly important for the assessment of the impact of various programmatic and technologic interventions.

a. Demographic trends: Crude birth, crude death, total fertility and infant mortality rates in the Matlab surveillance area since 1966 are shown in Table 1. The moderately high birth rate remained basically stable over the ten-year period, except during 1975, one year following a severe national food shortage. The death and infant mortality rates similarly fluctuated during the 1974 crisis and also during the War of Independence in 1971.

More detailed analyses of the fluctuating fertility rates have identified the important role of social dislocation - including temporary migration,

Table 1

Trends in Fertility and Mortality in the Matlab
Field Study Area, 1966 - 1975^a

Year ^b	Crude Birth Rate	Crude Death Rate	Infant Mortality Rate	Total Fertility Rate
1966	46.8	16.0	111	6.7
1967	45.2	17.2	125	6.4
1968	46.4	15.7	124	6.7
1969	45.2	15.1	128	6.6
1970	43.6	14.6	131	6.4
1971 ^c	44.5	21.3	147	6.5
1972	41.8	16.4	129	6.1
1973	47.8	14.6	129	7.3
1974 ^d	40.1	20.0	167	6.1
1975	27.6	18.2	150	4.2
1976	(43.2) ^e	(14.8) ^e		

^a These data are for 110 villages (original population 113,000).

^b Twelve months beginning April of each year.

^c War

^d Food shortages

^e Provisional data from 228 villages.

separation and delayed marriage - and possibly biological variables such as malnutrition, disease, and fetal losses in reducing fertility during periods of crisis. Malnutrition and diarrhea and other infectious diseases, operating independently and in combination during the crisis, were shown to be important contributors to mortality rises, particularly among pre-school children and the elderly. The data also indicate that the poor and other disadvantaged sub-groups are the primary victims of disaster. The findings highlight the importance of effective food distribution to areas of greatest need and certain types of health services for disaster relief.

b. Quality of the Matlab Vital Registration Data: A special survey was carried out to examine the quality and completeness of the Matlab registration system. The unusual reliability of the current system was confirmed. Only 1.1% of birth events and 1.9% of death events were missed by the basic field workers but detected by supervisory staff. The most common omissions (5.9%) were marital unions and dissolutions.

c. A new simplified survey technique for the measurement of fertility: Mr. A.K.M. Alauddin Chowdhury has developed a new survey method with a high degree of accuracy for estimating the current annual fertility rate in a population. The "Chowdhury technique" involves taking two cross-sectional surveys for the same group of women at an interval of six months. During each survey the woman is questioned in detail about her current reproductive status, that is whether she is menstruating, is pregnant (and if so the duration of gestation) or experiencing amenorrhea. The second survey after six months obtains the identical information, and by looking at pregnancy outcomes validates the responses of the first survey. The data obtained from these two pregnancy prevalence surveys can then be used to obtain the seasonal pattern of birth, the crude birth rates, and the age-specific fertility rates.

This survey technique was applied in ten sample villages drawn from the Matlab registration area and was shown to give results closely comparable to those obtained by the entire registration system. For example, there was less than a one percent difference in the estimates for the crude birth rate and the marital age-specific fertility rates.

To test the usefulness of the "Chowdhury technique" under less controlled circumstances, a study is being carried out in collaboration with the Division of Population of the Government of Bangladesh. The technique will be used to provide base-line estimates and follow-up estimates of trends in fertility in one of the Government's "zero population growth (ZPG)" project areas. These extended trials should establish the utility of this technique which could be useful in estimating vital rates for other less developed regions without reliable statistical information.

d. Sociocultural correlates of fertility: Utilizing census registration data, a preliminary investigation was undertaken on the socioeconomic correlates of fertility performance in Matlab. Surprisingly, the findings demonstrated a positive association between fertility and education, land-holding, and household agricultural production. These findings challenge the conventional "demographic transition" theory, developed from the historical European experience, that higher socioeconomic families have lower fertility and higher receptivity to family planning than poorer families. Although the analysis cannot identify the factors responsible for this unexpected finding, future research would explore the role of: varying breast-feeding and other health practices; the status and work of women; and socioeconomic value of children. At the minimum, the tentative results suggest that caution should be applied in transferring the development experience of industrial nations to less developed countries, such as Bangladesh, which are ethnically, culturally, and historically different.

e. Birth spacing and infant mortality: A series of analyses were undertaken on the effect of birth spacing on fetal and infant mortality. The studies demonstrate that short birth intervals (less than 12 months) are strongly associated with higher fetal losses, and poorer survivorship of the older child. Possible explanations of this higher risk are: overlap between lactation and pregnancy; poor breast-feeding; and competition between the fetus and the nursing infant for maternal resources, both biological and social.

A projection of these findings was made to estimate the health impact of better spacing among mothers in Bangladesh. Although the effect of optimal spacing on still-births and neonatal mortality would be marginal, its impact on early fetal and postneonatal mortality could be substantial. The overall conclusion of these studies is that prolonged pregnancy spacing can contribute substantially toward the prevention of unnecessary fetal and infant deaths.

2. CONTRACEPTIVE DISTRIBUTION PROJECT

In collaboration with the Ministry of Health and Population, the CRL has been operating since October 1975, a contraceptive distribution project (CDP) in the Matlab surveillance area. The study design consists of the provision of non-clinical contraceptives (oral pills and condoms) to every household in half the study population (150 villages, population 125,000). The remaining control population of 135,000 residing in 84 villages is serviced by the regular Government program. The aims of the study are: (1) to assess the level of contraceptive demand in rural Bangladesh when service delivery of non-clinical methods is fully adequate; (2) to measure the demographic impact of such a program; (3) to identify the factors influencing acceptance, continuation, and rejection; and (4) to derive information that may improve the efficiency and effectiveness of delivery systems in Bangladesh and other similar countries.

a. Acceptance and demographic impact: Initially 65% of married couples agreed to accept the supply of oral contraceptives in their homes although there was no commitment to use them. Subsequent quarterly prevalence surveys on a 20% sample population showed that in the first three months the prevalence of use in the distribution area increased sharply from 2% to 17%; no significant changes were noted in the control area. Over the ensuing two years, the prevalence of use has steadily decreased in the distribution area to a level of less than 10%.

Studies currently underway indicate that the decline is due both to poor continuation of use as well as diminishing numbers of new acceptors. Since births lag behind conceptions, it is premature to quantitate the demographic impact of the CDP. Initial results on pregnancy prevalence between the program and control populations suggest that, although small, fertility rates may be lower in the program area.

b. Delivery system constraints: Preliminary results from the CDP suggest several constraints to more efficient and effective delivery of services. In addition to problems of demand for contraception and technology appropriateness, users and continuers of oral pills have tended to cluster in pockets within the distribution area. We do not now know whether this clustering phenomenon is due to worker variability or differences in family/community attitudes, modernity, and communications.

Several indepth worker and client surveys have shown other program deficiencies such as infrequency of household visits, limited nature and quality of information provided by the field worker, and lack of effective reassurance and treatment of presumed or actual side-effects. Furthermore, there is evidence that the current field workers may not be optimally suited for their assigned task, since most are elderly women who have never practiced contraception themselves, who may be socially inferior to their clients, and who may accord the extra work of contraceptive delivery (without extra compensation) lower

priority than their customary demographic and diarrheal surveillance activities. More experimentation with field worker training, supervision, deployment, and support services are needed to determine an optimal service delivery strategy.

c. Contraceptive technology: While non-clinical contraceptives possess the advantage of facilitating wide distribution without sophisticated support services, they are nevertheless alien technologies transferred into traditional societies with potential problems of acceptability and use-effectiveness. Special surveys in the CDP indicate that both oral pills and condoms have encountered such problems in rural Bangladesh. The most common complaints from pill drop-outs are: dizziness, irregular bleeding, and other symptomatic complaints and one year continuation rates are less than 30%. Despite intensive publicity, condom knowledge was shown to be limited; only 47% of men correctly identified the method and fewer could describe its proper use. Condoms also presented problems of storage, use, and disposal in village settings.

Smaller scale studies, accordingly, were undertaken to study injectable contraception. Again the results were mixed. Trials of injectable contraceptives in six distribution villages suggested that this method may be an acceptable "back-up" for some dissatisfied pill users, but side-effects including dizziness, weakness, and menstrual irregularities led to poor continuation rates. These studies indicate that the introduction of technologies developed in industrialized countries and for affluent women may not necessarily be the most appropriate in geoculturally different and less affluent populations.

d. "Need" or "Demand" for contraceptives: Although at least 17% of eligible couples demonstrated a desire, by practice, to space or cease child-bearing, an even more important question is why the remaining 83% failed to do so. Preliminary exploration of this and related

issues were addressed by two knowledge, attitude, and practice (KAP) surveys. To estimate the theoretical level of "demand" or "need" for contraception, women were classified according to desired family size and number of living children. Those whose number of children equalled or exceeded reported desires were classified as in "need" of contraception. Such computations suggest that 38.4% of eligible women were potentially in need of contraception. A significant portion of these women, however, expressed a reluctance to contracept in the future. Discounting this group implies that an optimal level of prevalence of use would not exceed 26%.

These estimates were reinforced by surveys utilizing more sophisticated tests of family size preference. These revealed that most women in rural Bangladesh want large families, particularly sons. Thus, despite a substantial unmet "need" for contraceptives, birth rates are high because most women want large families. Unless social and economic change occurs, there is every likelihood that high fertility will persist.

3. DETERMINANTS OF NATURAL FERTILITY

Fertility is the outcome of an interaction between behaviour and biology. To investigate these bio-social determinants of reproduction in rural Bangladesh, the CRL initiated in November 1975 a prospective study of 2,500 women ages 15-45 residing in ten Matlab villages. Every month these women are visited by female workers who enquired about their reproductive, health, and marital status, breastfeeding practices, and separation from spouse, and who obtained nutritional measurements by simple anthropometry. Two years of longitudinal follow-up has provided an unique data base for unravelling some of the biological and behavioural determinants of reproduction in rural Bangladesh.

a. Menarche: The biological land-marks of female reproduction are menarche and menopause. It has been hypothesized that menarche is related to nutrition through the attainment of a critical body weight. Such a relationship has now been clearly established

in Bangladesh. Cross tabulations of girls by age (10-20 years old) and nutrition status body weight indicate that within any age group, the attainment of menarche is strongly associated with body weight. Interestingly, the findings further suggest that nutrition status may relate to age of first marriage, since the onset of menarche may trigger marriage. For example, in the two age groups 10-15 and 16-20, among premenarcheal girls only 2% and 5% respectively are married, while among post-menarcheal girls 27% and 55% respectively are married. This relationship between nutrition, menarche, and marriage takes on added significance because the cohort of girls born in 1961 or later attained menarche at least one year older than earlier cohorts, possibly due to the nutritional crises in the early 1970's. Thus, the widely believed increase in the age of marriage in Bangladesh may have been influenced as much by social response to biological change as by social change per se.

b. Birth intervals: The average interval between births in Bangladesh is approximately three years. This is surprisingly long in a non-contracepting population. The DNF study has shown that the major factor contributing to this "natural spacing" between births is prolonged breast-feeding with lactational amenorrhea averaging 18-22 months. The duration of lactational amenorrhea is briefer among upper socio-economic groups, apparently due to more limited practice of breast-feeding. The duration of lactational amenorrhea was not significantly influenced by maternal nutritional status, contrary to some widely held theories.

Factors that lower the rate of conception when women are ovulating regularly include temporary absences of husbands for occupational purposes, and an unexplained seasonal pattern of conceptions. Nutrition status had little effect on the rate of conception.

These studies underscore the importance of breast-feeding for birth spacing as well as infant

nutrition. This factor becomes particularly important with the introduction of modern contraceptives such as the pill which may interfere with breast-feeding and, if used inappropriately, may provide limited additional protection to couples because of overlap of use with amenorrhea. Further studies on the interaction between breast-feeding, nutrition, birth spacing, and contraception are in progress.

TRAINING

1. RESEARCH TRAINING

a. University Overseas Population Interns: Dr. Sandra Huffman, Graduate Student from the Department of Population Dynamics, Johns Hopkins School of Hygiene, carried out her field investigations for her thesis at Matlab. She was at the Laboratory from January 1975 through January 1977. She received her doctoral degree in June 1977, from Johns Hopkins University. Her thesis topic was "Maternal Nutrition, Breast-Feeding and Lactational Amenorrhea in Rural Bangladesh".

The CRL served in part as a host institution for Mr. Ray Langsten, a Graduate Student from the University of Michigan who was in Dacca for a two year period. During Mr. Langsten's tenure here he completed two KAP (Knowledge Attitude Practice) Surveys, in conjunction with the Contraceptive Distribution Project. Mr. Langsten left Bangladesh in May 1977, and has returned to the Department of Sociology at the University of Michigan where he is now completing his doctoral studies.

b. Oxfam Fellow: Oxfam sponsored Mr. Richard Daniel from the Department of Microbiology, University of Surrey for a research training program in Bacteriology. The program was from September 1976 until August 1977.

c. Rajshahi University - CRL Collaborative Training: Mr. K.M.A. Aziz, CRL Investigator completed a thesis on "Kin Terminologies and Family Structure of Muslims and Hindus in Matlab Thana, Rural Bangladesh" and was awarded the M.Phil. degree from the Institute of Bangladesh Studies, Rajshahi University, in May 1977. He is continuing in this training program for studies leading to the Ph.D. degree.

- d. National Council of Science and Technology Fellows: The CRL is providing a one year research training program for three fellows sponsored by the N.C.S.T.. These are:

<u>Name</u>	<u>Research Area</u>
Khalida Begum, M.Sc.	Microbiology
Md. Serajul Islam, M.Sc.	Ecology
M.H. Chowdhury, M.Sc.	Microbiology
A.S.M.M. Haque, M.Sc.	Ecology

2. 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: WHO sponsored Dr. Nader Nassif Tanious from the Ministry of Public Health, Egypt, on a training course in Cholera and Diarrheal Diseases. The course was from 16 May, 1977 until June 6, 1977.

The Center for Disease Control, Atlanta, sponsored Dr. Mark Oberle who joined the CRL for a three month field research training experience in Epidemiology.

- b. Bangladesh Trainees:

<u>Topic</u>	<u>Trainee Group</u>	<u>Trainees</u>	<u>Courses</u>	<u>Period</u>
Treatment of Cholera	<u>Dacca Medical College Hospital</u>			
	Physicians	41	5	3 days
	Medical Students	18	2	3 days
	Nurses	5	1	1 week
	<u>Ministry of Health</u>			
	<u>Family Welfare</u>			
	Visitors	154	12	1 day- to 2 weeks

<u>Topic</u>	<u>Trainee Group</u>	<u>Trainees</u>	<u>Courses</u>	<u>Period</u>
Basic Micro- biological Procedures	<u>Institute of Public Health Student Lab. Technicians</u>	24	2	9-12 days
	<u>Jahangir Nagar University Laboratory Technician</u>	1	1	3 weeks
	<u>Radder Barner Laboratory Technician</u>	1	1	2 weeks
Animal Caretaking	<u>Atomic Energy Center Scientific Assistants</u>	2	1	2 months
Clinical Pathology	<u>Save the Children Fund Lab. Technician</u>	1	1	2 months
	<u>Institute of Public Health Student Lab. Technicians</u>	20	1	1 month
Parasitology	<u>Johns Hopkins Center for Medical Research Lab. Technicians</u>	3	1	1 month
Fluorescent Antibody Conjugation	<u>Institute of Public Health Lab. Technicians</u>	2	1	2 weeks

<u>Topic</u>	<u>Trainee Group</u>	<u>Trainees</u>	<u>Courses</u>	<u>Period</u>
Laboratory Instrument Analysis	<u>Institute of Public Health Special Trainees</u>	61	1	2 days
Outboard Motor Maintenance	<u>Bangladesh Army Maintenance Technicians</u>	2	1	3 months

3. CRL STAFF DEVELOPMENT

The following CRL employees received special training under CRL sponsorship:

<u>Position of Staff</u>	<u>Course Title</u>	<u>Duration</u>
Private Secretary	Office Management and Communication	2 weeks
Head, Electro- Mecha- nical Branch	Industrial Accidents and Safety Devices	5 days
Statistician (2) Research Associate (1)	Population Research and Evaluation	6 weeks
Special Assistant, Supply Management	1. Personnel Management 2. Office and Adminis- tration Management	1 week 6 weeks
Maintenance Superintendent	Electronics and Tele- communication	6 months (Australia)
Research Assistant (Teknaf)	Nutrition Field Studies	2 weeks (India)

COLLABORATIVE RESEARCH

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

<u>Scientists and Institutions</u>	<u>Nature of Work</u>
Dr. Habib Rahaman Division of Animal Husbandry, Dacca	Parasitological Studies
Atomic Energy Commission, Dacca	Wholesomeness of Fish
Dr. John V. Lee, Public Health Laboratory, Kent, U.K.	Collaborative Work on Vibrio Phage Typing
Dr. G.S. Tawil, Regional Advisor in Health Laboratory Services, WHO, New Delhi	Antibiotic Sensitivity pattern of the commonly occurring pathogens
Mrs. Qudsia Akhtar, Dept. of Biochemistry, Dacca University	Enzymes of bacterial strains
Dr. R. Colwell Dept. of Microbiology, University of Maryland, U.S.A.	Genetic Analysis of <u>Vibrio</u> isolates
Dr. Kamaluddin Ahmed Professor & Director of Nutrition Dacca University	Nutrition Clinical Research
Dr. A.G. Kapikian National Institutes of Health U.S.A.	Special tests for Rotavirus
Dr. George Morris, Microbiologist Center for Disease Control, U.S.A.	Bacteriologic studies of cholera and <u>E.coli</u>
Dr. Bernard Rowe Salmonella and Shigella Reference Laboratory Central Public Health Laboratory Collindale, Avenue London NW9 5HT	Study of enterotoxi- genic <u>Escherichia coli</u>

Scientists and InstitutionsNature of Work

Dr. Atiqur Rahman Khan
Population Division, Ministry
of Health & Population

Contraceptive Distri-
bution Project

Dr. Robert Potter
Professor, Dept. of Sociology
Brown University, U.S.A.

Analytical models on
the interrelation-
ships of contraceptive
practice, breast-
feeding and child
spacing

Dr. John Kantner, Chairman
Dept. of Population Dynamics
Johns Hopkins University

Demographic data
analysis

Dr. Bradley Sack
Department of Medicine
Johns Hopkins University
Baltimore, Maryland

Enteric disease
immunology and
clinical studies

Dr. Nate Pierce
Department of Medicine
Johns Hopkins University
Baltimore, Maryland

Enteric disease
immunology and
clinical studies

Cholera Panel
National Institutes of Health
Bethesda, Maryland, U.S.A.
and
Bangladesh Medical Research Council
Dacca
and
Wellcome Research Laboratories
Wellcome Foundation
Kent, England

Cholera vaccines
development

PUBLICATIONS AND PAPERS

1. PUBLICATIONS

Ali, S. and Aziz, K.M.S., A Systematic Account of Molluscan Fauna of the St. Martin Island, Bangladesh. Bangladesh J. Zool. 4 (2):85-95. 1976.

Aziz, K.M.A., Kin Terminologies & Family Structures of Muslims and Hindus in Matlab Thana and Neighbourhood. Rural Bangladesh. Research Bulletin. Institute of Bangladesh Studies. University of Rajshahi, Vol. 2 in press 1977.

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Aziz, K.M.S., Toxic phytoplankton in some aquatic environments in Bangladesh. Proceedings of the Conference on Human Ecology, Atomic Energy Centre, Dacca. (In Press). December, 1976.

Chowdhury, A.K.M.A., Double Round Survey on Pregnancy - Prevalence and estimate of traditional fertility rates: Proceedings of International Population Conference, Mexico City, 1977. Published by IUSSP, Liege, Belgium.

Chowdhury, A.K.M.A., and Chen L.C., Dynamics of the Contemporary Famines: Proceedings of International Population Conference, Mexico City, 1977. Published by IUSSP, Liege, Belgium.

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~~doi~~ Haq, I. and Aziz, K.M.S., Changing antibiotic sensitivity pattern of the commonly occurring organisms causing dysentery. Bangladesh Med. J. 5(4): 119-125. 1977.

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* Huq, M.I., Kibryia, G., and Huber, D., Isolation of Urease Positive *Vibrio Parahaemolyticus* Strain from Human Cases - Infection & Immunity, (in Press), September, 1977.

~~Am~~ Huq, M.I., The Efficacy of Enrichment Media in the Diagnosis of Inapparent Infections with *Vibrio Cholera*. Bangladesh Medical Journal, (in Press), September, 1977. Vol. 6(2) Oct

* Huq, M.I., Alam, A.K.M.J., Studies on the *Aeromonas Shigelloides* Isolated from Cases of Human Diarrhea. Journal of Medical Microbiology, September, 1977.

✓ Huq, M.I., Intestinal Bacterial Flora in Normal Healthy Adults in Bangladesh. Indian Journal of Medical Research, July, 1977.

* Mosley, W.H., Osteria, T., Huffman, S.L., Interactions of Contraception and Breast Feeding in Developing Countries. Social Biology (in Press), 1977.

✓ Rahaman, M.M., Majid, M.A., Alam, A.K.M.J., and Islam, M.R., Effects of Doxycycline in Actively Purging Cholera Patients: A Double-Blind Clinical Trial. Antimicrobial Agents & Chemotherapy. 10:610-612, 1976. 10(4) Oct

~~Am~~ ✓ Rahaman, M.M., Mia, M.A.L., Khan, A.R., Khan, A.K., Rahman, Mahbubur, Huq, Mostaqul, Khan, A.Q., and Zoha, M.S., A Survey of Basic Health Information of Rural Bangladesh. BMRC Bulletin. 3:70-76, June, 1977. 3(4) Jun

~~Am~~ ✓ Swenson, I., Expected Reductions Fetal and Infant Mortality by Prolonged Pregnancy Spacing in Rural Bangladesh. Bangladesh Development Studies. 5:1-16, 1977.

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2. ABSTRACTS

Quader, S.Z.A., Al-Mahmud, K.A. and Aziz, K.M.S., Laboratory animal production in Bangladesh with indigenous feedstaff diet. Abstracts of the Second Annual Conference of the Bangladesh Association for the Advancement of Science, University of Mymensingh, p.C-23-24. January, 1977.

Ali, A. and Aziz, K.M.S., A modified method for the determination of copper in human serum. Ibid, p.C-25. January, 1977.

Aziz, K.M.S., Rahaman, M. and Ali, A., Nutritive Value of some fruits and vegetables of Bangladesh. Ibid, p.C-25. January, 1977.

Aziz, K.M.S., Rahaman, M. and Ali, A., Vitamin C, B Carotene & Vitamin A levels of some fruits of Bangladesh. Abstracts of the First Bangladesh Botanical Convention, University of Dacca, p.11.

3. CRL PUBLICATION SERIES

<u>Author</u>	<u>Title</u>	<u>Date</u>
CRL	Annual Report 1976	May, 1977
George T. Curlin, K.M.A. Aziz and M.R. Khan	The influence of drinking tubewell water on diarrhea rates in Matlab Thana, Bangladesh	June, 1977
A.K.M. Alauddin Chowdhury	Double round survey on pregnancy and estimate of traditional fertility rates	July, 1977
Moslemuddin Khan, George T. Curlin and Md. Shahidullah	Pattern of medical care for diarrheal patients in Dacca urban area	August, 1977
W. Henry Mosley	The effects of nutrition on natural fertility	August, 1977

<u>Author</u>	<u>Title</u>	<u>Date</u>
Ingrid Swenson	Early childhood survivorship related to the subsequent interpregnancy interval and outcome of the subsequent pregnancy	August, 1977
Atiqur R. Khan, Douglas H. Huber and Makhlisur Rahman	Household distribution of contraceptives in Bangladesh - The rural experience	Sept. 1977
John Briscoe	The role of water supply in improving health in poor countries (With special reference to Bangladesh)	Sept. 1977

4. PAPERS PRESENTED AT SCIENTIFIC MEETINGS

Symposium on Microbiology, Second Annual Science Conference, Bangladesh Association for the Advancement of Science, University of Mymensingh, Mymensingh, January, 1977.

Ahmed, A., and Aziz, K.M.S., Role of Micro-Passive-Agglutination Assay in Antibody-Studies in Blood Dysentery caused by Shiga bacillus.

Huq, M.I., Studies on Cholera Toxin.

First Botanical Convention, Dacca University, Dacca, November, 1976.

Aziz, K.M.S., and Huq, I., Role of Microbiology in the Economic Development of Bangladesh.

Aziz, K.M.S., and Huq, I., Change of Biotype and Serotype of Vibrio cholerae in Cholera Epidemics in Dacca, Bangladesh.

Huq, M.I., Role of Microbiology in the Economic Development of Bangladesh.

National Marine Fisheries Seminar, Department of Marine Biology, University of Chittagong, Chittagong, March, 1977.

Aziz, K.M.S., Pharmacologically Active Compounds from the Sea.

UNESCO Seminar on Man and Biosphere & Social Sciences. Atomic Energy Center, July, 1977.

Aziz, K.M.S., and Rahaman, M.M., Some Aspects of Environmental Health in Rural Bangladesh.

Seminar on Herbal Medicine & Indigenous Systems in Bangladesh. Organized by Proshika (former CUSO), ADAB Auditorim, Dacca, Bangladesh, August 8-10, 1977.

Aziz, K.M.S., Some Aspects of Folk Medicine in Bangladesh.

Aziz, K.M.S., Toxic Aspects of Indigenous Medicine.

Aziz, K.M.S., Aegle marmelos as a Potential Indigenous Medicine for Diarrhea.

First National Statistical Conference, Bangladesh Statistical Association, (March 7-9, 1977).

Aziz, K.M.A., The Methodology of Vital Events Registration in Rural Bangladesh.

Seminar on Association of Bangladesh Scientific Development, February, 1977.

Aziz, K.M.S., Rahaman, M. and Ali, Akbar, Nutrition Value of some Fruits & Vegetables of Bangladesh.

Sanitation in Developing Countries Today - sponsored by OXFAM, Ross Institute of Tropical Hygiene, London, July, 1977.

Briscoe, J., The Organization of Labour & the Use of Human Excreta & Other Organic Resources in Rural Areas of the Indian Sub-Continent.

Workshop on Bio-Gas Systems; sponsored by the Management Development Institute, New Delhi, March 1977, New Delhi.

Briscoe, J., The Role of Bio-Gas Plants in Improving Health in Rural India.

Workshop on Effective Interventions to Reduce Infection in Malnourished Populations; sponsored by U.S. National Academy of Science, Haiti, June 13-16, 1977.

Briscoe, J., The Role of Water Supply in Improving Health in Poor Countries (with special reference to Bangladesh).

Chen, L.C., Morbidity and Mortality Control of Diarrheal Disease: Some Strategic Issues.

Seminar on Fertility in Bangladesh. Cox's Bazaar, Bangladesh, 13-15 December, 1976.

Chen, L.C., Huffman, S.L., and Satterthwaite, P., Recent Fertility Trends in Bangladesh. Speculation on the Role of Biological Factors & Socio-economic Change.

Chowdhury, A.K.M.A., and Curlin, G.T., Recent Trends in Fertility & Mortality in Rural Bangladesh.

Huber, D.H., Khan, A.R., Curlin, G.T. and Langsten, R., Contraceptive Distribution Project in Rural Bangladesh.

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Chowdhury, A.K.M.A., Double Round Survey on Pregnancy & Estimate of Traditional Fertility Rates.

Chowdhury, A.K.M.A. and Chen L.C., The Dynamics of Contemporary Famine.

Huber, D.H., An Experimental Design for Assessing the Effectiveness of Household Contraceptive Distribution.

Swenson, I., Early Childhood Survivorship Related to the Subsequent Interpregnancy Interval & Outcome of the Subsequent Pregnancy.

Conference on Nutrition & Reproduction. National Academy of Sciences and the National Institutes of Health, Bethesda, Maryland, February 13-16, 1977.

Chowdhury, A.K.M.A., Effect of Maternal Nutrition on Fertility in Rural Bangladesh.

World Population Society Conference, Washington, D.C., 5-7 December, 1976.

Chowdhury, A.K.M.A. and Huber, D.H., Fertility & Mortality - Recent Changes in Matlab, Bangladesh.

Annual Meeting of the Population Association of America, St. Louis, Missouri, 21-23 April, 1977.

Chowdhury, A.K.M.A., Huber, D.H., and Curlin, G.T., Fertility & Mortality - Recent Trends in Rural Bangladesh.

Huffman, S.L., Chakraborty, J., and Mosley, W.H., Nutrition & Post Partum Amenorrhea in Rural Bangladesh.

U.S.-Japan Joint Cholera Conference, Sapporo, Japan, October, 1976.

Curlin, G.T., The Effect of Installation of Tube Wells on the Incidence of Cholera in Rural Bangladesh.

Verwey, W.F., Current Concepts of the Pathogenesis of Cholera Infection.

Annual EIS Conference, Atlanta, Georgia, April, 1977.

Huber, D.H., Demographic Impact of Household Contraceptive Distribution in Rural Bangladesh.

Annual Conference of the Bangladesh Medical Association, Dacca, January, 1977.

Hug, M.I., Changing Antibiotic Sensitivity Patterns of the Commonly Occurring Organisms Causing Dysentery.

Khan, M.U., Curlin, G.T., and Chakraborty, J.,
Growth & Development Studies, Meheran, Comilla.

Khan, M.U., Curlin, G.T., and Chakraborty, J.,
Incidence of Blindness in Rural Bangladesh.

Second International Conference on the Rapid Methods & Automation in Microbiology, Cambridge, U.K., September, 1976. Sponsored by UNESCO/IUBS/WHO and Cambridge.

Hug, M.I., A Simple Laboratory Method for the Diagnosis of Vibrio Cholera.

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Khan, M.U., Chakraborty, J., Sarder, A.M., and Khan, M.R., Role of Sources of Water in the Incidence of Cholera.

Rahaman, M.M., Majid, M.A. and Verwey, W.F., Evaluation of Hydration with Oral Electrolyte Solution in Moderate Dehydration Caused by Acute Diarrhea.

Regional Conference "Village and Household Availability of Contraceptives", Tunis, 27-30 March, 1977.

Khan, A.R., and Huber, D.H., Household Distribution of Contraceptives in Bangladesh - Rural Experience.

Thirteenth Joint Conference on Cholera. The U.S.-Japan Co-operative Medical Science Program, Atlanta, Georgia, 1977.

Merson, M.H., Sack, R.B., Islam, S., Saklayen, G., Huda, N., Kibriya, A.K.M.G., Mahmood, A., Ahmed, Q.S., Quader, A., Yolken, R.H., Rahaman, M., and Kapikian, A.Z., Enterotoxigenic Escherichia coli (ETEC) Disease in Bangladesh: Clinical, Therapeutic & Laboratory Aspects.

Seminar on Natural Fertility. International Union for the Scientific Study of Population, Paris, 21-24 March, 1977.

Mosley, W.H., The Effects of Nutrition on Natural Fertility.

Workshop on Regulation of Fertility During Lactation.
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Foundation and the Ciba Foundation, London, November 23-
24, 1976.

Mosley, W.H., Osteria, T., and Huffman, S.L., Interactions of Contraception & Breast-feeding in Developing Countries.

WHO Research Study Group Meeting on Diarrheal Disease
of Children, New Delhi, September, 1977.

Mosley, W.H., Some Epidemiological Considerations in Research on Diarrheal Diseases in Children.

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Studies. Organized by JHU Fertility Research Project &
Bangladesh Fertility Research Program, Dacca, July, 1977.

Rahman, Makhlisur, A follow-up Survey of Sterilization Acceptors in Matlab, Bangladesh.

Bangladesh Workshop on the National Sterilization Program,
Dacca, June, 1977.

Rahman, M., Huber, D.H., and Chakraborty, J., A Follow-Up survey of Sterilization Clients in Matlab, Bangladesh.

IUNS Conference on "Practical Approaches to Combat Mal-
nutrition". Cairo, Egypt, May 25-29, 1977.

Rahaman, M.M., and Mosley, W.H., Malnutrition & Family Planning.

Bangladesh Workshop "The Role of Injectable Contracep-
tives in Bangladesh". Dacca, 1 March, 1977.

Huber, D.H., Rahman, M. and Chakraborty, J., Injectable Contraceptives in Six Villages of Matlab Thana, Bangladesh - Initial Experience.

5. PAPERS SUBMITTED FOR PUBLICATION

Ahmed, A., Immunologic in-vitro identification of Labile Toxin (LT) Producing Escherichia coli. Lancet.

Aziz, K.M.A., Kin Terminologies & Family Structures of Muslims & Hindus in Matlab Thana & Neighbourhood Rural Bangladesh. M.Phil. Thesis. J. of Institute of Bangladesh Studies, Vol. 2.

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Khan, A.R., Huber, D., Household Contraceptive Distribution in Bangladesh: The Rural Experience in Village & Household Delivery of Contraceptives. Battelle Memorial Institute, June, 1977.

Merson, M.H., Cholera in Nelson's Textbook of Pediatrics, Eleventh Edition. V.C., Vaughn, R.J. McKay, R.E. Behrman (eds), W.B. Saunders Co., Philadelphia.

Palmer, D.L., Koster, F.T., Islam, A.F.M.R., Rahman, A.S.M.M. and Sack, R.B., Comparison of Sucrose & Glucose in the Oral Electrolyte Therapy of Cholera & Other Severe Diarrheas. New Engl. J. of Medicine.

~~done~~ Rahaman, M.M., and Alam, A.K.M.J., Rose Spots in Shigellosis Caused by Shigella Dysenteriae type 1 Infection. British Medical Journal. 1977 Oct 27; 2 (6095): 1123-24

Rahaman, M.M., Majid, M.A., and Monsur, K.A., Intravenous Fluid Therapy in Cholera & Non-cholera Diarrhea: A Comparative Evaluation of Two Solutions Containing Different Concentrations of Sodium. Bulletin of the World Health Organization.

- Rahaman, M.M., Alam, A.K.M.J., Islam, R., Sy.
Dysenteriae l Bacteremia in Children. Journal
of Pediatrics.
- Rahaman, M.M., Majid, M.A., Alam, A.K.M.J., and
Islam, R.M., Effects of Doxycycline in Actively
Purging Cholera Patients: A Double Blind Clinical
Trial. Antimicrobial Agents & Chemotherapy.
- Swenson, I., The Relationship Between Early Fetal
Wastage, Stillbirth & Pregnancy Spacing in Rural
Bangladesh. International Journal of Fertility.
- Yolken, R.H., Greenberg, H.B., Merson, M.H., Sack,
R.B., and Kapikian, A.Z., An Enzyme Linked Immuno-
sorbent Assay (ELISA) for Detection of Escherichia
coli Heat-Labelled Enterotoxin. J. Clin. Microb.

6. CRL SEMINAR PROGRAM

<u>Speaker and Affiliate</u>	<u>Topic</u>	<u>Date</u>
Dr. Brown CRL	Vitamin A	Oct. 8, 76
Dr. M.R. Khan Dacca University	Acidophilic Microorganisms	Oct.22, 76
Dr. Shamsur Rahman Inst. Pub. Health	Quality Control of Drugs	Oct.29, 76
Dr. A.T.M.F. Rahman Sr. S. Officer	Food Resources & Pop. in Bangladesh	Nov. 5, 76
Dr. Michael Merson CRL	<u>E. coli</u> Diarrhea	Nov.12, 76
Dr. John Lee Pub. Hlth. Lab., U.K.	Vibriosis in Britain	Dec.10, 76
Dr. John Briscoe CRL	Rural Sanitation	Dec.15, 76
Dr. Majid Molla Physician, U.K.	Malabsorption in Childhood (Coeliac Disease)	Dec.24, 76
Dr. W. Spira CRL	Environmental Factors in water and food borne diseases	Jan. 7, 77
Mr. Bruce Currey JHU	Areas liable to famine in Bangladesh	Jan.14, 77
Dr. Kenneth Brown JHU	Clinical Aspects of Vitamin A Deficiency	Jan.21, 77
Mr. K.M.A. Aziz CRL	Medical consultation prior to death in rural Bangladesh	Feb. 4, 77
Dr. Akhtar Hussain Imperial Chemical Industries Dacca	Stability of oil in water emulsion by Macromolecules	Feb.11, 77

<u>Speaker and Affilliate</u>	<u>Topic</u>	<u>Date</u>
Dr. Edwin McDaniel McCormack Hospital Thailand	Injectable contracep- tive programs in Northern Thailand	Mar. 4, 77
Dr. W.E. van Heyningen Oxford	The Bipartite Toxin	Mar.10, 77
Dr. Mohiuddin Alamgir Bangladesh Institute for Development Studies	Poverty & social structure of our society	Mar.11, 77
	Film show - The Bare- foot Doctors	Mar.18, 77
Mrs. P. Curlin, Dr. A.R. Khan & Dr. D. Huber CRL	Household Distribu- tion of Contraceptives in Bangladesh - Rural and Urban Experience	Mar.23, 77
Dr. David A. Sack JHU	Enterotoxigenic <u>E.coli</u> in Kenya	Apr. 1, 77
Dr. Trinidad Osteria School of PH, University of Philippines	A prospective study of lactation, contra- ception and birth spacing in urban Manila, Philippines	Apr.22, 77
Dr. Brian Seaton CRL	Reproduction at the zoo: An unusual view of fertility control	Apr.29, 77
Dr. K. Hughes Epidemiologist, WHO Smallpox Eradication Program	Smallpox pock mark and vaccination scar survey in Bangladesh	May 6, 77
Carol Vlassoff Michael Vlassoff Gokhale Instt. Univ. of Poona, India	Studies of Fertility Motivation Behaviour in rural Maharastra	May 12, 77

<u>Speaker and Affiliate</u>	<u>Topic</u>	<u>Date</u>
Dr. F.W. Sheppard Int. Rice Research Inst. Rep. in Bangladesh	A simplified approach to agricultural systems	May 13, 77
Dr. Alexander Langmuir Prof. Harvard Med. School	Solving the mystery of legionairres disease	May 18, 77
Dr. K.M.S. Aziz, I. Huq & Dr. J.Alam	Analysis of a recent diarrheal epidemic - Some clinical and microbiological aspects	May 20, 77
Ray Langsten Graduate Student Univ. of Michigan	Population growth in Bangladesh Recent data from Companiganj and Matlab and speculation about the future	May 27, 77
Dr. Shushum Bhatia Medical Director Kanpur, India	A rural health program in Barielly, India	June 3, 77
Drs. J. Alam & M.U. Khan, CRL	Epidemiology & Clinical Pattern in Non-cholera Vibrios	June 10, 77
Dr. M.M. Rahaman CRL	Practical approaches to combat malnutrition: Findings of the international conference in Cairo.	June 24, 77
Dr. David Sack CRL	Local Immunity and cholera	July 8, 77
Dr. David Nalin CRL	Recent Development in enteric disease research	July 15, 77
Mr. Imdadul Huq CRL	Microbiologic study of baby homes	July 22, 77
Dr. M.M. Rahaman CRL	Water usage and dysentery in Teknaf	Aug. 5, 77

<u>Speaker and Affiliate</u>	<u>Topic</u>	<u>Date</u>
Dr. Richard Feachem Ross Institute, U.K.	Water supply and control of diarrheal diseases	Aug.16, 77
Dr. M.U. Khan CRL	Role of sources of water in the incidence of cholera	Aug.26, 77
Mr. K.M.A. Aziz CRL	Cultural factors in population change	Sept. 2, 77
Dr. Michael Merson CRL	<u>E.coli</u> diarrhea in Dacca- clinical laboratory findings	Sept.13, 77

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 in the Directing Council in FY1977 are shown below:

	Tenure	
	From	To
<u>Government of Bangladesh</u>		
Dr. Mostaqul Huq, Director of Health Services (Preventive)	Jun. 1974	-
Dr. Abdul Quader Khan, Director, Institute of Epidemiology, Disease Control & Research (Malaria Institute).	Aug. 1975	-
Dr. Zakir Hossain, Chief, Health & Population Control, Planning Commission.	Mar. 1976	-
Dr. Yousuf Ali, Professor of Medicine, Dacca Medical College.	Oct. 1976	-
<u>United States Government</u>		
Mr. Michael R. Jordon Chief, Health & Population Division, U.S.AID.	Jun. 1974	Jun. 1977
Mr. Charles R. Gurney, Chief, Health & Population Division, U.S.AID.	Sept. 1977	-
Mr. William T. Oliver, Deputy Program Officer, U.S.AID.	Jul. 1977	Sept. 1977
Mr. Leighton Everson, Budget & Accounts Officer, U.S.AID	Oct. 1976	May 1977

	<u>Tenure</u>	
	<u>From</u>	<u>To</u>
<u>United States Government (Contd.)</u>		
Dr. James Levinson, Chief, Food & Nutrition Division, U.S.AID.	Sept. 1977	-
 <u>British Government</u>		
Mr. Michael C. McCulloch, First Secretary British High Commission.	Mar. 1976	-

SCIENTIFIC REVIEW AND TECHNICAL ADVISORY COMMITTEE

The Scientific Review and Technical Advisory Committee is appointed by the Director of the National Institute of Allergy and Infectious Disease, National Institutes of Health, U.S.A., from nominations received by each participating government and organization.

In FY1977 the Committee consisted of:

Dr. William S. Jordan (Chairman)

NIAID, National Institutes of Health, USA.

Prof. Derrick Rowley,

Department of Microbiology, University of Adelaide,
Australia.

Dr. Donald M. Mackay,

Deputy Director, London School of Hygiene & Tropical
Medicine, UK.

Dr. M.A. Latif,

Officer on Special Duty, Institute of Public Health,
Government of the People's Republic of Bangladesh.

The Committee held its meeting at the CRL from February 22 to March 1, 1977 and the following consultants were present:

Dr. John P. Craig,

Professor, Department of Microbiology and Immunology,
Downstate Medical Centre, State University of New
York.

Dr. Eugene Gangarosa,

Chief, Enteric Disease Branch, Centre for Disease
Control, Atlanta, Georgia.

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 in 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, 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 licence. 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. Licenced 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, Bangladesh. 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 History & Culture, Dacca University. Lay Person. Contribution as a woman and non-scientific person.

Dr. A.K.M. Jamiul Alam, B.Sc., M.B.B.S., Post Graduate Training in Medicine & Intestinal Diseases in the United Kingdom. Chief Physician, Cholera Research Laboratory, Dacca. Registered Medical Practitioner in Bangladesh. Clinician. Contribution as a clinician.

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 & Reproductive Endocrinology. Contribution in the field of laboratory sciences.

STAFF OF THE CHOLERA RESEARCH LABORATORY

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

Investigators:Research Area

Brian Seaton, Ph.D.	Biochemistry
David Sack, M.D.	Clinical-Immunology
John Briscoe, Ph.D.	Environmental Sciences
Kenneth Brown, M.D.	Pediatric-Nutrition
K.M.A. Aziz, M.A., M.Phil.	Anthropology
Md. Rafiqul Islam, M.B.B.S.	Clinician
Md. Serajul Islam, M.B.B.S.	Clinician
Md. Yunus, M.B.B.S.	Clinician
Michael H. Merson, M.D.	Epidemiology
Robert E. Black, M.D.	Epidemiology
Robert Gilman, M.D.	Clinical-Parasitology
Lado T. Ruzicka, M.A., Ph.D.	Demography
Shushum Bhatia, M.B.B.S., M.P.H.	Maternal Child Health
Trinidad Osteria, Sc.D.	Demography
William M. Spira, Ph.D.	Microbiology

Scientific Branch Heads:

Abdullah Al-Mahmud, M.Sc. (Vet.)	Animal Resources Branch
Akbar Ali, B.Sc.	Biochemistry Branch
A.K.M. Alauddin Chowdhury, M.Sc.	Statistics Branch
A.K.M. Jamiul Alam, M.B.B.S.	Physicians Branch
Ansaruddin Ahmed, M.B.B.S.	Immunology Branch
A.S.M. Mizanur Rahman, M.B.B.S.	Matlab Hospital Branch
Md. Imdadul Huq, M.Sc.	Microbiology Branch

Scientific Branch Heads: (Contd.)

Makhlisur Rahman, M.A.
 M.H. Munshi, M.B.B.S.
 Moslemuddin Khan, M.B.B.S., D.P.H.
 M.S. Islam Khan, M.A.

Matlab Field Surveillance Br.
 Teknaf Dysentery Project Br.
 Community Studies Branch
 Library & Publications Branch
 (Acting)

Mrs. P. Biswas

Dacca Hospital

Administrative Branch Heads:

Abul Kalam Azad, M.A., LL.B.

Personnel Management Branch
 (Acting)

Mr. Rabindra Nath Majumder
 Mr. A. Razzak
 Mr. M. Mujibur Rahman
 A.K.M. Abdul Matin, B.A.

Supply Management Branch
 Vehicles Maintenance Branch
 General Services Branch
 Matlab Administrative Branch

Mr. A.H. Chowdhury

Maintenance Superintendent

Mr. Noor Mohammad Mermalat
 Mr. M. Sobhani
 Mr. Md. Siddique

Transport Management Branch
 Electro-Mechanic Branch
 Instrument-Fabrication Branch

Personnel Summary:

On September 30, 1977, CRL had 598 fulltime employees and 290 contractual Females Field Workers. Of the total CRL staff, 278 are working in research areas. They may be classified as follows:

1. Scientists (Investigators)	24
2. Physicians	13
3. Technicians	110
4. Scientific Support	131
	<u>278</u>

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	74
3. Lower level	229
	<u>320</u>

CHANGES IN SENIOR STAFF IN FY 1977

	<u>Name</u>	<u>Position</u>	<u>Effective Month/Year</u>
(1)	<u>Promotion and Redesignation</u>		
	Dr. A.S.M.M. Rahman	Chief Physician, Matlab	Oct. 1976
	Dr. Md. Yunus	Dy. Chief Physician, Matlab	Oct. 1976
	Dr. Serajul Islam	Clinical Research Asst.	Jan. 1977
	Mr. Md. Shahabuddin	Controller	May 1977
	Mr. P.O. Weeks	Administrator	May 1977
	Mr. A.K. Azad	Head, Personnel Manage- ment Branch	May 1977
	Dr. K.M.S. Aziz	Scientific Director	July 1977
	Dr. M.M. Rahaman	Scientific Director	July 1977
	Mr. K.M.A. Aziz	Investigator	July 1977
	Mr. Makhlisur Rahman	Head, Matlab Field Surveillance Branch	July 1977
(2)	<u>New Appointment</u>		
	Dr. W.H. Mosley	Director	March 1977
	Dr. Brian Seaton	Biochemist	April 1977
	Dr. Lincoln Chen	Scientific Director	May 1977
	Dr. Robert E. Black	Epidemiologist	June 1977
	Dr. Trinidad S. Osteria	Demographer	July 1977
	Dr. W.B. Greenough	Scientific Director	July 1977
	Mrs. Shamima Moin	Budget Analyst	Aug. 1977
	Dr. Michael H. Merson	Epidemiologist	Aug. 1977
	Dr. Shushum Bhatia	Research Physician	Aug. 1977
	Mr. Badruddin Ahmed	Cost Analyst	Sept. 1977
	Dr. Lado T. Ruzicka	Demographer	Sept. 1977
(3)	<u>Departures</u>		
	Dr. W.F. Verwey	Director	Feb. 1977
	Dr. George Curlin	Division Head	June 1977
	Dr. Douglas Huber	Epidemiologist	June 1977
(4)	<u>Leave of Absence</u>		
	Mrs. Susan Alamgir	Head, Library Branch	June 1977

LIST OF VISITORS
TO THE CHOLERA RESEARCH LABORATORY
OCTOBER 1976 - SEPTEMBER 1977

OCTOBER 1976

- Dr. V.T.H. Gunaratne,
Regional Director, South-East Asian Regional Office,
World Health Organization, New Delhi, India.
- Dr. W.B. Greenough III,
Director, Clinical Scholar's Program, Johns Hopkins
University, Baltimore, Maryland, USA.
- Dr. Mark Oberle,
Epidemic Intelligence Service Officer, Center for
Disease Control, Atlanta, Georgia, USA.
- Professor Stephen J. Richardson,
Bowman Gray School of Medicine, Department of
Microbiology, Wake Forest University, North Carolina,
USA.

NOVEMBER 1976

- Dr. John Bresnan,
Head, Office for Asia & the Pacific, Ford Foundation,
New York, USA.
- Dr. David Bell,
Executive Vice-President, Ford Foundation, New York,
USA.
- Dr. John V. Lee
Public Health Laboratory Service, Public Health
Laboratory, Preston Hall Hospital, Maidstone, Kent,
UK.
- Dr. Nelo Hellman,
Executive Director, International Association of
Pediatricians, Helsinki, Finland.
- Mr. F.O. Pinkham,
Assistant Administrator, AID, Washington, USA.
- Mr. S.D. Biggs,
Fellow, Institute of Development Studies, University
of Sussex, Brighton, UK.

NOVEMBER 1976 CONTINUED

Mr. R.W. Smith,
Assistant Agricultural Adviser (Research),
Ministry of Overseas Development, London, UK.

Mr. J.M. Waller,
Ministry of Overseas Development, London, UK.

Mr. P.T. Walker,
Division of Ecology, Center for Overseas Test Research,
Ministry of Overseas Development, London, UK.

Mr. Barry Kramer,
Asia Correspondent, The Wall Street Journal,
Hong Kong.

Members of the Japanese Aid Mission:

Mr. Mitsuo Iijima,
Leader, Special Assistant, Economic Co-operation
Bureau, Ministry of Foreign Affairs, Tokyo, Japan.

Mr. Mikoto Usui, Professor of Tsukuba University,
Tokyo, Japan.

Mr. Noriyuki Kandori, Official, Planning Division,
Economic Co-operation Bureau, Ministry of Foreign
Affairs, Tokyo, Japan.

Mr. Kenji Miyata,
Official, South-West Asia Division, Asian Affairs
Bureau, Ministry of Foreign Affairs, Tokyo, Japan.

Mr. Akihiro Mitarai,
Deputy Director, Research Section, Japan International
Co-operation Agency, Tokyo, Japan.

Mr. Kojiro Noda, Deputy Director, International
Investment Department, Tokyo Bank, Tokyo, Japan.

Mr. Masaki Komatsu,
Research Officer, International Development Centre,
Tokyo, Japan.

DECEMBER 1976

Visit of Malnutrition Panel - Members:

- Dr. David Coursin, Chairman
Director of Research, St. Joseph's Hospital, Lancaster,
Pennsylvania, USA.
- Dr. Sheldon Morgen, Member
University of California, Berkeley, California, USA.
- Dr. Barbara Underwood, Member
Pennsylvania State University, Pennsylvania, USA.
- Dr. Harold Roth, Member
Associate Director for Digestive Diseases & Nutrition,
National Institute of Arthritis, Metabolism & Digestive
Diseases, National Institutes of Health, Maryland, USA.
- Dr. Josef Brozek, Member
Department of Psychology, Lehigh University,
Bethlehem, Pennsylvania, USA.
- Dr. Gerald F. Combs, Project Officer
Nutrition Program Director, Extramural Programs,
National Institute of Arthritis, Metabolism & Digestive
Diseases, National Institutes of Health, Maryland, USA.
- Mr. Samuel S. Liben,
Centre for Population Studies, Harvard University,
Cambridge, Mass. USA.
- Mr. Peter P. Roger,
Centre for Population Studies, Harvard University,
Cambridge, Mass. USA.
- Dr. L.T. Ruzicka,
Acting Head Department, Australia National University,
Research School of Social Sciences, Department of
Demography, Australia.

JANUARY 1977

- Dr. Andrew G. Dean,
Pacific Research Section, University of Hawaii,
Honolulu, Hawaii, USA.

JANUARY 1977 CONTINUED

Dr. Mahboobuddin Ahmed,
Staff, World Fertility Survey, London, UK.

Mr. Jerry Anderson,
Ford Foundation, New York, USA.

FEBRUARY 1977

Technical Review Committee Members:

Dr. William S. Jordon, Chairman
Director, Microbiology of Infectious Diseases Program,
National Institutes of Health, Bethesda, Maryland,
USA.

Dr. Donald M. Mackay, Member
Deputy Director, Ross Institute of Tropical Hygiene,
London School of Hygiene & Tropical Medicine, London,
UK.

Professor Derrick Rowley, Member
Department of Microbiology & Immunology, The
University of Adelaide, South Australia.

Dr. John P. Craig, Consultant
Department of Microbiology & Immunology, Downstate
Medical Centre, University of New York, USA.

Dr. Eugene J. Gangarosa, Consultant
Chief, Enteric Diseases Branch, Centre for Disease
Control, Atlanta, Georgia, USA.

Dr. William B. Greenough III, Observer
Director, Clinical Scholar's Program, Johns Hopkins
University, Baltimore, Maryland, USA.

Dr. Michael H. Merson, Observer
Johns Hopkins University, School of Medicine,
Baltimore City Hospitals, Baltimore, Maryland, USA.

Dr. Carl E. Miller, Observer
Cholera Program Officer, GMB/NIAID, National Institutes
of Health, Bethesda, Maryland, USA.

FEBRUARY 1977 CONTINUED

- Dr. W. Henry Mosley, Observer
Chairman, Department of Population Dynamics, Johns
Hopkins University, Baltimore, Maryland, USA.
- Dr. Abram S. Benenson,
Department of Microbiology, University of Melbourne,
Australia.
- Dr. Isaiah A. Jackson,
Chief, Health & Nutrition, Asia Bureau, AID, Washington,
USA.
- Dr. Bradley Sack,
Professor of Medicine, Johns Hopkins University,
Baltimore, Maryland, USA.
- Dr. William Brace,
Head, International Population Centre, London School
of Hygiene & Tropical Medicine, London, UK.
- Dr. J.G.C. Blacker,
Consultant, World Fertility Survey, London, UK.

MARCH 1977

- Dr. W.E. Van Heyningen,
The Master, St. Cross College, Oxford, UK.
- Dr. C. Gary Merritt,
Research Division, Office of Population, USAID,
Washington, USA.
- Dr. Rafael A. Esmundo,
ICOMP, The Philippines.
- Miss Margaret Fairlie,
South Asia Department, Ministry of Overseas Development,
London, UK.

APRIL 1977

- Dr. Trinidad S. Osteria
Assistant Professor, Institute of Public Health,
University of the Philippines, The Philippines.

APRIL 1977 CONTINUED

- Dr. Hideo Fukumi,
Director, National Institutes of Health, Tokyo,
Japan.
- Dr. Barry Lloyd,
Department of Microbiology, University of Surrey,
Guildford, UK.
- Dr. Majorie A. Koblinsky,
Program Officer, Health Sciences, International
Development Research Centre, Tanglin, Singapore.
- Mrs. S. Kosciielecki,
Program Officer, Population & Health Sciences,
International Development Research Centre, Ottawa,
Canada.
- Dr. Poeewono Rabardje,
Faculty of Medicine, Gadjah Mada University, Yogyakarta,
Indonesia.
- Mrs. Nirmala Narula,
Head, Asia Program, Pathfinder Fund, Boston, USA.

MAY 1977

- Dr. Saribin Hasibuan,
Faculty of Medicine, Gadjah Mada University,
Yogyakarta, Indonesia.
- Dr. Michael Vlassoff & Dr. Carol Vlassoff,
Gokhale Institute of Politics & Economics, Poona,
India.
- Dr. Jon. E. Rohde,
Faculty of Medicine, Gadjah Mada University, The
Rockefeller Foundation, Yogyakarta, Indonesia.
- Dr. Alexander D. Langmuir,
Health Clark Lecturer, London School of Hygiene &
Tropical Medicine, London, UK.
- Dr. Stanley Becker, Department of Population Dynamics,
Johns Hopkins School of Public Health, Baltimore,
Maryland, USA.

MAY 1977 CONTINUED

Dr. James Levinson,
Director of Nutrition, AID, Washington, USA.

Dr. Nadir Nassif Tanious,
Ministry of Health, Cairo, Egypt (Trainee WHO Fellowship).

Dr. Shushum Bhatia,
Director, Rural Community Health Program, Faridpur,
Bareilly, India.

JUNE 1977

Mr. Henry Chuck,
Administrator, Department of Population Dynamics,
Johns Hopkins University, Baltimore, Maryland,
USA.

JULY 1977

Dr. John Kantner,
Chairman, Department of Population Dynamics, Johns
Hopkins University, Baltimore, Maryland, USA.

Ms. Wendy Dobson,
Department of Economics, Princeton University,
Princeton, New Jersey, & International Development
Research Centre, Ottawa, Canada.

Dr. Salie S. Nelson)
Mr. Bardin H. Nelson) International Rice Research
Ms. Florita Sheppard) Institute, Manila, Philippines.
Mrs. F.W. Sheppard)

De. Leslie Corsa,
Chairman, Population Centre, University of Michigan,
USA.

Dr. David R. Nalin,
Assistant Professor, Johns Hopkins University, School
of Public Health, Baltimore, Maryland, USA.

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AUGUST 1977

Dr. Richard Feachem,
Lecturer in Tropical Public Health Engineering,
London School of Hygiene & Tropical Medicine,
London, UK.

Mr. Roger Kramer,
Staff Demographer, International Statistical Program,
US Bureau of Census, Washington, USA.

Dr. Thomas C. Butler,
Assistant Professor, Case Western Reserve University,
Cleveland, Ohio, USA.

SEPTEMBER 1977

Dr. Donald M. Mackay,
Deputy Director, Ross Institute of Tropical Hygiene,
London School of Hygiene & Tropical Medicine,
London, UK.

Mr. Harold N. Graves,
Consultant, 4816 Grantham Ave., Chevy Chase,
Maryland, USA.

Dr. Ron Gray) WHO Team for Research on Human
Dr. E.S. Grech) Reproduction, World Health
Dr. Kanti Giri) Organization, Geneva, Switzerland.

Dr. Ismail Sirageldin,
Professor, Department of Population Dynamics, Johns
Hopkins University, Baltimore, Maryland, USA.

Dr. L.T. Ruzicka,
Acting Head of Department, Australian National University,
Research School of Social Sciences, Department of
Demography, Canberra, Australia.

George Zeidenstein,
President, Population Council, New York, USA.

Andruh Jain,
Staff Associate, International Program Division,
Population Council, New York, USA

Dr. W.L. Reyes,
WHO Sanitary Engineer, Community Water Supply & Sanitary
Division, World Health Organization, New Delhi, India.