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INTERNATIONAL CENTRE FOR
DIARRHOEAL DISEASE
RESEARCH, BANGLADESH

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INTERNATIONAL CENTRE FOR
DIARRHOEAL DISEASE
RESEARCH, BANGLADESH

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The ICDDR,B publishes a journal, a newsletter, scientific reports, monographs, annotated bibliographies and many other items in the field of diarrhoeal diseases and on related subjects. Details of some of these publications may be found at the end of this report.

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PREFACE

This is the ninth Annual Report of the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B).

The ICDDR,B was established in December 1978, succeeding the former SEATO Cholera Research Laboratory which had been founded in 1961. The mandate of the ICDDR,B is to undertake and promote research on diarrhoeal diseases and on the related subjects of nutrition and fertility, to train people and disseminate knowledge in these fields of study, and to develop improved means to prevent and control diarrhoeal diseases in developing countries.

The ICDDR,B has its headquarters in Dhaka, the capital of the People's Republic of Bangladesh. The Centre, as it is known, runs two field stations, one in Matlab Upazila of Chandpur District and the other in Teknaf Upazila of Cox's Bazar District. The Centre has research projects in several parts of Dhaka, in several areas of rural Bangladesh and provides technical assistance at two Diarrhoea Control Centres in Saudi Arabia.

The Centre is organised into four Divisions of scientists with similar interests: Community Medicine, Clinical Sciences, Laboratory Sciences, and Population Sciences and Extension. Research proposals from scientists are first reviewed within the Division and then by two committees: the Research Review Committee and the Ethical Review Committee. At the head of each Division is an Associate Director who answers to the Director. The Director in turn answers to an international Board of Trustees containing eminent scientists and representatives of the Government of Bangladesh.

This report describes many aspects of the work of the staff of the ICDDR,B during 1987, including research, support for research and health care services. The articles published by scientists during the year are also listed here and, when possible, are cross-referenced with reports in the text, although much of the research published in 1987 was done in previous years.

If you have any comments on this report or would like more information about the work described here, then please write to the Director at the address given opposite.

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DIRECTOR'S INTRODUCTION

Nineteen hundred and eighty-seven has been the most favourable financial year the ICDDR,B has had since its inception. Prudence in all financial matters and generous support from donors have made it possible not only to initiate new research, to maintain health care and training activities, and to continue with the renovation of the laboratories, but also to end the budgetary year with a respectable cash surplus.

The maternal and child health activities in Matlab were sizeably expanded during the year to provide comprehensive preventive health care. This is largely a result of a growing awareness of the plight of women and children in rural Bangladesh by studies of causes of death: many women die during maternity while children are most at risk of dying during the first year of life. The importance of acute respiratory tract infections as a cause of infant mortality has been clearly established and measures to prevent such deaths will begin in 1988. Also in Matlab the usefulness of measuring the circumference of the middle of the upper arm (MUAC) has been further confirmed by research: MUAC seems a better means of identifying children most at risk of dying than any other body measurement or index of malnutrition. Now the question of treating such children is being addressed: is it done better in the surroundings of the malnourished child's home or in a special hospital unit?

Successful innovations in maternal and child health or in family planning have to be practicable within state health care systems before they can become widely adopted practices. With practicability in mind, the Maternal, Child Health and Family Planning Extension Project has continued to examine within the Government health services the effectiveness of successful aspects of the programme in Matlab. Another considerable and highly rewarding task of the Project was the continued collaboration with the Government of Bangladesh during the process of hiring 10,000 Family Welfare Assistants.

With the help of consultants from the Canadian International Development Agency, the Centre's staff established a new database on the mainframe computer for the demographic data collected in Matlab. This will allow much easier access to data for the Centre's demographers and should improve current studies of the impact of health services on people living in a poor community in a developing country. A sound and accurate description of a population under study is a very important part of field research, as several studies in Matlab have shown.

In the clinical sciences research on improved oral rehydration solutions and the complications of invasive diarrhoea were continued, while studies on persistent diarrhoea — which had been identified in 1986 as a research priority within the Centre — were started with the aim of carefully defining the condition and the extent of the problem. Generous help from the Danish aid agency DANIDA has provided support for the

diarrhoea treatment centre run in Dhaka by the Centre, as well as for the unit providing treatment for malnourished children. Danish aid will allow an expansion of services to include other activities related to child survival including vaccination and follow-up of children who are more likely than others to develop complications after their discharge.

By the end of 1987 there had been 2½ years surveillance in the Oral Cholera Vaccine Trial. It seems likely that the trial will add not only to our knowledge of cholera vaccines, but to our knowledge of the oral route of immunisation, and will provide answers to several other biologically important questions as the vast amounts of data are being further analysed.

During 1987 the ICDDR,B was honoured to receive a Science and Technology for Development Award from the United States Agency for International Development and the National Research Council (see picture, page 3). The citation accompanying the certificate, which is shown above, stated: 'To the International Centre for Diarrhoeal Disease Research, Bangladesh for its diarrhoeal disease research and its substantial contributions to global child survival, most importantly through the development of the technology known as oral rehydration therapy (ORT)'. The ICDDR,B was one of nine organisations to receive this award and one of only two medical research institutions, the other one being the Johns Hopkins School of Hygiene and Public Health, Baltimore, USA. The award is a tribute to all the people who have served the Centre and its predecessor the Cholera Research Laboratory, over the last 25 years.

Collaboration and exchanges with organisations both within and outside Bangladesh continued during the year. The collaboration with the Centre for Diarrhoeal Disease Control and Research in Henan, the Peoples' Republic of China, was further expanded and several Chinese scientists and physicians worked at the Centre during 1987. Research on oral rehydration solutions based on starchy staple foods continued during 1987 in collaboration with the Kenyan Medical Research Institute. Institutional collaboration was established between the Centre and Tufts University in Boston, USA, while links were maintained with Johns Hopkins University, who were the source of two new members of staff, and with the University of Maryland in the field of Environmental Microbiology. Generous financial support from donors made it possible to strengthen the Centre's links with the London School of Hygiene and Tropical Medicine in the fields of nutrition, parasitology, and water and sanitation; with the Department of Gastroenterology in the University Hospital in Basel, Switzerland; with INSERM in Paris; and with the Department of Microbiology of the Free University of Brussels. The Centre's research work and its staff have profited greatly from these links.

It is most rewarding that a growing number of donors are helping the Centre to maintain and expand the collaboration with institutions in developed countries, which is so important to its development. Much remains to be done however to establish strong links with institutions in the developing world, and financial constraints are still a severely limiting factor. The Scientific Working Groups of the WHO Control of Diarrhoeal Disease Programme are supporting a growing number of ICDDR,B research studies, as can be seen from this report. The financial support from the WHO has been most welcome but the scientific collaboration is of even greater value.

During 1987 Bangladesh was hit by some of the worst flooding in recent history. Emergency aid from several donors allowed the Centre to contribute to the national relief effort during this potential catastrophe, mainly through its Epidemic Control Preparedness Programme.



Agency for International Development and the National Research Council
*Science and Technology
for Development Award*
1987

*A special tribute to an institution whose use of science and technology
over the past twenty-five years has dramatically benefited millions of people
in developing countries, the award is presented to the*

**International Centre for
Diarrhoeal Disease Research, Bangladesh**



*Done in the City of Washington
this 22nd day of June 1987*



M. Z. M. Khan

Administrator

Robert A. ... Chairman

At the close of 1987 optimism seems to be warranted. The Centre's recovery is accelerating, scientific priorities are now more clearly defined and the Centre's research, training and service activities are being pursued vigorously. Two meetings of donors, one of which was held in Dhaka, have allowed a better understanding of the donors' views and the Centre's needs. Yet there is no room for complacency. Much hard work lies ahead, and while the inherited problems are being solved new ones will have to be faced. But the Centre's mandate, to fight one of the most important group of diseases in the developing world today, must be continued with diligence and determination.

Roger Eeckels MD DTM
Director

CHOLERA

In early 1985 the ICDDR,B began a large field trial in Matlab of two orally administered vaccines against cholera in collaboration with the Government of Bangladesh and the World Health Organization. The efficacy of the vaccine has been assessed since then by "active surveillance", in which fieldworkers search for cases of cholera in the community where vaccination was carried out, and by "passive surveillance", waiting for patients with cholera to attend the Centre's hospital in Matlab.

Oral cholera vaccine trial

Principal Investigator: John Clemens

Funded by: United States AID and WHO

Over 60,000 people living in Matlab received either one of two vaccines or placebo. The results of surveys for subsequent cases of cholera revealed that during the first 4 to 6 months after immunisation one of the vaccines, the one which contained the B-subunit of cholera toxin as well as killed whole cells (BS-WC vaccine) conferred 85% protection against cholera, while the second vaccine, which contained only killed whole cells (WC vaccine), conferred 58% protection.

During the remainder of the first year after immunisation, a period in which two major epidemics of cholera occurred in Matlab, the protection provided by both vaccines declined so that over the entire first year the protective efficacy was 62% for the BS-WC vaccine and 53% for the WC vaccine. However there were differences in the protection afforded by the vaccine to different age groups. At the end of the first year of surveillance the vaccines appeared to afford negligible protection to children while they still gave good protection to older people: 78% who received the BS-WC vaccine were protected compared with 67% who received the WC vaccine. So in older people there appeared to be no decline in protection during the year.

The vaccine also appears to provide some protection against diarrhoea due to enterotoxigenic *Escherichia coli* (ETEC). People who received two or three doses of the BS-WC vaccine showed a 67% reduction in the incidence of diarrhoea due to the strains of ETEC which produce a heat labile toxin, and the incidence of life-threatening illness was reduced by 86%. This finding suggests that the BS-WC vaccine elicits antibodies which cross-react with the heat labile toxin of ETEC.

During the first year after immunisation admissions to hospital for diarrhoea of whatever cause were reduced by 25%. This effect was particularly marked for watery diarrhoea, again whatever the cause: it was reduced by 52% for people who had received the BS-WC vaccine and by 32% for those who received the WC vaccine. The advantage of the BS-WC vaccine appeared once again to be due to cross-protection against strains of ETEC producing the heat labile toxin.

A preliminary analysis of the results of surveys in the second year after immunisation indicate that both vaccines confer a protection of about 60% against cholera. This duration of sustained protection has never been achieved before by a cholera vaccine. Surveillance will continue for a third year.

The observation that the vaccines used in this trial seem to confer some protection against diarrhoea due to certain strains of bacteria of a different genus is very interesting and suggests that the toxin these bacteria produce may be similar to cholera toxin. Yet what about protection against other members of the genus Vibrio which cause disease?

Antitoxic immunity conferred against non-O1 Vibrionaceae by one of the vaccines used in the cholera vaccine trial

Principal Investigator: Bradford A Kay

Funded by: UNDP and WHO

The aim of this study was to assess the potential of the BS-WC vaccine to protect individuals against infections with other vibrios. This was undertaken because some non-cholera vibrios produce a toxin similar to that produced by V.cholerae and so vaccination with part of cholera toxin may produce cross-protection. In order to test this hypothesis, two approaches were taken. First, non-cholera vibrios isolated from patients taking part in the vaccine trial were tested to see if they produced this similar toxin. Secondly, cross-reactions between somatic antigens of V.cholerae and selected members of the vibrionaceae were studied using antisera raised against V.cholerae.

A total of 735 isolates of non-cholera Vibrionaceae from 11 species were tested for their ability to produce a toxin similar to cholera toxin by means of a variety of media, propagation conditions and test methods. The GM1 ganglioside ELISA was used to screen organisms then the Y-1 adrenal cell test was used to confirm toxin production. The results of these experiments identified only two toxin producing isolates, both Vibrio mimicus.

In the second approach significant cross-reactivity was found between V.cholerae O1 and the Vibrionaceae tested. However, much less cross-reactivity was noted when using antiserum from vaccinated people than against antiserum from patients who had recovered from cholera.

Vibrio cholerae O1 is usually identified by lengthy and costly biochemical tests on organisms isolated from faeces on nutrient media. There is a need for a diagnostic test which is simple to perform in circumstances where facilities are poor, even if the process or manufacturing the reagents is complicated. Coagglutination is one such simple test in which the presence of the organism causes clumping of bacteria which have been coated with antibodies to that organism. This clumping or "coagglutination" is easy to see with the naked eye.

Diagnosing *Vibrio cholerae* 01 by coagglutination

Principal Investigator: Mahbubur Rahman

Funded by: UNDP and WHO

Faecal samples from 240 people with suspected cholera were tested for *Vibrio cholerae* using two culture media. A coagglutination test detected all the 200 infections diagnosed by these means, giving a sensitivity and specificity of 100%. Once the reagents have been prepared the test is simple and the results are available 24 hours earlier than conventional diagnostic methods. Research has also shown that this test can be used successfully to diagnose cholera using culture media inoculated with faeces and stored at room temperature for 4 hours. This would be particularly useful for laboratories without an incubator.

In the human body the first line of defence against diarrhoeal disease is the acid secreted by cells lining the stomach: few pathogens can survive strongly acid conditions for very long and *V. cholerae* dies at a pH of less



than 5.5. People who produce little or no gastric acid are known to be highly susceptible to diarrhoeal diseases, so is there a direct relationship between gastric acidity and the chances of contracting a disease such as cholera? But measuring gastric acidity directly can be physically difficult and invasive, so an indirect estimate of acidity has been developed and used to measure the gastric acidity of people who have had cholera to answer the question: are they poor secretors of acid?

A new test to assess gastric acidity as a risk factor for cholera

Principal Investigator: FPL van Loon

Funded by: UNDP

The test involves measuring the concentration of hydrogen in the breath after first consuming a stimulant to provoke the normal secretion of stomach acid and then a dose of magnesium: the magnesium reacts with the acid to release hydrogen which can be measured in expired air (see picture above: a subject breathes into a bag while listening to music). This estimate of gastric acidity was used to compare people who had recovered from cholera at least six months before with controls of the same age in the same family who were likely also to have been exposed to the disease. In 12 of 15 pairs studied the breath hydrogen of the people who had had cholera was lower than the controls and the average difference between the two groups was significant. This result confirms the role of gastric acidity as non-specific protection against cholera.

SHIGELLOSIS

Dysentery caused by species of *Shigella* is a large and growing problem in Bangladesh and many other developing countries. Of the four main species, *S. dysenteriae* type 1 causes the most serious disease and, as reports from Teknaf indicate (see p 49), most strains are rapidly becoming resistant to the commonly used antibiotics.

Research on *Shigella* burgeoned during the year with the award of a major grant from the United States Agency for International Development. The Centre has facilities for field, clinical and laboratory research and this grant will allow studies to be undertaken on risk factors for shigellosis in the community, on treating shigellosis and its complications in hospital, and on studies of potential antigens for a vaccine in the laboratory.

Developing a scheme to diagnose and treat dysentery based on a few simple signs and symptoms

Principal Investigators: C Ronsmans, ML Bennish and T Wierzba

Funding: Medecins sans Frontières, Belgium and Lutheran World Services, Switzerland

This study had three aims. First, to determine by surveillance for one year the prevalence of different forms of diarrhoea in a rural community of about 900,000 people in northern Bangladesh. Secondly, to diagnose the actual cause of diarrhoea in three groups of about 100 young children with either watery, bloody or mucoid diarrhoea, to test the species of *Shigella* isolated for their resistance to antibiotics, and to describe the clinical features of the children's illness. Finally, using this information, to develop a scheme or algorithm based on a few simple signs and symptoms which might enable community health workers (CHWs) to diagnose and treat dysentery and diarrhoea.

A total of 46,607 cases of diarrhoea were recorded during the year: 41% were classified as watery, 39% were bloody and 20% were mucoid. There were 198 deaths, 62% of which were associated with bloody diarrhoea.

Species of *Shigella* were isolated from the stools of 50% of 101 children with bloody diarrhoea compared with 16% from the stools of 199 children with other forms of diarrhoea. Of the 82 isolates of *Shigella*, 41% were resistant to ampicillin, 33% to cotrimoxazole and 27% to both drugs. Thus a report of bloody diarrhoea was likely to be shigellosis in 50% of cases, and 86% of cases reported to be watery or mucoid diarrhoea were unlikely to involve species of *Shigella*. The predictive value of a report of bloody diarrhoea alone was found to be as good as schemes which only involve a microscopical examination of stools in addition to a clinical examination.

Reducing morbidity and mortality due to diarrhoea will depend considerably on treating and controlling shigellosis. As a result of this study CHWs are now providing antibiotics to treat bloody diarrhoea in addition to providing oral rehydration.

Shigellosis can be a serious illness for young children and can have long lasting effects on their growth.

A prospective study of risk factors for the occurrence of shigellosis and its clinical sequelae in rural Bangladeshi children

Principal Investigator: Faruque Ahmed

Funded by: United States AID and WHO

The aim of this study is to identify factors which put children up to 4 years old at risk of contracting shigellosis and, if they get shigellosis, to identify the factors which put them at risk of the common sequelae of this disease, such as persistent diarrhoea and a failure to grow. Children in Matlab who are close contacts of cases of shigellosis will be visited on alternate days for 10 days, then weekly for another 21 days; the final visit will be 12 weeks after the first. The risk factors for shigellosis under study are: low body stores of vitamin A, breast milk as a proportion of the diet, weaning practices, nutritional status, recent measles, personal hygiene of the child and the mother, water supplies and water storage, and the food handling practices of the family. In addition to these factors, the diet during shigellosis and antibiotic treatment are being studied as risk factors for the common sequelae of shigellosis.

Hyponatraemia, a dangerously low concentration of sodium in the blood, is a potentially fatal complication of shigellosis.

Hyponatraemia in shigellosis, its causes and treatment

Principal investigators: I Kabir and ML Bennis

Eighteen patients with shigellosis and a serum sodium concentration of less than 125 mmol/l were studied. Their mental status was assessed and the osmolality and sodium concentration of their serum and urine was measured before and after infusing a 3% solution of sodium chloride for 2 hours.

Only 3 patients had evident dehydration. Before the infusion 16 patients were either lethargic or unconscious compared with 4 after the infusion. The mean serum sodium concentration rose from 119 mmol/l to 129 mmol/l while osmolality rose from 264 to 281 mosmol/l; both increases were significant ($P < 0.001$). The mean urine sodium concentration rose from 4 to 13 mmol/l and the osmolality dropped from 543 to 534 mosmol/l; neither changes were significant.

Six patients were freely offered liquids to drink during the study. During the 2 hours before the infusion they drank an average of 23 ml of liquid; afterwards they drank an average of 365 ml in two hours. Five of them specifically requested something to drink at the end of the infusion.

This study suggests that hyponatraemia is not related to a major loss of body fluids. The lack of evidence of dehydration, the high urine osmolality and the low serum osmolality suggest that the problem may be related to the inappropriate secretion of anti-diuretic hormone.

The rapidity with which strains of *Shigella* can develop resistance to antibiotics is well illustrated by the results of surveillance over recent years in Teknaf (p 49). For this reason there is a continual search for drugs which are effective treatments for shigellosis.

Ciprofloxacin compared with ampicillin for treating shigellosis

Principal Investigators: MA Salam and ML Bennish

Funded by: Miles Pharmaceuticals, USA

The aim of this study is to assess the effectiveness of treating shigellosis with ciprofloxacin, one of the newer quinolone antimicrobial drugs, by comparing it with ampicillin. During the course of the study the sample size had to be increased as many of the strains of *Shigella* spp isolated were resistant to ampicillin so there were insufficient controls to be able to assess the efficacy of ciprofloxacin. Of the 161 patients studied *Shigella* spp were isolated from the stools or rectal swabs collected from 127. Tests on stool samples collected for alpha-1-antitrypsin and Shiga toxin are still continuing. When the tests are complete the results can be analysed and the coded treatments revealed.

One way of developing a vaccine is to use strains of a pathogen which don't cause severe or prolonged disease but do stimulate the body to produce protective antibodies. These strains can be developed either by screening wild organisms and selecting or breeding avirulent strains, or by manipulating the genetic material of strains to introduce lethal genes which either kill the organism before it can do any harm or which diminish its virulence. The one major provision is that the modified strain should not regain its virulence when it is introduced into the vaccinated host.

Isolating attenuated mutants of *Shigella flexneri* Y and evaluating their potential as a live oral vaccine

Principal Investigator: Zia Uddin Ahmed

Funded by: United States AID

Mutant strains of both *Shigella flexneri* Y and *S. dysenteriae* type 1 have been isolated that do not grow well at a temperature of 37°C, the temperature of the human body, but can be grown at 30°C. However these mutants are not stable enough for use in a vaccine: about one cell in every 10⁵ can grow at the higher temperature and thus has the potential to cause disease. For this reason an attempt was made to add a second mutation to the temperature-sensitive strain by introducing a gene which results in a requirement for thymine. No organisms with this mutation and without a requirement for thymine have been found in 10⁹ cells, which indicates that the mutant is very stable. The double mutant strain -- temperature sensitive and thymine requiring -- has a theoretical chance of reverting to the wild, pathogenic strain of less than one in 10¹⁴.

Experiments with the double mutant in rabbits have shown that it is not virulent and that it provides protective immunity to a challenge with a usually lethal dose of live cells of the highly virulent parent strain. This mutant will now be tested for safety using experimental monkeys.

Most pathogenic organisms can only grow in certain hosts and often only within certain tissues of that host. To begin growing the infective stage must respond to some sort of trigger, a component or condition in its environment. For many bacteria it seems likely that the trigger to begin growth is a reaction between the surfaces of the pathogen and the host which leads to attachment: *Shigella* must stick to the surface of the gut for example, before they can penetrate the tissues and begin to multiply. In simple terms if attachment to the host is an important trigger in the start of the processes of disease then the reaction between surface of bacteria and the surface of host is worthy of study because if attachment could be prevented then so would disease.

The next two studies reported here are concerned with the structural components of species of *Shigella* and the immunity elicited in people during disease. An examination of the reactions between the surface components of *Shigella* and the antibodies produced during disease can show which components produce the strongest immune reactions for example.

Studies on the outer membrane proteins of species of *Shigella* and their relationship with virulence
Principal Investigator: Firdausi Qadri
Funded by: United States AID

This research has three main components. First to develop simple laboratory tests which estimate the virulence of species and strains of *Shigella*. Secondly, to extract and purify important proteins produced by *Shigella* such as toxins. Finally, to study the properties of the surface of species of *Shigella*, the main point of contact between pathogen and host and probably crucial in the process of pathogenesis.

Research on the first aim has shown that virulent and avirulent strains of *Shigella* can be differentiated by the colour of the colonies which grow on culture media containing the dye Congo Red. In addition there appears to be a relationship between the degree of pathogenicity of different species of *Shigella* and their relative hydrophobicity as measured by their ability to aggregate in different strengths of salt solution. These tests provide a simple and rapid means of assessing the virulence of strains of *Shigella* without the need to use experimental animals.

Research on the second aim has shown that shigella toxin is present on the cell envelope and in the peri-plasmic space of *S.dysenteriae* type 1. Extracting and purifying this toxin in the past has involved using large volumes of filtered culture medium or lysed cells and two or three steps in a process of purification by chromatography. The yields of toxin by this process are also poor. A new process has been developed involving a one step chromatographic process with high yields of toxin.

Crossed immunoelectrophoresis (CIE) is a technique in which proteins are placed in a small well at one corner of a thin gel on a glass plate and then separated in one direction, towards the anode (+), by an electric current. The distance each protein moves is proportional to its size and electrical charge. Except for the column of separated proteins, most of the first gel is then replaced with a second gel containing antibodies to the proteins. The current is then applied at an angle of 90° to the first direction. The proteins separate in the second dimension and react with antibodies to form a precipitate when they meet at the optimum concentration. This is then stained. This picture shows CIE of outer membrane proteins of *Shigella dysenteriae* type 1.



Research on the third aim has shown that some outer membrane proteins of *Shigella dysenteriae* type 1 cause red blood corpuscles (RBCs) to clump together indicating that they are binding to the RBCs. This reaction is called haemagglutination and has not been reported before for *S.dysenteriae* type 1. Research has shown that *S.dysenteriae* type 1 only produces this substance when it is grown under certain highly specific conditions, the same conditions shown by earlier work to result in the production of the most protein antigens. The substance causing haemagglutination is heat labile and is not inhibited by the presence of sugars which typically inhibit such binding.

The immunity stimulated by a pathogen during disease is often much stronger than the immunity which can be generated by vaccinating people with any form of artificially prepared vaccine. Studying naturally derived immunity is an important aspect of research on vaccines.

The immune responses of patients with dysentery to structural components of species of *Shigella*

Principal Investigator: Ivan Ciznar

Funded by: UNDP

The aim of this research is to identify the cellular components of *Shigella* which stimulate immunity during disease. Serum samples are being collected from patients during the acute phase of illness and during convalescence in order to examine the systemic immune response to the infection. In addition, liquid washed from the intestine is being collected and tested for secreted antibodies in order to estimate the local immune response.

Strains of *Shigella* belonging to all four species causing disease in man have been isolated from 25 patients studied so far. The serum and intestinal fluid samples collected indicate that outer membrane proteins,

lipopolysaccharides and Shiga toxin are the major antigens and that some antigens appear to occur also in non-pathogenic strains of E.coli.

What makes some strains of organisms cause disease and not others is a question which, if answered, can lead to a better understanding of the processes of disease as well as improving the chances of developing a vaccine. The severity of disease in strains of Shigella often appears to be associated with circular pieces of DNA outside the chromosomes called plasmids which can be passed between strains and even species of bacteria. Some of these plasmids may be responsible for resistance to particular antibiotics.

The role of plasmids in producing structural components associated with the virulence of Shigella dysenteriae type 1
Principal Investigator: Khaleda Haider
Funded by: UNDP and WHO

Four plasmids with sizes of 140, 6, 4 and 2 megadaltons (Mdal) are commonly found in strains of Shigella dysenteriae type 1 isolated from all over the world. The first aim of this research was to compare in various strains of S.dysenteriae type 1 the presence or absence of these plasmids with the lipopolysaccharides (LPS) they produce. Tests were also carried out to examine differences in the degree of the immune response to different lipopolysaccharides.

The results indicate that the 6 Mdal plasmid is associated mainly with the synthesis of LPS but the other 3 plasmids are also necessary for some components. Strains containing none of these plasmids only produce the core sugars without any O-antigen side chains.

Other research has shown that the large plasmid in species of Shigella is responsible for some properties associated with virulence. Thus the second aim of this research was to examine the relationship between this large plasmid and virulence. The analysis has shown so far that a small deletion in the plasmid of about 12 mdal results in a loss of virulence. This loss does not affect the production of the proteins present in the outer membrane of strains of Shigella dysenteriae type 1. This suggests that a strains of Shigella with this deletion could stimulate immunity yet not be pathogenic.

Similar techniques to those described earlier for detecting Vibrio cholerae in the stools are being used to try to improve the diagnosis of shigellosis.

Diagnosing shigellosis
Principal Investigator: Mahbubur Rahman
Funded by: UNDP and WHO

A coagglutination test using bacteria coated with antibodies to species of Shigella has been developed to try to detect the pathogen in faeces, in culture plates using different media and in broths used to increase the number of organisms.

PERSISTENT DIARRHOEA

Diarrhoea which lasts for 14 days or more is often classified as "chronic" or "persistent". This is a rather arbitrary duration but it does indicate that something abnormal has happened -- diarrhoea does not usually last that long. This is because the majority of pathogens which cause diarrhoea are said to be self-limiting: the organism multiplies, the host produces an immune response, the multiplication of the pathogen is inhibited and the patient recovers. By this process most people with diarrhoea caused by a pathogen usually get better without treatment within 10 to 14 days, as long as they are adequately rehydrated, although there are some exceptions: organisms such as *Giardia intestinalis* or *Entamoeba histolytica* seem to be able to evade the immune response and cause long lasting disease.

Persistent diarrhoea may not always be caused by a pathogen: intolerance to certain substances such as lactose in milk or gluten in wheat can also cause diarrhoea, while in some cases of diarrhoea no biological cause or pathogen has yet been found (see section on Other Pathogens, p 21). Persistent diarrhoea can have serious effects on nutritional status, particularly in children. The causes and treatment of persistent diarrhoea have been somewhat neglected in recent years, but in 1986 persistent diarrhoea was identified as a research priority for scientists and physicians at the ICDDR,B.

Persistent diarrhoea and malnutrition in urban and rural Bangladesh
Principal Investigator: FJ Henry
Funded by: FAO

This study has several aims. First, to determine the proportion of episodes of diarrhoea in young children in urban and rural Bangladesh which last for 14 days or more and are classified as persistent diarrhoea. Secondly, to examine the effect of persistent diarrhoea on growth and to assess the impact of different pathogens. Thirdly, to determine whether the frequency of acute illnesses is related to the duration of persistent diarrhoea and to malnutrition. Finally, to examine whether treatment or changes in the diet during the acute phase of diarrhoea affects the duration of the episode.

Episodes of diarrhoea are being studied in 600 children aged less than 4 years in two sites, one urban and one rural. Faecal samples and rectal swabs are being collected from children with diarrhoea and from healthy controls, and are being tested for bacteria, viruses and evidence of parasitic infections. Dietary information is being collected during regular home visits to find out about illnesses, and the nutritional status of children is assessed each month. So far over 600 episodes of diarrhoea have been studied of which about 4% of them have lasted for more than 14 days. The study is continuing.

There is evidence that in some cases persistent diarrhoea can be treated by dietary means such as removing items which may contain components which are responsible for food intolerance: foods based on milk and wheat are good examples. Research at the ICDDR,B is showing that a diet based on comminuted chicken can help to treat persistent diarrhoea in young, malnourished children.

Dietary treatments for persistent diarrhoea
Principal Investigators: SK Roy and R Haider
Funded by: United States AID

The aim of this study is to examine the absorption of nutrients from a simple diet developed to treat persistent diarrhoea. The intake and absorption of nutrients from all food consumed over a period of 72 hours will be estimated for 30 male children aged 4 to 24 months with persistent diarrhoea and 20 healthy children of the same age and sex. The study is still in progress.

In many gut diseases the intestinal wall may become abnormally permeable. This can result in a loss of tissue fluids and proteins and such losses may exacerbate malnutrition. There are several ways of estimating an intestinal loss of protein. The most common is to measure the concentration in the stools of a blood protein called alpha-1-antitrypsin (α -1-AT) which is not broken down in the gut but is excreted intact in faeces. But this only estimates protein loss, one feature of damage to the gut wall: a changed gut permeability can affect absorption as well as causing leakage. One technique to estimate a change in permeability involves giving an oral dose of two sugars which are not metabolised by man: lactulose, which is normally poorly absorbed by a healthy gut, and mannitol, which is normally well absorbed by a healthy gut. A rise in the ratio of lactulose to mannitol in the urine can indicate abnormal permeability. Both these tests are being used at the ICDDR,B in studies of gut damage due to intestinal pathogens, their effect on the nutritional status of children and on the impact of nutritional supplements.

A study of the effect of zinc supplements on mucosal permeability
persistent diarrhoea in children
Principal Investigator: SK Roy
Funded by: The Wellcome Trust

The trace element zinc has profound effects on protein synthesis and growth, as well as on cell membranes and the transport of water and electrolytes. The surface of the intestine is extremely active both in terms of transport and growth: the cells lining the intestine are the first barrier between the gut lumen and body tissues, so all absorbed nutrients have to cross this barrier; the cells are also constantly being replaced as they only have a life of about 2 days. To test the hypothesis that zinc supplements can reduce diarrhoea by improving mucosal permeability and improving water and electrolyte transport, this study is being undertaken in children with both acute and persistent diarrhoea.

In 1987 130 children with persistent diarrhoea were studied. The children were aged between 3 and 24 months and were given either zinc acetate or a placebo for 14 days in a double-blind study. Stool samples

were collected regularly in order to measure α -1-AT and intestinal permeability was estimated by the lactulose/mannitol test. Children were then visited at home once a week after their discharge for 3 months in order to collect data on illnesses, growth, nutritional status and their diet. The study will continue until the middle of 1989.



Skin lesions in a child with zinc deficiency

Giardia intestinalis is a protozoan parasite of the small intestine. It rarely causes an acute diarrhoea but there is evidence that the first infection with *Giardia* is associated with frequent liquid stools, often with malabsorption of nutrients. The infection and the loose stools can last for several months and persistent infections in children are associated with a failure to thrive.

Giardia and persistent diarrhoea in young children

Principal Investigator: Andrew Hall

Funded by: United States AID and British ODA

This study involves a prospective investigation of the acquisition of infections with *Giardia* by young children living in an urban slum, the association of infections with persistent diarrhoea and the effect of *Giardia* on growth and nutritional status. By the end of the year about 50 children aged between 2 and 8 months had been recruited for the

investigation, which will involve studying 200 children for up to 2 years. The health of each child is recorded every week and it is weighed and measured once a month. Stool samples are being collected for microscopical examination each month and if children develop diarrhoea then samples are submitted for microscopical examination and for microbiological culture.

There is no adequate explanation yet for the range of symptoms seen during giardiasis -- from asymptomatic infections to persistent diarrhoea with malabsorption. One explanation may lie in differences between strains of Giardia. Strains of many species of protozoa have been distinguished on the basis of differences in the movement of enzymes during electrophoresis when different molecular forms of the same enzyme exist within different strains. The movement of these "isoenzymes" can be used to distinguish between strains and may perhaps be used to distinguish between pathogenic and non-pathogenic strains as well.

Identifying and characterising strains of Giardia intestinalis

Principal Investigator: Andrew Hall

Funded by: United States AIL and British ODA

The aim of this investigation is to identify isoenzymes to act as markers in studies of strains of Giardia. Two isolates from Bangladesh, 11 clones from these isolates and 3 isolates obtained from other countries are being grown in vitro to provide enzymes for electrophoresis. These isolates and strains are being screened using cellulose acetate electrophoresis for the presence of over 25 different enzymes. If isoenzymes are identified then polyacrylamide gel electrophoresis and isoelectric focusing will be used to characterise the isoenzymes in more detail before studying organisms obtain from symptomatic and asymptomatic people.

TREATMENT FOR DIARRHOEA

There is always a possibility that bias may affect the results of clinical research. For example, the response to a treatment may be altered if the patient knows which treatment is being given, or the physician may treat the patients receiving an experimental drug differently from those who are given the placebo. For these reasons experiments are often performed either in a single-blind manner in which the patient is unaware of the treatment being given, or in a double-blind manner in which both the patient and the physician are unaware of the treatment being given. Many of the clinical trials of treatments at the ICDDR,B are double-blind: only the pharmacist or someone not involved in the experiment knows which treatments are being given to whom. This information, such as the code for each of two apparently identical capsules, is usually divulged at the end of the experiment and after the results have been analysed. These research methods are being applied to studies of oral rehydration solutions in the Dhaka Treatment Centre of the ICDDR,B.

The standard WHO formula of oral rehydration salts contains sodium bicarbonate in addition to sodium chloride, potassium chloride and glucose. This mixture has one disadvantage: in warm, humid environments the bicarbonate reacts with glucose to form brown furfural compounds and the storage life of the salts is shortened. This has been overcome by replacing the bicarbonate with citrate. This new ORS is now being given a clinical trial at the ICDDR,B.

A comparison of the efficacy of bicarbonate ORS with citrate ORS to treat acute diarrhoea

Principal Investigator: RN Mazumder

Funded by: WHO

In this double-blind study 180 male with acute diarrhoea for less than 48 hours will be randomly assigned to two groups. After initial intravenous rehydration, both groups will receive oral tetracycline for 48 hours and either citrate or bicarbonate ORS. Both the volume of ORS consumed and of stools produced will be recorded for each patient until the diarrhoea has ceased. The cause of the diarrhoea will be determined by microbiological culture. The study is due to end in 1988 when the results will be analysed and the codes for the treatments revealed.

Oral rehydration using glucose ORS supplemented with alanine.

Principal Investigators: FC Patra and DA Sack

Funded by: WHO

Studies on human volunteers have shown that the presence of the amino acid alanine in ORS enhances the absorption of water and electrolytes from the intestine. The aim of this study was to compare the effectiveness of the

standard glucose ORS with the a solution containing alanine at a concentration of 90 mmol/l and with a slightly reduced concentration of glucose. All other ingredients were the same.

In a double-blind study 98 male patients older than 6 years were randomly assigned to receive either the alanine and glucose or the normal glucose rehydration solutions. All patients were initially rehydrated with an intravenous acetate solution. All received oral tetracycline for 48 hours and all were fasted for 24 hours after starting to receive their assigned type of ORS. This study finished in December 1987. A preliminary analysis of the data shows that patients who received the alanine glucose ORS passed significantly less stools compared with the patients who received only glucose ORS.

Research at the ICDDR,B and elsewhere has shown that starchy cereals such as rice are as effective, if not more effective than glucose in oral rehydration solutions. This is probably because the carbohydrate is digested slowly to release sugars and because simple sugars have been shown themselves to draw water from tissues. Solutions based on starchy foods have also been shown to be superior to the traditional glucose ORS in their ability to reduce the volume of stool, to reduce the duration of diarrhoea, to reduce the volume of ORS required and to reduce vomiting. So in fact the next question could be asked . . .

Does solid food potentiate the efficacy of ORS?

Principal Investigator: N Hague Alam

Funded by: UNICEF

Work at the Centre has shown that the superiority of rice ORS over the WHO glucose ORS is only demonstrable in patients with cholera as long as they are not given any food. The aim of this study is to examine whether solid food potentiates the effects of both types of ORS. The experimental design involves studying patients with moderate or severe dehydration due to cholera and treated in one of four different ways: (1) given glucose ORS and no food for 24 hours; (2) given glucose ORS and food throughout treatment; (3) given rice ORS and no food for 24 hours; finally (4) given rice ORS and food from the beginning. The effects of these treatments will be assessed every eight hours by measuring the volume of ORS consumed and the volume of stools, vomit and urine produced. Serum electrolytes and body weight will also be measured. During 1987 119 patients were studied, bringing the total to 136.

The next four studies are all concerned with treating diarrhoeal diseases with drugs.

Berberine sulphate for treating childhood diarrhoea

Principal Investigators: M Shahriar and GH Rabbani

Funded by: UNDP/WHO

The plant alkaloid berberine is found in plants used in India and China to treat diarrhoea, while a pure preparation is marketed by pharmaceutical companies in both India and Japan. A recent study at the ICDDR,B showed

that berberine given as a single dose of 400 mg reduced fluid loss by 30% to 50% in adults with secretory diarrhoea induced by toxins. This encouraging result stimulated the present study.

Two hundred children with diarrhoea aged from 1 to 15 years will be randomly assigned to receive either berberine sulphate given at a dose of 10 mg/kg body weight in 3 divided doses for 3 days, or a placebo. The consumption of fluids and the volume of diarrhoea, urine and vomit produced will be measured. Eighty eight patients have been studied so far.

Cholestyramine is drug which is normally used to lower blood cholesterol concentrations. It does so by binding to bile acids. In the intestinal tract bile acids are thought to aggravate diarrhoea.

Cholestyramine as an adjunct treatment for acute diarrhoea in children treated according to WHO guidelines

Principal Investigator: Tarja Rautanen

Funded by: WHO

The aim of this study was to find out if treatment with cholestyramine decreases the volume of diarrhoea. This would indicate that it has an anti-secretory effect.

A double-blind study was carried out on 150 children admitted to the wards of the Dhaka Treatment Centre with acute diarrhoea and moderate dehydration to find out if cholestyramine decreases the volume of stools produced. After initial rehydration the patients were randomly divided into two groups to receive either cholestyramine or a placebo. The effect of cholestyramine will be evaluated by comparing the duration of diarrhoea, stool output and the total amount of ORS required for rehydration between groups. The study has been completed and the data are being analysed.

Treating a disease with a single dose of drug has obvious attractions and advantages: there are no problems with compliance in taking medicine and no need for further medical supervision.

A single dose of doxycycline to treat cholera

Principal Investigator: AN Alam

Funded by: WHO

The aim of this study was to compare the efficacy of a single dose of doxycycline with the antibiotic tetracycline in the treatment of cholera. A total of 249 patients were randomly assigned to three groups: one received 200 mg of doxycycline and another group 300 mg, both drugs given orally on the first day in hospital, while the remainder received 500 mg of tetracycline given 6 hourly for 2 days. The study was performed in a double-blind manner with the people being treated with doxycycline receiving dummy capsules after their single dose of drug and at the same time tetracycline was being given.

The success of the treatments was assessed by comparing the amount of ORS consumed, the volume of stools produced and for how long V.cholerae were excreted in the stools. No results are available yet.

Chloramphenicol, cotrimoxazole and ampicillin are all effective treatments for typhoid fever but they require frequent doses of the drugs for quite long periods. Ceftriaxone, a third generation cephalosporin, has been found to be quite effective in both experimental and clinical studies of typhoid fever.

A comparative trial of chloramphenicol and ceftriaxone for treating typhoid fever-

Principal investigator: Asma Islam

Funded by: Case Western Reserve University, USA

In this study chloramphenicol was given at a dose of 60 mg/kg body weight each day in 4 divided doses for 14 days and its efficacy compared with ceftriaxone given as a single daily dose of 75 mg/kg body weight for either 5 or 7 days. The 7 days of treatment with ceftriaxone were effective in clearing the pathogen, Salmonella typhi, from the blood in less than 48 hours. The trial of 5 days of treatment with ceftriaxone has just been completed and results are being analysed.

The incorrect or unnecessary use of antibiotics has had some adverse consequences, the most serious of which is the development of resistance to the antibiotics used as treatment. For this reason alternative treatments are being sought which do not involve drugs. One theoretical means of treating the excessive growth of an organism which causes diarrhoea would be to inhibit or prevent the multiplication of a pathogen by a harmless species. In this way a biological treatment would have been achieved by a process of competitive exclusion. The aim of treating diarrhoea with "Bioflorin", a freeze dried preparation of a group D Streptococcus S.faecium, is to do just this.

Treating diarrhoea with "Bioflorin", a preparation of dried Streptococcus faecium

Principal Investigator: AK Mitra

Funded by: WHO

A total of 200 adult males with diarrhoea, aged from 16 to 60 years, and who had not received any drug treatment, were enrolled in the study and randomly assigned to receive either "Bioflorin" or a placebo. The treatments were given as capsules every 8 hours for 3 days in a double-blind manner. Stool samples were collected for microbiological culture at enrolment and every two days, and the volume and pH of the stools was measured. Dehydration was treated with intravenous saline, and if after 3 days there was no improvement in the patient's condition, conventional drug treatment was started. A normal diet was given. The results are still being analysed.

OTHER PATHOGENS

Cholera may be the archetypal watery diarrhoea and shigellosis the archetypal dysentery, but they are not the only causes of watery diarrhoea or dysentery. Other pathogens are being studied at the ICDDR,B and there may be others so far unknown or undetected: even in the best diagnostic laboratories a putative pathogen is found in less than 70% of stool samples.

Although diarrhoea may not always be caused by a pathogenic organism, new causes are found occasionally. Until about 10 years ago for example, a protozoan parasite called Cryptosporidium was thought to be a fairly common cause of diarrhoea in calves and an opportunistic infection in immunocompetent patients. It is now known to be a cause of travellers' diarrhoea, post-measles diarrhoea and has been found in about 4% of stool samples during routine surveillance at the Dhaka Treatment Centre. What is the next pathogen to be shown to be important: Bacteroides fragilis? Plesiomonas shigelloides? Enterocytozoon bieneusi?

A recent report has indicated that enterotoxigenic strains of Bacteroides fragilis, an anaerobic bacterium, are associated with diarrhoea in both domestic animals and man. The work reported here is only the second time this organism has been isolated in people with diarrhoea and it is the first report from Asia.

A search for Bacteroides fragilis in patients with diarrhoea
Principal Investigator: Bradford A Kay
Funded by: United States AID

Stools from patients were cultured for Bacteroides fragilis only if species of Shigella and Salmonella or V.cholerae were not found. Four enterotoxigenic strains of B.fragilis were isolated from 21 patients who had symptoms lasting from 12 to 25 days.

Research using experimental animals showed that injecting cultures of whole cells at a concentration of 10 cells/ml into the jejunum of rabbits brought about their death. Filter sterilised supernatants of the culture medium also induced a fatal, but less rapidly fatal, diarrhoea. A histopathological examination of the gut revealed marked destruction of tissues and necrosis. Nontoxigenic B.fragilis were unable to kill rabbits or cause histopathological changes. Toxicity was not observed in conventional tests using three sorts of sensitive cells grown in vitro or in suckling mice, but toxic effects were seen in HeLa cells and in primary cultures of intestinal cells from newborn rabbits.

Plesiomonas shigelloides is a bacterial species which has been found in the stools of some patients with diarrhoea but has not yet been confirmed as the cause of diarrhoea. One way to assess any potentially pathogenic effect is to infect experimental animals and examine any effects. Even if disease is not caused in animals this does not mean that the organism is not pathogenic because the gut of a rabbit for example is very different from the gut of a human.

Plesiomonas shigelloides infections in experimental animals

Principal Investigator: KA Chowdhury

Funded by: United States AID

Five groups of 5 rabbits were treated as follows: three groups were infected orally with one of three strains of Plesiomonas shigelloides, one group was fed a pathogenic species of Shigella (S.sonnei) and the final group was left uninfected to act as a control. The rabbits were observed for symptoms of diarrhoea for 7 days and rectal swabs were cultured daily. Four rabbits in each group were killed after 7 days and their intestines examined for signs of damage. The fifth rabbit in each group was killed after 28 days and the serum was tested for antibodies to the organisms used to infect them.

Plesiomonas shigelloides was detected in faeces from infected rabbits and the organisms were excreted for the same period as S.sonnei, but there were no symptoms of diarrhoea and only mild lesions were observed in the intestinal wall. In contrast, the rabbits infected with S.sonnei showed acute inflammation and moderate to severe intestinal lesions. There was no evidence that antibodies were produced against P.shigelloides.

Diarrhoea can sometimes occur after treatment with an antibiotic. One possible explanation for this may be that the normal balance of species living in the alimentary ecosystem is perturbed by the death of species which ordinarily compete and inhibit the growth of each other, so a normally harmless organism which is insusceptible to the drug becomes dominant and grows unchecked. This abnormal growth of a normal commensal may lead to diarrhoea.

This may be theory but one organism which has been associated specifically with diarrhoea after treatment with certain antibiotics is Clostridium difficile. The evidence indicates that this organism is present but undetectable in the intestinal flora, and only multiplies to detectable numbers after antibiotic treatment.

Antibiotic-associated diarrhoea in Bangladesh and the role of Clostridium difficile

Principal Investigator: SQ Akhtar

Funded by: United States AID

Stool samples were collected from 71 people with diarrhoea which had occurred after treatment with antibiotics. Another 100 patients with diarrhoea who had not received antibiotics were used as controls. The faecal samples were cultured anaerobically on highly selective media to isolate C.difficile, and extracts of organisms were tested for their

ability to produce toxins by using cells grown in culture which are highly sensitive to toxins. Clostridium difficile was isolated from 5 patients who had developed diarrhoea after antibiotic treatment and from none of the controls. Two of the five strains isolated produced toxins.

Antibiotic-induced diarrhoea in animals and the role of Clostridium difficile

Principal Investigator: SQ Akhtar

Funded by: United States AID

The aim of this study was to try to induce diarrhoea in animals by treating them with the broad spectrum antibiotics lincomycin and ampicillin. Before administering the drugs to the rabbits and guinea-pigs used in these experiments, stools from the animals were cultured for Clostridium difficile; the organism was not found.

All the animals given lincomycin developed a profuse, watery diarrhoea within 48 hours and 75% died within 10 days; animals fed ampicillin developed a less severe diarrhoea; the untreated animals remained healthy. Clostridium difficile was isolated from animals given antibiotics and the strains were shown to produce a toxin. This indicates that antimicrobials induce a diarrhoea in animals which is probably due to C.difficile. The organisms may have been present in the animals' intestines before treatment but were undetectable.

TRANSMISSION OF DIARRHOEA

Clean piped water and a closed sewage system are basic utilities in many developed countries of the world and are largely responsible for preventing disease which are transmitted by the faecal-oral route. In rural Bangladesh similar services can be provided by tube wells and latrines.

Mirzapur Handpump Project

Principal Investigators: KMA Aziz and Bilqis Amin Hoque

Funded by: CIDA through UNDP

The main objective of the Project is to measure the impact of installing handpumps and latrines on the health of people living in Mirzapur, a rural area of Bangladesh, and of the effects of health and hygiene education. A secondary objective is to test a new design of handpump, a locally manufactured, non-suction handpump, particularly suitable for the ground-water conditions in many parts of Bangladesh (see photograph, page 25).

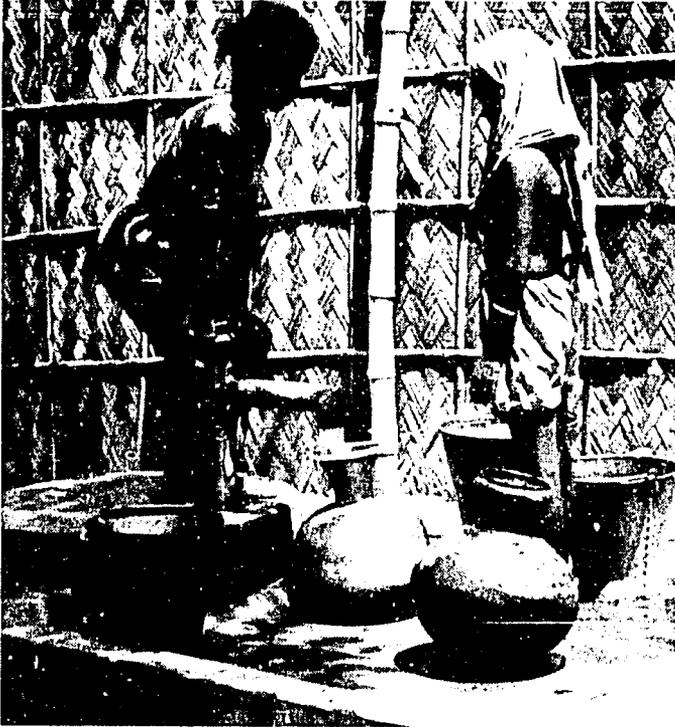
The project began in 1984 with the installation of handpumps and latrines in two villages comprising about 800 households and 4,500 people, the intervention area. Three nearby villages without any special amenities are being studied as a control area. Every week information about episodes of diarrhoea has been collected, every three months children have been weighed and measured, every six months surveys of "knowledge, attitudes and practices" have been conducted and every year surveys of the prevalence of parasites have been done. Information on water consumption, water quality and on the performance of latrines and handpumps has also been collected.

The handpumps were well accepted by the community and virtually all households use them as their source of drinking water. They were also used by a large majority of households for most domestic activities, but an observational study conducted in May 1987 showed that the use of surface water sources was still widespread, particularly for bathing. The consumption of handpump water per person was found to be related to several factors including household size, the distance to the handpump and to the number of people served by a pump.

Surveillance showed that each pump required on average 4 to 5 minor repairs a year. The pumps are designed so that they can be maintained by the community and groups of women volunteers have been servicing 30 pumps with very encouraging results. Early in 1988 the maintenance of all handpumps will be passed to the community.

Double-pit, water-sealed latrines have been installed in more than 95% of households in the intervention area (a figure far exceeding the Bangladesh target for the end of this decade of 13% of households). They were less readily accepted by the community than the water component of the Project, but are now used by most adults, though not so much by young children. The severe flood of 1987 caused damage to many of the latrines, the extent and effects of which are currently being analysed.

Initially the health education programme was conducted by project staff. From 1985 a new community-based approach was used involving local women volunteers. At the end of 1987 women from every household had been trained as health educators.



A Tara handpump in operation in Mirzapur. Over 150 of them have been installed in two villages as part of a study of the effects of improved water supplies, sanitation and health education on the incidence of diarrhoeal diseases. The handpumps are simple to operate: water is drawn by pulling up on handle rather than by a traditional crank. They are also simple to repair: a task which is now being done by local women. The study is due to finish at the end of 1988.

A detailed analysis of its impact on health is underway and the results will be available in 1988. So far it has been shown that the incidence of diarrhoea among children less than 5 years of age was similar in both areas before the handpumps and latrines were installed, at 3.9 and 3.8 episodes/child/year respectively. After 1984 the incidence rate declined in both areas but substantially more so in the intervention area.

When children are weaned from breast milk they are often exposed to disease because of unhygienically prepared weaning foods.

Sanitation, weaning and diarrhoea
Principal Investigator: FJ Henry
Funded by: FAO

The main aim of this study is to determine what foods and food preparation practices expose children being weaned to diarrhoeal diseases. The second aim is to assess the effect of interventions such as installing tube-wells and giving health education on the contamination of food.

Bacterial contamination with intestinal pathogens is being assessed by testing food and water samples for the presence of coliform bacteria. These bacteria are present in the gut of everybody so their presence in food and water indicates faecal contamination. Nine hundred samples of infant foods and drinking water have been collected from the intervention and comparison areas of the Mirzapur Handpump Project (see above). The mean faecal coliform count in different types of foods, expressed as the logarithm of the mean numbers of organisms in millions per unit weight or volume, was 5.2 in left-over rice, 2.4 in other types of rice, 2.2 in milk, 0.6 in drinking water, 0.5 in bread and cakes and an average of 1.5 in all other foods. There was found to be an exponential increase in the degree of contamination with an increasing gap between food preparation and its consumption.

Most children appeared to be able to tolerate considerable contamination of food and water before experiencing diarrhoea. The analysis of results will examine the role of the nutritional status of the child in this apparent insusceptibility to infection, as well as confounding social and environmental factors.

The pattern of susceptibility or insusceptibility of strains of bacteria to viruses called bacteriophages can be used to characterise and distinguish between strains if enough bacteriophages are used. This method is being used to study the transmission of diarrhoea due to enterotoxigenic strains of *Escherichia coli* (ETEC) among cases of diarrhoea and the contacts of cases in the cholera vaccine trial (see page 4).

Using bacteriophages to identify strains of enterotoxigenic *E.coli*
Principal Investigator: KA Monsur
Funded by: UNDP and WHO

The phage sensitivity pattern of labile-toxin producing strains of ETEC isolated from stools collected during the cholera vaccine trial was examined. Of 111 strains identified serologically the largest group comprised 42 isolates of the 078 serogroup while out of 24 isolates of the 06 serogroup, 19 belonged to another 'phage pattern.

There is a theory that between epidemics of cholera the organism which causes the disease, *Vibrio cholerae*, survives in fresh water.

Studies on the seasonal distribution of *Vibrio cholerae* in natural fresh waters in Bangladesh

Principal Investigator: Anwarul Haq
Funded by: United States AID

The aim of this 3-year study is to investigate the seasonality of the occurrence of *Vibrio cholerae* in the fresh waters of Bangladesh and to relate the presence and absence of the organisms to physical, chemical and biological changes in the environment. Water samples are being collected bi-weekly from 10 sites in Matlab and tested for physical properties such

as pH, for the concentration of minerals and ions and for plankton and algae. The presence of V.cholerae is being detected using conventional culture techniques and by immunofluorescence microscopy using monoclonal antibodies. This research is a part of the work of an Environmental Microbiology Unit.

MORTALITY, MORBIDITY AND MALNUTRITION

Child survival was identified last year as a priority for research at the ICDDR,B. If the means are to be found to decrease the death rate of over 200 infants in every 1000 live births, then research to identify the principal causes of death must be undertaken in circumstances where those deaths occur. This must include research on the health of mothers as well, because a child's health depends to a large part on the mother's ability to look after it. Two studies of deaths among children and women in rural Bangladesh, where over 90% of the people live, are reported here.

The causes of death of children in Matlab

Principal Investigator: V Fauveau

Funded by: NCRAD MCH-FP Programme and CIDA via the DSS

Based on the new procedure established by the DSS in 1986 to assess the causes of death (see Annual Report 1986), the causes of deaths of children in Matlab were analysed for the year 1986. One of the most significant findings was that deaths due to neonatal tetanus had previously been largely over-reported because the criteria to define a case were not precise. As a result neonatal tetanus dropped from first to third place as a cause of neonatal mortality, and now comes below complications of a low birth weight and trauma at birth.

The causes of death of women in Matlab

Principal Investigator: V Fauveau

Funded by: NORAD MCH-FP Programme and CIDA via the DSS

An analysis was completed in 1987 of causes of death of women of reproductive age in Matlab during the ten years between 1976 and 1985. The maternal mortality rate was 5.5 per 1000 live births. In 77% of cases it was due to direct obstetric complications with the following order of importance: post-partum haemorrhage, induced abortion, eclampsia, post-partum sepsis and obstructed labour. The rest of the deaths were due to concomitant medical causes and injuries. Excluding abortions, 43% of all maternal deaths occurred during labour or in the two days following the end of the pregnancy, and 80% of all maternal deaths took place in homes without medical care. These findings have served as a basis for planning a maternity care programme in Matlab (see page 46).

During the same 10-year period it was found that infectious diseases were the major cause of death of women of reproductive age, between 15 and 44 years old. They comprised 24% of the total deaths and most were due to diarrhoeal diseases and respiratory tract infections. Direct obstetric complications accounted for 29% of all deaths, injuries and violence for another 12%, while suicide alone accounted for almost 5% of deaths. Direct obstetric complications and injuries were particularly frequent in young women while infectious diseases were the main cause of death in older women. The two most significant underlying conditions for these causes of death were a high fertility and poor access to modern medical care.

Although much of the work of the ICDDR,B concerns diarrhoea, this often overlaps with other problems of health. For example: patients are often admitted to hospital with other disease as well as diarrhoea, so the question arises: are they related in any way?. In particular, how are respiratory tract infections, recently identified as a major focus of attention in the Matlab MCH-FP Programme (see p 45), related to diarrhoeal diseases?

Acute lower respiratory tract infections in children with and without diarrhoea

Principal Investigators: M Rahman, Farida Huq (IPH) Nazmun Nahar (DMCH)
Funded by: United States Board of Science and Technology for International Development (BOSTID)

The aim of this study, which began in 1986, is to examine the causes of acute lower respiratory tract infections in children aged less than 5 who attend either the ICDDR,B with diarrhoea or the Dhaka Medical College Hospital without diarrhoea. The viral and bacterial causes of these infections are being sought by testing nasopharyngeal aspirates, throat swabs and blood.

An adequate period of breast feeding is crucial for the health and growth of infants. Breast milk is nutritionally adequate for the first few months of life, breast milk contains antibodies to help protect the infant against infections, and above all it is sterile. The hazards begin when infants are first fed on other foods: they may be nutritionally inadequate as they are often made from highly diluted powdered cows milk, and they are rarely sterile. For these reasons weaning is often associated with growth faltering.

Breast feeding, weaning and infant growth in rural Bangladesh

Principal Investigator: Shameem Ahmed
Funded by:

The objective of this study is to examine the effect of the introduction of supplementary foods on the growth of breast-fed infants. A cohort of 146 children in a rural area of Chandpur district were studied from birth until one year of age. The children were weighed and measured every 15 days, illnesses were recorded and a 24 hours dietary recall of foods given to the infant was recorded. Breast-milk samples were collected from 30 randomly selected mothers every 3 months and the nutrient content of the milk was measured.

An analysis of the relationship between growth, morbidity, the nutrient content of breast milk and food intake is under way and will form part of a dissertation for a Ph.D. at the Institute of Child Health, University of London, U.K.

The second phase of data collection is now underway to assess the effect of the different patterns of feeding and morbidity on the growth of the same children during the second and third years of life. It will

examine the following questions. Does growth faltering occur if a child is exclusively breast-fed for more than 12 months of age? What is the incidence of diarrhoea and other illnesses in breast-fed children during the second and third years of life? Do children whose growth has faltered during the first year of life regain their initial growth velocity in the second and third years of life?

Breast-feeding, nutritional status and child survival

Principal Investigators: A Briend, B Wojtyniak and MGM Rowland

Funded by: NORAD MCH-FP Programme and CIDA via the DSS; ORSTOM

This prospective study was linked with the next investigation reported here and was conducted to examine the effect of breast-feeding on nutritional status, morbidity and child survival. Every month for 6 months, health workers enquired about breast-feeding and illness in about 4600 children aged 12 to 36 months, and measured their arm circumference. Information about children who died within one month of a visit was then compared with information about those who survived.

Approximately one third of the deaths in the age range 18-36 months was attributable to the lack of current breast-feeding. Within this age range the protection conferred by breast-feeding was independent of age but was evident only in severely malnourished children. In communities with a high prevalence of malnutrition, prolonged breast-feeding for up to 3 years may substantially enhance child survival.

Malnourished children are known to have a greater risk of dying -- for whatever cause -- than well nourished children, but there is still great debate about the best means of assessing a child's nutritional status in relation to the risk it has of dying. A simple and sensitive indicator is needed to enable health workers to identify children who need help, preferably before they have got to a stage when they are beyond help. Arm circumference may provide the best indicator of the risk of dying of all nutritional measurements and indices currently in use.

Detecting children in the community most at risk of dying

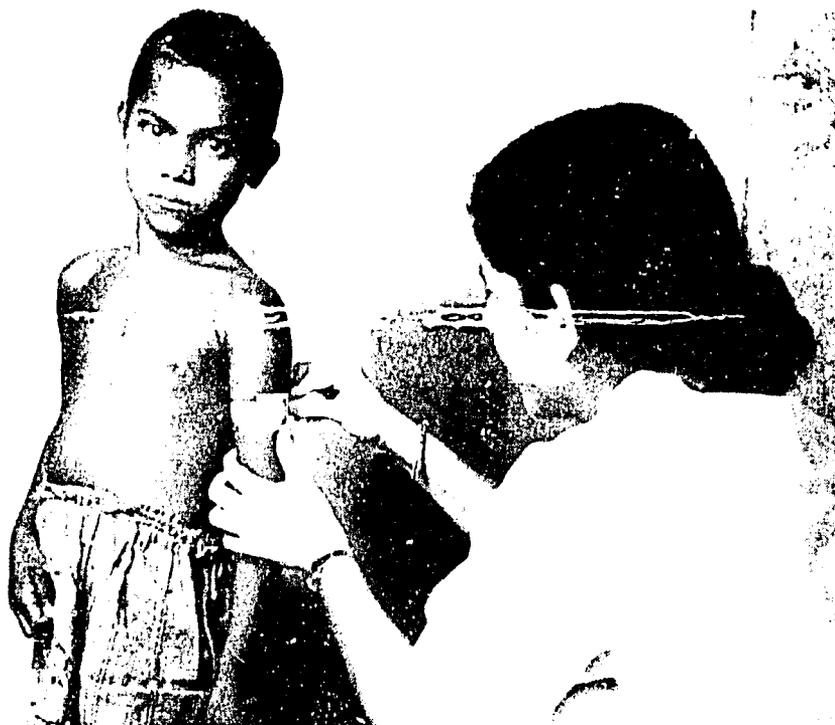
Principal Investigator: A Briend

Funding: NORAD MCH-FP Programme and CIDA via the DSS; ORSTOM

The aim of this project was to test the value of measuring mid-upper arm circumference as a means of detecting children most at risk of dying. The research for this project was undertaken between 1985 and 1986 in Matlab, and was analysed in 1987 (see Publication B 12).

The mid-upper arm circumference (MUAC) of about 5,000 children aged between 6 and 36 months was measured monthly for 6 months. Using the MUAC it was possible to identify children who died within one month of the measurement with 94% sensitivity and 46% specificity - almost twice the sensitivity achieved by other anthropometric measurements or indices for that level of specificity. The specificity was slightly improved when the absence of breast-feeding, concurrent diarrhoea, oedema, and acute respiratory tract infections were taken into account.

This study indicates that children most at risk of dying can be detected by a simple measurement which could be used as a screening process for specific treatments and nutritional rehabilitation.



Measuring arm circumference with a simple waxed paper tape

Recent studies in Indonesia suggest that a deficiency of vitamin A may be responsible for an increased susceptibility to diseases and may increase the risk of dying. This research is now being critically appraised by studies in many other parts of the world where vitamin A deficiencies are common, including Bangladesh.

Evaluating the risk of dying in the interval between doses of vitamin A six months apart

Principal Investigators: A Brand and V Fauveau

Funding: United States AID; OREGON

This research project is designed to test indirectly the hypothesis that vitamin A may reduce infant and child mortality. Villages in Matlab have been divided into two groups so that capsules of vitamin A are given at different times of the year. Variations in the number of deaths during the interval between giving capsules are being studied.

The concentration of vitamin A in breast milk is crucial to breast-fed infants as it is their only source of this vitamin after stocks laid down in the liver in utero have been exhausted.

The concentration of vitamin A in breast milk after supplements

Principal Investigators: SK Roy and Asma Islam

Funded by: UNDP

The aim of this study was to examine the effect of providing a single dose of 200,000 units of vitamin A to mothers after childbirth on the concentration of vitamin A in breast milk and on the subsequent health and growth of their children. The controls received a placebo. The concentration of vitamin A and retinol binding protein was estimated in blood before supplementation and at regular intervals for 9 months after; the same measurements were also made on breast milk for 9 months after delivery. The effect of the dose of vitamin A lasted for 3 months. There were no differences between groups in the incidence of diarrhoea and other illnesses.

Two hospital studies of factors which might contribute to malnutrition are reported next. The first involves examining the nutritional consequences of intestinal damage caused by pathogens while the second study involves an examination of the way the pancreas functions during acute diarrhoea.

Protein loss into the gut in childhood diarrhoea

Principal Investigator: AN Alam

Funded by: United States AID

Protein losses into the intestine and intestinal permeability are being measured in both malnourished and well nourished children with diarrhoea of different causes. The techniques being used to estimate intestinal permeability are described in more detail on page 14. In addition, nitrogen losses in the faeces and urine are being measured. Zinc supplements are also being given to examine any effects on intestinal permeability. In 1987 20 children were studied.

One of the two functions of the pancreas is to secrete inactive forms of several enzymes into the small intestine where they are then activated to begin digesting proteins and carbohydrates. The pancreas is therefore intimately concerned with the digestion of food in a part of the gut often severely affected by pathogens which cause diarrhoea.

Pancreatic exocrine function in acute diarrhoea

Principal Investigator: PK Bardhan

Funded by: Swiss Development Corporation and United States AID

Studies at the Centre have shown that a transitory malabsorption of nutrients occurs in most gut infections, but the mechanism of this has not been explained. The aim of this study is to assess the function of the pancreas and its secretions in patients with acute, infectious diarrhoea. The study began in September 1987 and of the 30 patients and 10 volunteers required, 14 patients and 1 volunteer had been studied by the end of 1987.

POPULATION STUDIES

Since 1963 the ICDDR,B has been studying the population of a large part of Matlab Upazila, a region about 45 km south-east of Dhaka. The Centre's Demographic Surveillance System (DSS) as it is called, involves periodic censuses and socio-economic surveys in addition to a continuous recording of vital events: all births, deaths, migrations, marriages and divorces. At the beginning of 1987 there were 194,757 people living in 143 villages within the DSS area.

In 1976 the ICDDR,E began a similar process of demographic surveillance in Teknaf, a rural area near the extreme south-east border of Bangladesh. At the beginning of 1987 the population of the area under study was 77,316. Some demographic trends in Matlab and Teknaf are presented in Table 1.

Demographic Surveillance System

Principal Investigator: Bogdan Wojtyniak

Funded by: Canadian International Development Agency

An improvement in reporting causes of migration in and out of both Matlab and Teknaf DSS areas was achieved during 1987 which now enables distinctions to be made between different reasons for moving. For example, people may move to accompany their families; they may move to get better jobs or because of marriage or to study; they may be forced to leave in order to find work, or alternatively, may arrive to take up employment. The last two reasons for moving are termed "push" and "pull" migration.

To improve data recording and allow it to be done using microcomputers at field stations, the currently used registration forms were redesigned, the layout was standardised and redundant information was removed.

DSS Database Development

The main work during the year was the continuing process of transferring data recorded on paper into a computer database: most of the work in 1987 involved the Census and the Socio-economic Survey of 1982. In this process once each record is entered into the computer it has to be checked carefully against the written record to make sure it was entered accurately, and against other records which might show up inconsistencies. This can involve comparing the same information about a person, such as age, in several different parts of the database to make sure it is consistent, or may involve comparing it against a range of possible values: someone is unlikely to be 120 years old for example.

Once all the data recorded for 1982 had been entered into the computer and exhaustively checked, it was then transferred into the main DSS database. This involved making sure that the right data went into the right place and that it conformed with the format in which the larger

database expects its data. This process can also act as a way of identifying errors. Once within the larger database, it was then necessary to establish links between related data. For example, links between information collected about the same person at different times or for different reasons. The computer programmes for this process of building a database, in which the data is related in logical links with other data so that for example, information about a woman is linked with her husband, uses software called Standard Query Language or SQL (sometimes pronounced "sequel"). The result of database building and SQL is that an ICDDR,B demographer can sit at a screen and keyboard terminal to the mainframe computer and have easy access to all the information and related information about any person or topic of interest stored in the DSS database. In computer jargon this is called an "on-line interactive interface for end-users".

Table 1

Population dynamics in the Matlab treatment area (M treat.), in the Matlab comparison area (M comp.) and in Teknaf, from 1979-1986. The Matlab treatment area is served by the Centre's MCH-FP Programme (see p 45) while the Comparison area is served by the government health services alone.

Vital rates (per 1000)	Area	1979	1980	1981	1982	1983	1984	1985	1986
All deaths	M treat.	12.1	11.3	11.9	12.5	12.1	13.4	10.0	9.9
	M comp.	15.6	14.8	14.4	15.9	18.0	17.3	14.1	12.1
	Teknaf	15.9	12.8	14.2	13.6	14.7	17.1	12.8	13.4
Neonatal deaths	M treat.	70.9	59.3	66.4	58.1	56.4	57.9	50.0	49.6
	M comp.	74.6	72.7	69.5	68.1	70.3	71.4	67.9	51.8
	Teknaf	85.6	75.0	88.3	72.8	88.4	96.0	77.4	81.0
Post-neonatal deaths	M treat.	43.5	32.6	36.1	47.5	41.8	56.9	34.4	37.5
	M comp.	43.5	41.3	45.0	50.2	42.2	55.7	49.3	37.7
	Teknaf	57.1	46.8	51.2	46.1	65.4	57.3	45.9	46.2
Child (1-4 y) death	M treat.	17.1	18.6	19.1	18.8	21.6	23.1	14.7	13.1
	M comp.	26.2	25.4	24.8	27.4	35.3	39.2	21.5	20.1
	Teknaf	16.9	13.7	14.9	10.6	12.3	22.1	11.8	12.5
Births	M treat.	34.9	37.1	35.3	36.9	33.8	30.7	34.3	33.3
	M comp.	47.0	45.5	43.8	44.6	42.4	37.3	42.5	40.0
	Teknaf	55.6	52.4	51.5	54.2	53.4	54.8	54.4	55.5
Total fertility*	M treat.	4.8	5.1	4.8	5.0	4.5	4.0	4.5	4.3
	M comp.	6.9	6.7	6.3	6.3	6.4	5.1	5.9	5.5
	Teknaf	8.1	8.1	7.7	7.9	7.5	7.8	8.1	8.1
Natural increase	M treat.	22.9	25.8	23.4	24.3	22.3	17.3	24.3	23.4
	M comp.	31.4	30.6	29.4	28.8	25.8	20.0	28.4	27.9
	Teknaf	39.7	39.6	37.3	40.6	38.7	37.7	41.6	42.1

* per woman

Research

The DSS database allows many aspects of life, health and death to be studied on a large scale from behind a computer terminal.

A study of data from Teknaf examined the effect of mothers' personal and domestic hygiene on the incidence of diarrhoea among 327 children aged 6-23 months. These children were living in an area where tube-well water and latrines had been provided by the ICDDR,B and were compared with 339 children in a similar area with no such new facilities. A number of hygienic practices were found to be related to a 40% decrease in the annual incidence of diarrhoea among children in the first area, and included using hand-pump water for drinking and washing, as well as washing hands before handling food and after defaecating.

Using data from Matlab it has been possible to see if there are any sustained effects of the 1974 - 1975 famine on children born around that period. A total of 7,264 births were studied in three groups: children born during the famine, children conceived during the famine and children born after the famine. The death rates among these children during the first 5 years of life were studied and found to be higher during the first two years of life among children born during the famine.

A third study examined in both Matlab and Teknaf the effect of consanguineous marriage on the number of miscarriages, still-births and live-born children, and on infant mortality in general. In both regions no significant general relationship was found. However, there was a significantly higher mortality among the children of marriages between first cousins. It is probable however that the large number of still-births, miscarriages and deaths in childhood which occur anyway may obscure any effect of parental consanguinity.

It has been observed that the likelihood of divorce in rural Bangladesh is related to age, the duration of marriage and to socio-economic status. An analysis of 5 years of data performed during 1987 indicated that divorce in rural Bangladesh tends to occur early in marriage. In addition it was found that a difference in ages has a strong impact on the incidence of divorce, which is also related to education, the husband's occupation and religion. Divorces were found to be substantially more common among people with no schooling or Koranic education and were more common among farm labourers compared with other occupational groups.

A cohort of 518 first marriages which took place in 1975 was examined for 10 years to study fertility and divorces in relation to the distance separating the bride and groom before their marriage. The mean fertility of women was inversely and significantly related to this distance while the risk of divorce was significantly higher among couples who lived within 10 kilometres of each other before their marriage. However, socio-economic status was also found to be related to the distance which had separated a couple before their marriage: people who married someone from nearby tended to be poorer while richer people tended to find partners from further away.

HEALTH CARE RESEARCH

The Maternal, Child Health and Family Planning (MCH-FP) Extension Project was established in 1982 at the request of the Planning Commission of the Government of Bangladesh. Its aim is to test in rural Bangladesh the ability to transfer successful aspects of the maternal, child health and family planning services in Matlab (see page 45) to the Government health services. This research is being carried out in the Upazilas of Sirajgonj and Abhoyanagar.

The MCH-FP Extension Project

Principal Investigator: Michael Koenig

Funded by: United States AID and the Population Council

In contrast to the services provided in Matlab and other similar pilot programmes, the Extension Project tests the effectiveness of services within the Government organisation, thereby facing the same constraints in terms of finance, resources and management as the Government MCH-FP programme. During its five years of operation, the wide ranging research of the Extension Project has generated much that is relevant to policy in general, some of which has been incorporated into national policy. During 1987 the activities of the project continued and in some areas were expanded.

Matlab: research

A major emphasis was placed on obtaining a more detailed understanding of the dynamics of contraceptive use in the Matlab treatment area.

A study examined trends in family size in relation to contraceptive use in Matlab and concluded that the adoption of contraception for the purpose of spacing births was the primary factor behind the rise in contraceptive prevalence in the Matlab treatment area during the period between 1977 and 1984 (see Publication B. 40). The success of the Matlab family planning programme is noteworthy in that it has occurred within a setting where the demand for family planning services is widely believed to be very weak or entirely absent.

A second study examined the factors underlying the success of family planning in the Matlab programme. The principal conclusion of the study was that the presence of a strong service programme in an environment where the demand for such services is highly fragile has been a primary factor behind the high rate of contraceptive use in the treatment area.

A third area of research has involved more detailed investigations of the effectiveness of contraceptive use and the rates of their continued use. A study of IUD users was undertaken during the year and similar studies of other contraceptive method users are in progress.

A second major focus of research has been a collaborative evaluation of the impact of family planning and MCH services upon mortality. In addition, studies based upon both aggregate-level time series data as well as individual-level longitudinal data have explored the impact of services such as family planning, tetanus and measles immunisation upon declines in mortality among neonatal, post-neonatal and 1-4 year old children. This is part of an effort to understand more fully the potential as well as the limitations of such interventions for improving child survival in settings such as rural Bangladesh.

The Matlab Record-keeping System (RKS)

A key component of the Matlab MCH-FP programme is a computerised system of record-keeping for about 15,000 women of reproductive age and 18,000 children under 5 years old. Community Health Workers (CHWs) collect information each month from women about their use of contraceptives, reproductive status, breast-feeding and about tetanus immunisation. Mothers are also asked other questions about their children which provides information on immunisation, diarrhoea, treatment for diarrhoea, the administration of vitamin A capsules, nutritional status, and acute respiratory tract infections.

In addition to its central role in providing MCH-FP services in Matlab, the information stored on computer in the RKS provides the basis for much of the research undertaken within the treatment area. Efforts were directed in 1987 to further modifying and expanding this data system. In addition, preliminary work was begun on transferring the RKS from the mainframe computer in Dhaka to microcomputers in Matlab, with the primary objective of developing a record-keeping system which is more efficient and which could be used in other MCH-FP programmes which do not have access to a mainframe computer.

The Extension Areas: the Sample Registration System (SRS)

A major innovation of the Extension Project has been the development of the Sample Registration System (SRS), a computerised system providing rapid feedback about the impact of the Extension Project on service operations and about demographic rates. At intervals of 90 days teams of interviewers visit a representative sample of roughly 10,000 households to collect information on vital events, contraceptive use, and contacts with the Government health and family planning service programme during the preceding period. Within three weeks of the end of a round of visits the data has been edited and indicators of the impact of the programme are available. Moreover, the data can be readily linked to previous records to allow detailed longitudinal analyses to be undertaken of specific issues concerning service operations and demography. The SRS produces highly accurate and reliable data, yet it avoids the lengthy delays which characterise other surveillance systems (see Table 2).

In collaboration with the Population Council efforts were concentrated during the year on adapting the SRS to microcomputers so that it might be used elsewhere. In addition, the Extension Project provided technical assistance to a team of Indonesian investigators in order to adapt the SRS to the surveillance of diarrhoeal diseases in rural Sumatra.

Table 2
The birth, fertility rate and death rates in the two areas of the MCH-FP
Extension project, Sirajgonj and Abhoynagar.

Vital rates (per 1000)	Sirajgonj				Abhoynagar			
	1984	1985	1986	1987	1984	1985	1986	1987
Crude birth rate	46.6	44.5	39.6	40.6	29.5	33.2	26.7	29.5
General fertility rate ^a	206.0	194.6	172.1	176.1	125.3	139.1	110.8	121.6
Total fertility rate ^b	6.4	6.1	5.4	5.3	3.8	3.9	3.1	3.4
Crude death rate	19.3	14.5	13.8	13.3	11.3	11.3	10.0	7.8
Infant death rate ^c	175.3	166.7	149.4	149.4	145.8	121.1	138.2	105.8
Neonatal death rate ^c	105.3	97.2	95.3	91.9	75.6	54.0	91.5	60.2
Post-neonatal death rate ^c	69.9	69.4	54.2	57.5	70.1	67.1	46.7	45.6
Age specific death rates:								
- 1-4 years	36.1	22.9	23.0	18.4	10.5	9.5	9.2	4.6
- 5-14 years	3.9	2.4	1.8	2.6	2.5	1.3	1.3	0.6
- 15-44 years	2.7	1.2	2.7	2.0	2.4	3.3	2.0	2.5
- 45 + years	30.4	23.1	23.0	24.2	28.5	31.1	30.1	19.9

^a Per 1000 women of child-bearing age

^b Per woman

^c Per 1000 live births

Operations Research

In 1987, the Extension Project continued to test interventions in the Government service programme which had been shown to be effective in Matlab. Of particular interest was the assessment of the impact of increased numbers of female fieldworkers upon the delivery of services, an innovation which was tested in the Extension Areas prior to its introduction nationally. The initial results from this study showed that increasing the number of female fieldworkers has resulted in a significant rise in the frequency of visits to rural households as well as a substantial rise in the contraceptive prevalence.

A series of studies were also undertaken during 1987 on specific aspects of the Government service programme. These operations research studies included: the management of the Government IUD programme; an analysis of trends in sterilisation performance; factors accounting for variation in the performance of female fieldworkers; a time-use analysis of male health workers; and differences between male and female workers in patterns of work and services provided.

Technical Assistance at the National Level

The Extension Project has been increasingly recognised by policy makers as a resource not only for testing innovative approaches to service delivery in its field sites, but for providing direct technical assistance to the Government to improve the national programme. A major Project activity during 1987, in response to a request from the Government of Bangladesh, was to assist the Government with planning and implementing the recruitment of 10,000 additional female fieldworkers (FWAs). The decision to increase the number of FWAs was based largely upon the findings of research from the Extension Project which showed that the inadequate number of female fieldworkers was a key barrier to a more effective functioning of the Government service programme. The recruitment of these additional workers represents one of the most ambitious expansions of staff ever undertaken by a government health and family planning programme. A team of Extension Project staff, working with Government officials at the District and Upazila levels, has greatly assisted the Government in planning and executing recruitment. The findings of research from the Extension Project have contributed significantly to strengthening the process of recruitment and deployment of the new FWAs.

PROVIDING HEALTH CARE

The ICDDR,B provides free treatment for diarrhoea for anyone who attends its Treatment Centres in Dhaka, Matlab and Teknaf. Many small research projects also provide free medical care as a part of their work. The main Treatment Centre is on the site of the Centre itself in Mohakhali, Dhaka.

Dhaka Treatment Centre

Head of Hospital: AN Alam

Funded by: DANIDA and core support

During 1987 a total of 70,739 patients attended the Dhaka Treatment Centre, an increase of 10% compared with the previous year. Some diagnostic tests were performed on stools collected from every twenty fifth patients (see Table 3).

Table 3
Results of the microbiological culture of stools from a systematically selected sample of 4% of patients who visit the Dhaka Treatment Centre of the ICDDR,B.

Month	Number of patients	Salmonella spp	Shigella spp	Vibrio cholerae	Other vibrios
January	198	0	39	33	44
February	120	0	5	13	19
March	189	0	11	33	24
April	289	0	18	37	71
May	287	0	23	52	46
June	236	1	26	21	32
July	168	2	16	20	20
August	274	3	27	41	56
September	326	1	38	67	70
October	260	1	28	71	53
November	169	0	24	49	41
December	305	1	35	131	62
Total	2821	9	290	568	538
Percent	100%	0.3%	10.2%	20.1%	19.1%

The percentage of patients actually admitted to the wards dropped slightly from 8.9% to 8.5% even though the the total number of admissions increased by over 5%, from 5,712 to 6,033. Of the patients admitted to the wards of the Treatment Centre, 1,015 had shigellosis and 1,100 had cholera. The death rate was very similar to that in 1986: 390 people died, 0.6% of all patients who came for treatment and 6.5% of all patients admitted. Shigellosis was responsible for 25% of those deaths.

Just over 240,000 litres of ORS were consumed in the Treatment Centre during the year and over 49,000 litres of intravenous solution. The ratio of ORS used to i.v. fluid was about 5 to 1.

Three departments were created within the Dhaka Treatment Centre during the year. A Clinical Services Department, a Clinical Research Department and a Child Health Department.

It is estimated that roughly 1 million people live in the slums of Dhaka and that about 200,000 of them are less than 5 years old. These children and their mothers are the targets of a project to study the means of providing them with health services largely using volunteers based within the slum communities themselves. In the course of this operations research many services are provided to the slum dwellers of Dhaka.

Urban Volunteer Programme (UVP)

Project Director: Diana Silimperi

Funded by: United States AID; Belgian Administration for Development Co-operation; French Government Relief Fund

The main priorities of the health services provided by the UVP are to treat and prevent diarrhoea, to vaccinate, to improve nutrition and to provide the means to plan families. In addition, the Programme collects information from 70 clusters of households in the slums in order to study the epidemiology of diarrhoea and nutritional deficiencies, to identify means to prevent diarrhoea, malnutrition and deaths in childhood, and to test services for possible use within the whole Programme.

Although the training of community volunteers began in 1981, it was not until 1987 that funding was obtained to allow significant expansion of the programme. During 1987 attention has focused on refining the Programme's goals and objectives; describing its organisational structure, its supervisory system and jobs; improving training and the data collection system, and providing the means for assuring the quality of services and evaluating their effect. Some new objectives were also defined and include teaching people how to read and write, and teaching skills that could be used to make money: both these activities will be undertaken while at the same time promoting an awareness of how to improve health.

As a part of the process of formal self-description, maps of the slums in Dhaka were commissioned and a new census was undertaken. This will enable an analysis of the distribution of volunteers and will assist in evaluating the impact of the Programme.

While this was going on the UVP was still providing services to urban slum dwellers. Here are some statistics about a few of those services provided during the year:

- 109,421 patients with diarrhoea were treated and 768 who were severely dehydrated were referred to the ICDDR,B Treatment Centre
- 385,463 packets of ORS were distributed
- 2,213 children with xerophthalmia were detected and treated with oral vitamin A

- 477 children received food at three nutritional rehabilitation centres in slum communities
- 3,513 bars of Neem soap were distributed to promote personal hygiene and to treat scabies
- 7,976 mothers and children were encouraged by volunteers to be vaccinated
- 9,469 mothers were referred by volunteers for family planning services

An analysis of volunteers

A review was undertaken in 1987 of the activities of all the 1822 urban volunteers trained since the Programme began in 1981. About 1550 were found still to be active in 1987 while about 250 volunteers had stopped their activities or could not be found. Most of the volunteers who had given up had done so because they had moved or had lost contact with their supervisors. The survey found that the active volunteers spent from 2 to 60 hours on promoting health. About 10% of them currently had paid employment while another 10% received stipends from the UVP for their work as supervisors, for training or for other specialised work. A 9 month study of contacts between 21 UVP supervisors and 1,269 active volunteers recorded a total of 6,299 contacts, but only 7% of volunteers had contact with their supervisors every month. On average for the whole Programme there was one supervisor for every 75 active volunteers, a high ratio which will be reduced to about 1:40 in 1988 by plans to increase the number of supervisors.

Data collection

A thorough review of the system for recording the work of volunteers indicated that the field notebook system was not accurate, since it largely depended upon memory: most volunteers are illiterate and rely on memorising what they do and then reporting it to field supervisors who write in the notebooks. Because volunteers may have few contacts with their supervisors an alternative system of record-keeping was devised based on a calendar with pictures and symbols. The results of a trial of this system have been used to improve the calendar and it will be brought into full operation in 1988 after the volunteers and supervisors have been trained.

Distributing ORS

A preliminary survey revealed that although the activities of the urban volunteers are directed at children younger than 5, many recipients of ORS were not aware of this, a significant number did not give it to their young children because they didn't like it, and most ORS was consumed by older children and adults. A full evaluation of ORS use is underway.

In the past packets of ORS were collected from the central office by supervisors who simply estimated the number they needed for their volunteers. No records were kept about how many packets were collected by each volunteer or about how many packets were left over each month. In addition the figures for the total number of packets supplied each month showed little seasonal variation even though diarrhoeal disease is highly seasonal, while there were large differences in requirements for the same month in different years.

In 1987 a new system to register the number of packets supplied to each volunteer was set up based on estimates of their requirements. This

information is now being recorded on computer. With details of the number of packets remaining from the previous distribution, it will allow requirements to be calculated both for the project and on an individual basis. A regular van delivery of ORS to supervisors was also started. During September, the first month of the new system, a record number of 52,000 packets of ORS were distributed. The first 4 months of the new system coincided with an increased incidence of diarrhoea due to the severe flooding which hit many parts of the country including Dhaka (see below), which resulted in increased diarrhoea and an greater demand for ORS. The new system proved itself by working well.

The severe flooding which hit Bangladesh in 1987 was reported to be the worst in living memory. Bangladesh contains most of the Ganges delta and the average height of the country is only about 10 metres above mean sea level. Even during the monsoon in normal years many parts are liable to flooding and, as in many other parts of the world, the poor in Bangladesh tend to live on the lowest lying land. One major consequence of flooding is that when surface waters get into pit latrines people's water supply can become contaminated and so diarrhoeal diseases often break out.



The hospital volunteer project

During the year a formal description of the purpose and procedures of this project was undertaken, the general aim of which was to provide a few urban volunteers with one year's advanced training in nutrition, in treating diarrhoea and in preventing epidemics. The knowledge and skills acquired by the volunteers during their training in the Dhaka Treatment Centre can then be used to improve the health of their community.

Immunisation

During 1987 a trial project using 29 volunteers to motivate and refer mothers to have their children immunised was conducted in two areas of Dhaka. The general volunteers provided basic knowledge about immunisation to 7,976 mothers; 794 children were actually taken to immunisation centres. An evaluation of the project showed that it involved a considerable

commitment by both volunteers and supervisors. Not all aspects of the project will be used by the whole Programme, but in 1988 volunteers will be taught about immunisation and how to get mothers to have their children vaccinated.

As a result of this pilot project a network of organisations involved in immunisation has evolved within Dhaka. A Dhaka EPI Co-ordination Committee was formed, including a representative of the UVP, and a conference was held in November to co-ordinate the EPI in metropolitan Dhaka.

Nutritional activities

During 1987 two new nutritional rehabilitation centres were started using UVP trainees, bringing the total to three, and 477 children were treated during the year. A project was also begun in one slum to evaluate the effect of combining maternal education, growth monitoring and supplementary feeding. In the same community a feeding programme was instituted during the serious floods which seriously affected many slums in Dhaka.

As a part of the process of internal self-evaluation during the year, the operation of the nutritional rehabilitation units was also assessed. This indicated that improvements were needed in terms of training and supervising staff, treating and referring sick children, and visiting children at home after discharge. Measures to bring about improvements have been introduced.

Training

During 1987, 69 volunteers took part in training courses at the Dhaka Treatment Centre and at the Nutritional Rehabilitation Units. Despite a temporary lull during the review of the whole UVP training programme, basic training was also given to 311 volunteers, revision training to 84 and training in immunisation to 61. The expertise of supervisors was also improved by an advanced course on immunisation, while the competence of field research officers to determine causes of deaths by interviews and to perform anthropometry was improved.

The UVP also provided specialised training for volunteers from other organisations during the year, including the Village Education Resources Centre and the New Life Centre.

Research

The number of families being studied in each of the 70 clusters of slum households served by the UVP was increased to 50 during the year. The criteria used to select families was refined and each cluster was mapped. The routine collection of information on illnesses, vital events and nutritional status continued, with particular emphasis being placed on checking information at all stages of its transformation into data and statistics. In addition, a questionnaire about health and about peoples' knowledge about health was given in all 70 clusters of families.

Little information has been collected about causes of death in urban slums because it is very difficult to obtain accurately: it relies heavily on interviews with family members rather than a physician's report. A new questionnaire was prepared which attempts to determine the cause of death by asking pertinent questions about symptoms. When this questionnaire has

been refined it will become a routine form for use among the clusters of families being studied by the UVP.

Although the main emphasis during the year was critical self-evaluation and a process of formal description of the Programme, several papers were published on earlier research (see Publications list no B.66 to B.69).

Towards the end of 1977 a family planning and health services programme was launched in half of the the Matlab project area with the objectives of reducing fertility and improving child survival. This has now become the Matlab MCH-FP Programme. The Demographic Surveillance System in Matlab (see p 33) makes it possible to assess the impact of the services provided by the Programme in comparison with the remainder of the population in the DSS area who receive the normal government services. These two areas are called the Treatment and Comparison areas.

The design, implementation and monitoring of the MCH-FP Programme in Matlab Programme Heads: MGM Rowland and V Fauveau
Funded by: NORAD

Health care is provided during fortnightly visits to homes by 80 Community Health Workers (CHWs) who give advice on family planning and nutrition and provide a wide range of contraceptive methods, vaccinations, safe birth kits and vitamin A capsules. Mothers and children can also obtain treatment for diarrhoea and other illnesses at the Matlab Treatment Centre or at four smaller clinics. The CHWs are supervised by male Senior Health Assistants who counsel husbands when needed and by female Family Welfare Visitors who can treat women for family planning related infections and can insert intra-uterine devices.

The first objective of the programme, to lower total fertility, was accomplished by 1984: the fertility rate was then 3.9 in the treatment area compared with 5.2 in the comparison area, a 25% difference. Infant mortality rates however, were not significantly reduced and for this reason it was decided to place emphasis from the beginning of 1986 on child health interventions.

The comprehensive Expanded Programme of Immunization (EPI) was implemented uniformly in the four service blocks of the MCH-FP area in 1986, and a Nutrition Rehabilitation Unit was set up at the Central Matlab Clinic (see Annual Report 1986).

In 1987, based on the findings of an analysis of the causes of death during 1986 of mothers and children less than 5 years old in the MCH-FP and comparison areas (see page 28), the focus of interventions shifted towards the control of acute respiratory tract infections and to providing maternal care.

Controlling acute respiratory tract infections

Acute respiratory tract infections were found to be responsible for 39% of post-neonatal deaths and for 18% of child deaths during 1986. For this reason they have become a priority in the Centre's child survival programme. In accordance with the recommendations of the WHO, the

programme will aim to use CHWs and their paramedical supervisors to detect, assess and treat respiratory tract infections. Moderately severe infections will be treated at home by injections of penicillin while severely ill children will be referred to the treatment sub-centres or to the Matlab clinic. The training programme for CHWs, which includes finding cases, assessing their severity, and the use of injectable penicillin, was completed during the later part of 1987 and, depending on funding, the intervention itself will start in early 1988.

Improving maternity care

Based on the information provided by a recently completed study of maternal mortality in Matlab (see p 28), a programme of maternity care funded by the Ford Foundation was started in early 1987 by posting four professional midwives at two of the MCH sub-centres.

The four midwives have three main functions. First, whenever pregnant women have been identified they perform antenatal visits with CHWs to provide advice, treatment for mild problems and to refer mothers with complications to local hospitals. During these visits the CHWs vaccinate mothers against tetanus, provide iron and folic acid supplements and give safe delivery kits for use during labour. These kits contain among other items a bar of soap, a sterile blade, sterile thread and disinfectant.

Secondly, the midwives attend home deliveries with CHWs and Traditional Birth Attendants (TBA). During normal deliveries they encourage TBAs to follow hygienic practices and to avoid potentially harmful ones. If complications arise they assist the TBA and CHW using the equipment and drugs available in their kits or they organise the referral of the mother to the ICDDR,B clinic in Matlab or to the Chandpur District Hospital.

Finally, they perform postnatal visits during which they make sure both the mother and newborn are well. Again they either treat complications themselves or refer the patients.

By the end of 1987 the midwives had performed 1267 ante-natal visits to 46% of all pregnancies, attended 143 or 15% of all deliveries, performed 506 postpartum visits to 54% of all deliveries and had referred 40 patients to the District Hospital at Chandpur. There was only one known maternal death among the mothers they cared for during the year. Plans are underway to extend these activities to the other half of the MCH-FP area in 1988.

In February 1987, the ICDDR,B also organised a Workshop on Maternity Care at Nayergaon sub-centre. This was attended by 19 members of various NGOs and government officials and by 25 ICDDR,B staff working in Matlab. One outcome of the workshop was a set of specific recommendations for managing obstetric complications during home deliveries.

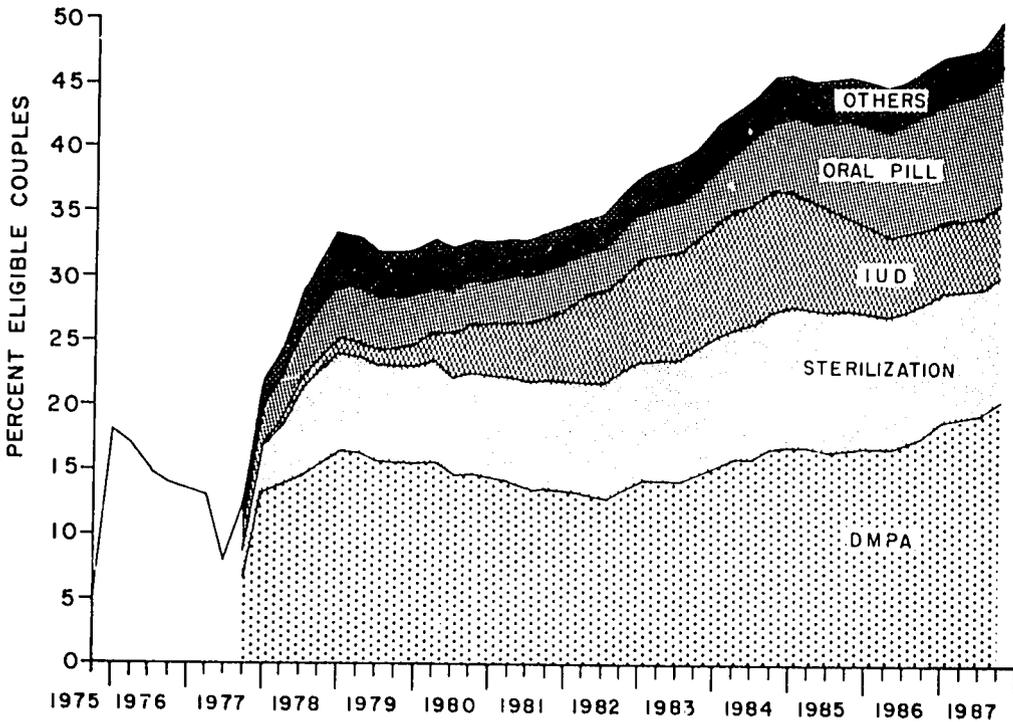
Other Services

The other MCH-FP services, together with their specific monitoring and evaluation, continued throughout 1987. They included: oral rehydration for diarrhoeal diseases; the Expanded Programme of Immunization; nutrition education; the distribution every six months of capsules of vitamin A; the referral of children with infectious illnesses to the MCH clinics; and domiciliary contraceptive services with treatment for any side effects.

The prevalence rate of contraceptive use rose once gain during 1987 from 45% of eligible couples to almost 50% at the end of the year (see Figure below).

Figure

Contraceptive prevalence in Matlab between 1975 and 1988 shown cumulatively by method used.



(IUD = intra-uterine device; DMPA = depot medroxyprogesterone acetate, an injectible contraceptive)

Nutritional activities

The Matlab Central Nutritional Rehabilitation Unit was set up in 1986 with the objective of intensively feeding children with severe malnutrition and treating their associated infections. During 1987 nearly 200 children with a mid-upper arm circumference of less than 110 mm were admitted for treatment. Most of the children were referred by CHWs during routine home visits. The average duration of stay in the unit, usually with the mother or another female attendant, was 19.5 days during which they received intensive feeding with local foods prepared according to local recipes and customs. The mothers were active participants in comprehensive nutrition education, including demonstration of food preparation. There were only five deaths, mostly as a result of infectious complications giving a case fatality rate of 2.6%.

Because of the distance of the Matlab Nutritional Rehabilitation unit from most people's home and the reluctance of husbands to let their wives stay away for up to 3 weeks, a day care NRU with 10 beds was set up in one of the MCH sub-centres in Nayergaon. In 1987 this unit admitted 84 children. Their stay was irregular and was on average shorter than for children admitted to the hospital rehabilitation unit.

Post-flood Nutrition Programme

The extensive floods in August and September 1987 also affected the Matlab area quite severely and raised fears of an increase in malnutrition. Using grants from the French and Dutch governments, Nutritional Rehabilitation Units were set up in November 1987 in three MCH clinics; 194 children had been fed by the end of the year.

Surveys of MCH-FP fieldworkers

A survey of contraceptive practices used by the female field workers themselves working in the project showed a rate of contraceptive use of 66%: the major methods used were the contraceptive pill, condoms and IUDs. Another survey conducted in 1987 with the objective of assessing the variability of CHW's performance showed a range of contraceptive use rate between 33% and 68%. The reasons for this variability either related to the area or to the workers, are being investigated.

The activities of the Matlab Field Station are organised into five parts, closely linked but functionally distinct, each under a supervisor. The parts are: Clinical Services, Health Services (MCH-FP), Demographic Surveillance System, Special Studies, and Administration. Their activities are supervised and co-ordinated by the Head, Matlab Station, although overall responsibility lies with the Associate Director in charge of the Community Medicine Division (CMD).

Matlab Station

Head of Station: M. Yunus

During 1987 more than 7,200 patients were provided with free treatment for diarrhoea at the Matlab Treatment Centre, 63% of whom came from outside the area of the Demographic Surveillance System. The case fatality rate was 0.7%. An additional 4,600 patients were treated at three Community Operated Treatment Centres (COTCs) run by volunteers trained and supported by Matlab Station. There were only 9 deaths at the COTCs, a case fatality rate of 0.2%.

In addition to supporting research investigations the Microbiology Laboratory cultured stools from 2,692 patients with diarrhoea who came from within the DSS area and isolated three main pathogens: Vibrio cholerae (17%), non-cholera vibrios (12%), and Shigella spp (16%).

The Clinical Pathology Laboratory performed microscopical examinations of 5,663 faecal samples, 1157 urine specimens and over 3,000 blood samples. The clinical laboratory also performed tests on more than 200 specimens for blood chemistry including sodium, potassium and glucose.

After the floods

Following the severe flood, Matlab Station organised three medical teams to provide relief in Matlab Upazila. From September to December these teams treated 4680 patients, mostly children suffering from infectious diseases including diarrhoea, dysentery, acute respiratory tract infections, fever and skin infections.

Teknaf Station

Head of Station: MH Munshi

Funded by: DANIDA and United States AID

Three treatment centres are operated in Teknaf and in 1987 they provided free care to 5,827 patients with diarrhoea. The number of patients seen in Teknaf during 1987 and the two previous years is shown in Table 4. There was a significant jump of 10% in the proportion of patients with dysentery, from 64% in 1986 to 74% in 1987.

Table 4
Clinical and laboratory services in Teknaf, 1985-1987

	1985	1986	1987
Total number of patients	3,631	5,565	6,240
Watery diarrhoea	1,152	1,780	1,203
Dysentery	2,253	3,572	4,624
All others	226	213	413
Deaths in treatment centres	1	9	6
Patient treated for > 12 hours	36	252	258
Total number of stools cultured	3,405	5,310	5,684
V.cholerae isolated	24	201	83
Shigella spp isolated	833	1,724	2,974
S.dysenteriae type 1	198	533	1,970
S.flexneri	590	1,166	957
Other Shigella spp	45	25	47
Total ORS used (litres)	6,915	12,550	11,223
Total IV fluid used (litres)	557	82	321

Much of the dysentery seen in 1987 was due to species of Shigella, and in particular, S.dysenteriae type 1: 66% of all diagnosed cases of shigellosis were due to this species and strain of Shigella compared with 31% in the year before. Shigella dysenteriae type 1 causes the most severe disease of any of the species and strains of Shigella and the growing problem of this form of shigellosis in Teknaf is compounded by the fact that the majority of the strains isolated during 1987 were resistant to the most commonly used drugs (see Table 5). Resistance to nalidixic acid, the former drug of choice for treating shigellosis, has developed considerably since 1986 and in most cases it is now useless for treating dysentery due

to S.dysenteriae type 1. Pivmecillinam is now being used to treat adults seriously ill with shigellosis while its use to treat shigellosis in children is being evaluated.

The emergence of strains of S.dysenteriae type 1 which are resistant to nalidixic acid has been found to be related to the presence of a plasmid with a size of 20 megadaltons (see Publication B.48). This association suggests that resistance to nalidixic acid may be encoded on the plasmid, but this needs to be confirmed, particularly as resistance to the quinolone group of antibiotics was never before thought to be plasmid mediated. The general danger inherent in plasmid mediated resistance to drugs is that plasmids are easily transferred between resistant and sensitive strains and even between resistant and sensitive species.

Table 5
Drug resistance of Shigella dysenteriae type 1 and S.flexneri isolated between 1985 and 1987 expressed as a percentage of all organisms isolated during each year.

Drugs	Species	1985	1986	1987
Ampicillin	<u>S.dys. type 1</u>	58	95	99
	<u>S.flexneri</u>	34	55	46
Tetracycline	<u>S.dys. type 1</u>	99	99	100
	<u>S.flexneri</u>	92	92	89
Chloramphenicol	<u>S.dys. type 1</u>	98	99	100
	<u>S.flexneri</u>	34	48	41
Trimethoprim- sulphanmethoxazole	<u>S.dys. type 1</u>	95	99	99
	<u>S.flexneri</u>	4	12	48
Gentamicin	<u>S.dys. type 1</u>	1	1	28
	<u>S.flexneri</u>	0	0	15
Nalidixic acid	<u>S.dys. type 1</u>	0	32	90
	<u>S.flexneri</u>	NT	2	1
Pivmecillinam	<u>S.dys. type 1</u>	NT	16	0
	<u>S.flexneri</u>	NT	4	5

NT = Not tested.

There are serious implications for Bangladesh if strains of S.dysenteriae type 1 resistant to all previously useful drugs are spread throughout the country. Meanwhile other drugs such as ciprofloxacin (see page 9) are being tested as treatments for shigellosis. The need for an effective treatment is urgent.

The Epidemic Preparedness Programme was started in July 1983 with a grant from the Ford Foundation. Its objective is to provide the Government of Bangladesh with expertise to control epidemics of diarrhoea by training Government health staff in diagnosis, treatment and prevention.

Epidemic Control Preparedness Programme

Head of Programme: AKM Siddique

Funded by: Ford Foundation

The specific aim of the programme during its first phase was to train health personnel from all the Upazilas and Districts of Bangladesh. In addition, after 2 years experience of 174 outbreaks of diarrhoea, the ECPP was able to identify factors associated with the high case fatality rate due to cholera in rural areas. The project made significant progress towards its goal of controlling epidemic outbreaks of diarrhoeal diseases and reducing mortality.

Following the success of the first phase, which ended in August 1986, and at the request of the Government, the project has been funded by the Ford Foundation for another two years (1987-1989). The plan for the second phase is to train 46 medical officers who will be responsible for implementing at the District level the National Diarrhoeal Disease Programme. In addition 64 District laboratory technicians will also receive training in essential laboratory methods to diagnose diarrhoeal disease.

The efforts to prevent epidemics will continue. This will contribute to a fundamental understanding of the transmission of diarrhoea and will provide opportunities to evaluate specific methods of preventing epidemic spread.

SUPPORT FOR SERVICES AND RESEARCH

Support for clinical services and research at the main part of the ICDDR,B in Dhaka is provided by a single department which performs routine tests in the fields of microbiology, immunology, clinical chemistry and pathology, and provides other vital support for research such as providing experimental animals or maintaining and repairing equipment.

Department of Laboratory Services
(Bradford A Kay)

The Department of Laboratory Services comprises nearly 140 professional and support staff organised into six sections, each of which has a defined role. The Research Microbiology Branch supports the activities of field and laboratory research. The Clinical Laboratory Branch meets the needs of research studies for routine tests, and the needs of physicians at the Dhaka Treatment Centre. The Animal Resources Branch supplies experimental animals for research and for routine laboratory tests. The pathologists and staff of the Anatomy and Histopathology Unit provide services for both human and veterinary histopathological studies. The results of biochemical, microbiological and clinical pathology tests are now being stored on computer by the Laboratory Information and Archive Unit. Finally, in the Bioengineering Cell, four engineers install, maintain and repair the Centre's electronic and electromechanical equipment.

The Laboratory Information and Archive Unit of the Department of Laboratory Services has undertaken an ambitious three-year plan to store all laboratory information on computer. A series of forms has been designed to record the results of most diagnostic tests done by the Microbiology, Biochemistry and Clinical Pathology branches. This information is already being used for cost accounting purposes and will also allow routine reports and collected statistics of results to be prepared. By the end of 1987 about 25,000 reports had been entered into a computer database with target of 120,000 reports for 1988.

In addition to entering this laboratory information into a computer database, the Archive Unit is currently creating a database of the Centre's bacterial culture collection of about 500,000 isolates. Most of them were isolated during the Oral Cholera Vaccine Trial and represent a unique collection of bacterial isolates.

The Research Microbiology Branch supported about 40 research projects in 1987. A number of changes were made in procedures during the year and enzyme-linked immunosorbent assays are now being used to detect the heat-labile (LT) and heat-stable (ST) toxins of *E.coli*. These assays have replaced conventional tests which used infant mice and rabbit ileal loops to detect the toxins, and as well as having the advantage that they do not use animals they are also cheaper to perform. Other new tests involved

detecting V.cholerae and Shigella spp in faecal samples by coagglutination (see pages 6 and 12). In addition three new cell lines are now grown in culture: HeLa, VERO and HEP2 cells.

The final phase of a 3-year plan to renovate the laboratories was nearly completed in 1987 and involved the Tissue Culture and Anaerobe Laboratories, the Media Preparation Laboratory and the Glassware Washing Room. New equipment during the year included a carbon dioxide incubator, a very low temperature freezer and a freeze-drier.

The Clinical Laboratories Branch has 51 employees working in four sections: Clinical Pathology, Clinical Biochemistry, Clinical Microbiology and Research and Development. The Clinical Laboratory serves the diagnostic needs of physicians in the Treatment Centre as well as providing diagnostic tests for research studies: 120,000 tests for 30 research projects were performed in 1987.

The new Clinical Laboratories Branch is based in the Dhaka Treatment Centre. The services it provides include microbiological culture, clinical pathology tests including blood and stool examinations, and biochemical tests on body fluids. Here two technicians are seen using a new Beckman E4 electrolyte analyser to measure sodium, potassium, chloride and carbon dioxide in serum. Such measurements are important because diarrhoeal diseases can lead to severe losses of these ions which can endanger life.



Although the main laboratory of this Branch is in the Dhaka Treatment Centre itself, the Research and Development Section is located in the main IPH building. This section is responsible for developing and performing specialised biochemical tests for research purposes. After its refurbishment during the year bench space will become available for

visiting scientists and specific projects which need to do laboratory work.

Several major items of equipment were purchased for the Clinical Laboratories during the year including a Beckman E-4 Automated Electrolyte analyser, a Waters HPLC and an LKB Kinetic spectrophotometer.

The Anatomy and Histopathology Unit moved into a new laboratory space on the top floor of the IPH building during 1987. This provided offices as well as more working and reading space. New equipment was also installed including an automatic tissue processor, a tissue embedding unit, a Fisher staining unit, a Reichert rotary microtome, a Reichert automatic microtome knife sharpener, and a fume hood.

The necropsy room was renovated and the range of services offered by the Unit was expanded to include tissue biopsies, frozen sections, necropsy of both humans and animals, bone marrow studies and cytology. Services are now being provided routinely for the physicians of the Treatment Centre and the number of research studies with histopathological aspects grew during the year to include studies on fatal complications of childhood diarrhoea, Plesiomonas shigelloides (see page 22), Bacteroides fragilis (see page 21), non-Shigella dysentery and on attenuated mutants of Shigella (see page 9).

A histopathology laboratory procedures manual was made available in 1987 and a laboratory user's manual is planned for release early in 1988. A number of training workshops for members of the Department of Laboratory Sciences was organised during the year, mainly concerned with routine laboratory procedures.

The Animal Resources Branch is composed of 16 members of staff in two sections: a Research and Treatment Section responsible for all tests and experimental procedures, and a Production and Nutrition Section concerned with maintaining and breeding animals.

During 1987 nearly 20,000 tests and procedures were performed while 20 research studies used the branch's facilities. The Branch was also responsible for producing antisera to Vibrio cholerae and other bacterial pathogens and established a rabbit caecal tie procedure and a lamb ileal loop procedure as research tools for studies on secretory diarrhoea.

During 1987 preparations were made to establish a breeding colony of Rhesus monkeys. The Government of Bangladesh has given permission for 120 monkeys to be provided to the Centre from local sources. The animal house was renovated to provide quarantine rooms and total containment areas. Cages were ordered from India and an incinerator was built for burning infected wastes. The monkeys will be used initially to test strains of Shigella which could be candidates for a vaccine. The long term goal is to provide Rhesus monkeys for research at the Centre which are free from disease. The monkey colony is scheduled to be occupied in the second quarter of 1988.

The equipment used in the Centre is valued at over US\$ 1.5 million and is therefore an important asset to be handled and maintained with care. This work is done by the staff of the Bioengineering Cell.

Many manufacturers of equipment used in the Centre do not have service engineers in Bangladesh so an important aspect of any major item of

equipment is being able to provide servicing and repair within the Centre. The ability to do this may involve periods of training abroad for particularly complicated items of equipment and during 1987 the Head of the Cell received training at Roche Diagnostics in Switzerland on the CobasBio, a centrifugal analyser soon to be installed in the Research and Development Section of the Centre.

During 1987 18 major items of equipment were installed in the Centre and several major pieces of equipment were overhauled or reconditioned. In response to a need for a low-technology answer to a scientific need, a battery powered bacteriological incubator was made using local materials. It is now being used in the laboratory of Teknaf Station.

In addition, free technical assistance was provided to 10 national institutions during 1987 including: the Institute of Public Health, the Defence Force laboratories, the Diabetic Association Hospital, Shishu Hospital, the Institute of Post-Graduate Medicine and Research and the Infectious Diseases Hospital.

Computer Information Services (Roma Ghosh and Ashraf Hira)

The Computer Information Services (CIS) continued during 1987 to improve and expand the hardware, software and facilities it offers to the Centre's scientists and administrators.

To improve the working environment for computer users, the IBM System 34 computer was moved to the premises of the IBM 4361 and the room housing its terminals was renovated. Three additional links were created to PC's, bringing the total linked to the mainframe to 9. Finally, plans were completed to add an additional hard disk and two more terminals.

A new release of SAS statistical software was installed during the year in addition to the Statistical Package for the Social Sciences (SPSS) already present. SQL software which allows data to be transferred from databases to SAS was installed, as well as a new COBOL compiler for administrative applications.

During the year there was a 40% increase in the number of users of CIS facilities, from 98 to 138. The DSS emerged as the major user of the computer occupying 42% of its CPU time, followed by the Cholera Vaccine Trial Project (18%), the MCH-FP Extension Project (7%) and the Finance Office (6%). The staff of CIS entered almost 4 million records for various projects during the year including over 1.2 million for the MCH-FP Extension Project.

For the administrators of the Centre an interactive payroll system was developed, the personnel management system developed in 1986 was enhanced to include details of leave and salaries, and a database of the Centre's fixed assets was created.

To meet the increasing demand for programming, data entry and computer expertise, an analyst programmer, two data entry technicians, three trainee programmers, a senior computer operator and a secretary were hired.

The CIS provided over 70 hours of training courses for 50 of the Centre's staff during 1987, and 12 people from outside the Centre attended two courses arranged in collaboration with the Staff Development Secretariat and IEM, Bangladesh.

The services of the CIS were also sought by many organisations in Bangladesh. Six students from the University of Dhaka processed data for their dissertations, while technical information about data processing was provided to institutions such as the Bangladesh University of Engineering and Technology and the Centre for Integrated Rural Development for Asia and the Pacific. UNICEF, the National Institute of Preventive and Social Medicine and UNDP were among several organisations who used the CIS data conversion facilities during the year.

The Data Management Branch
(Kashem Shaikh)

The Data Management Branch provided assistance to 20 scientific projects during the year in designing questionnaires, coding and editing data, and in preparing cross tabulations, graphs and charts. The Branch developed a comprehensive archiving system for all the Centre's research projects to include the title, the Principal Investigators, the duration of the study and any documents needed to understand the data. Finally the Branch continued its work on the medical records of the Centre's three diarrhoea treatment centres and prepared annual reports of statistics.

In addition to providing expertise for scientists at the Centre, help was extended to students and researchers from several national institutions such as the Bangladesh Medical Research Council and the Institute of Statistical Research and Training.

THE LIBRARY, PUBLISHING AND TRAINING

Information Services, Publications and Communications (M. Shamsul Islam Khan)

The Library is an important resource for the staff of the Centre and provides facilities and services unrivalled in Bangladesh. It also provides general and specialised help to many libraries and institutions within Bangladesh while its information service is utilised by several international institutions as well.

To illustrate these points here are some statistics for the year:

- 8,566 readers other than members of staff
- 316 new books procured of which 118 were purchased
- 227 journals subscribed to and 190 received either free or by exchange
- 147,854 pages photocopied of 8,187 items
- 16 computer literature searches obtained
- 13,628 books and journals loaned
- 621 duplicate books or journals provided free to Bangladeshi institutions
- 851 books provided on inter-library loan
- 24 issues of the Current Awareness Service Bulletin published.

Collaborative links were established during the year with the Nuffield Library of the British Medical Association. They have agreed to provide literature searches and photocopies of articles not held in the Library, a development which should speed up the time taken to obtain literature searches for the Centre's scientists.

Links with the British Council in Dhaka were strengthened during 1987 when the Council agreed to help develop the Library's collection by generously providing books costing £1,200. They also obtained photocopies of 45 scientific articles for the Library. It is hoped that this assistance will continue in the coming years and that new titles and up to date editions of reference books can be purchased for the library, a part of the Centre which has been particularly affected by the recent financial stringency.

During the year a new Library Advisory Committee was formed with the purpose of providing advice and expertise in the main fields of interest in the Centre as well as administrative weight. A thorough review of journal subscriptions was completed and several branches and research projects agreed to pay the subscriptions of titles relevant to their needs.

After the successful completion of the first phase of the Disc Project, a two-year second phase began in January 1986. The Disc Project is financed by the International Development Research Centre (IDRC), Canada and is the world's first and only information centre and clearing-house

devoted solely to acquiring, analysing, preparing and disseminating information and literature on diarrhoeal diseases. During the year the project was evaluated by an independent external consultant.

In 1987, the DISC Project enrolled 79 individuals, libraries and organisations as its members and received 174 subscriptions for the Journal of Diarrhoeal Diseases Research (JDDR). During the year, 4 issues of the JDDR were published with, as a separate section, 4 issues of the Annotated Bibliography of Asian Literature on Diarrhoeal Diseases. Another issue of the JDDR and the Annotated Bibliography was completed and sent to the press. Abstracts of 363 papers were included in the five issues of the annotated bibliography.

In the Specialized Bibliography Series, an annotated bibliography was published entitled "Water, sanitation and diarrhoeal diseases: roles and relationships" while another annotated bibliography entitled "Review articles and selective studies on diarrhoeal diseases" was completed. These bibliographies cited over 1,000 papers with abstracts of over 600. In addition, in response to specific requests from members, the DISC Project prepared and supplied 13 short bibliographies on different subjects.

To supplement the Centre's library collection, the DISC Project procured 86 reprints and papers on diarrhoeal diseases from authors and libraries. It also procured 5 MEDLARS searches on different topics concerning diarrhoeal diseases. The Project continued to undertake regular surveys of current diarrhoeal disease research projects in Asia. Of the 253 questionnaires sent, 24 responses were received in 1987; some of these were reported in Glimpse, the bi-monthly newsletter.

Glimpse continued to highlight research in progress at the Centre and provided abstracts of the Centre's publications, news on forthcoming meetings and conferences, and information on current research projects in Asian countries, as well as information on the programmes and activities of the DISC Project.

During the year a new brochure was published highlighting the activities and different features of the DISC Project. This can be obtained by writing to the Head, Library and Publications Branch at the address given at the back of this report.

During 1987, the Publications Unit had another active year which saw the production of:

- the Centre's 1986 Annual Report (3,000 copies)
- 2 issues of the newly introduced Technical Documentation Series (500 copies each)
- 7 issues of the bi-monthly newsletter, Glimpse (35,000 copies)
- 4 issues of the Journal of Diarrhoeal Diseases Research (1,000 copies each).

The Unit was responsible for mailing over 52,500 copies of publications to individuals, libraries and organisations throughout the world.

The Medical Illustration Cell (MIC) provides scientists with a range of services from preparing charts, graphs, illustrations and posters to book-cover design and developing audio-visual aids. The MIC has a fully equipped photographic laboratory and in 1987, with the help of IDRC, acquired a microfiche production unit. This new facility will help in storing the Centre's ever growing collection of journals and is already in use to produce microfiche copies of the papers covered by the Annotated Bibliography of the JDDR.

Training Branch
(RL Akbar)

During 1987, 633 researchers, physicians, health administrators and health personnel from 19 countries received training at the Centre. Although the total training activities decreased significantly compared with previous years, more people attended more national training course than in 1986.

International training courses

There were 5 international training courses attended by 56 participants from 10 different countries. The fees, travel and living expenses of the participants on these courses was funded by CIDA, United States AID, WHO, ICHF and Japan.

Forty physicians, nurses and diarrhoeal disease control programme managers from Ethiopia (5), Zimbabwe (3), Sierra Leone (2), Uganda (6), Zambia (2), Nepal (15), Tanzania (3), Mozambique (2) and Afghanistan (2) attended three courses on clinical aspects of diarrhoeal diseases, which provided them with skills in diagnosing and treating diarrhoea in both hospitals and the community. In addition the participants will now be able to organise training for health personnel in their own countries.

Eight physicians and diarrhoeal disease control programme managers from Indonesia attended a course entitled "Diarrhoeal Diseases: Epidemiological Aspects". The aim of this course was to provide information about recent advances in the epidemiology of diarrhoeal diseases with special reference to developing countries, and to improve the participants ability to apply epidemiological methods, to conduct surveys, to study transmission and to evaluate methods to control and prevent diarrhoea.

A course on "Laboratory Diagnosis of Common Diarrhoeal Disease Agents" was attended by 8 participants from the People's Republic of China and 2 from Bangladesh. In addition to training the participants in the fundamental principles of laboratory procedures to isolate and identify pathogens responsible for causing diarrhoea, the course also provided training to promote self-reliance in preparing culture media locally.

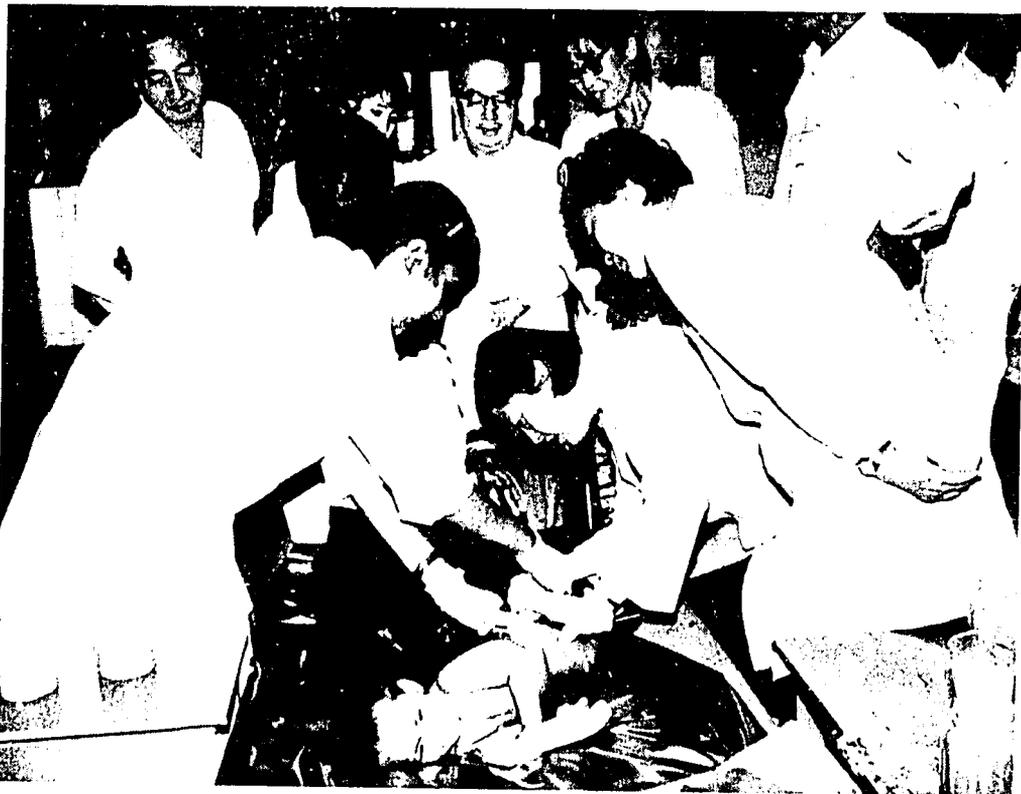
In addition to these training courses, the Training Branch also organised a two month group training programme for 6 doctors, nurses and laboratory technicians from the Kingdom of Saudi Arabia. This provided practical training in treating diarrhoea and laboratory procedures for isolating and identifying pathogens responsible for causing diarrhoea.

Study Visits

Two groups, one from India sponsored by the WHO and the other from Vietnam sponsored by Indvelop, were also arranged during 1987. The objective of

the study visit for the participants from India was to review approaches to planning, implementing and evaluating aspects of diarrhoeal diseases control programmes in both urban and rural areas. The Vietnamese participants visited the Centre to learn how to plan, develop, implement and evaluate the Primary Health Care in different settings.

National training courses In 1987 the Centre organised 12 training courses for 198 students, medical interns, trainee nurses and field supervisors of the Bangladesh Rural Advancement Committee (BRAC). These courses were on clinical aspects of diarrhoeal disease and provided training on treating and preventing diarrhoeal disease with special emphasis on nutrition and child survival.



A participant in the course on laboratory diagnosis of diarrhoeal disease from the People's Republic of China learning how to take a rectal swab.

Short-term training

During the year, a series of one or two day sessions were provided to 313 students from Medical Colleges and other government institutions on treating diarrhoea with ORS.

The Fellowship Programme

Through this programme 23 students, researchers and health professionals from 6 countries including Bangladesh received training in aspects of

diarrhoeal diseases under the supervision of preceptors.

The objectives of this informal training, which varied in duration from one week to one year, was to develop specialised skills and to provide an insight into research methods. The trainees either worked in current research studies or developed research themselves in collaboration with their preceptors.

Seminars

To provide opportunities for an exchange of information and views, 5 seminars were organised by the Training Branch in which both resident and visiting scientists presented talks on diarrhoea and other related topics. The Dhaka Hospital also organised 21 clinical seminars and case studies during the year, many of which involved eminent visiting physicians.

Staff Development Improving the skills, knowledge and productivity of members of staff members is one of the mandated objectives of the Centre. This is done by organising courses and by sending staff to national and overseas institutions. During the year 8 members of staff continued with their doctorates or degree courses, 12 more left the Centre to begin courses or training and 12 returned after completing their degrees or training. At the end of the year 8 staff members were overseas. More details of the people receiving the training can be found in the section entitled "People" beginning on page 70.

During 1987 34 people were sent to institutions within the country for short courses of training in fields such as computer programming, management, personnel management, maternity care, and 'trainers' training. In addition, the Dhaka Treatment Centre started a programme to exchange physicians with Dhaka Shishu Hospital. Under this programme in 1987, a physician from the Dhaka Treatment Centre received one year's training in paediatrics in Dhaka Shishu Hospital while three physicians from Shishu Hospital received training in treating patients with diarrhoea.

ADMINISTRATION

Personnel, Administration and Finance
Associate Director: MA Mahbub

During 1987 an appointment was made to a new Associate Directorship. The new position carries overall responsibility for the Centre's administration, procurement, personnel and finances.

Finance Office (Chief Finance Officer: HAN Janssen)
As a result of continued efforts to eliminate the Centre's deficit and after providing for depreciation of US\$ 500,000, the end of 1987 showed a surplus of US\$ 600,000. This resulted from an increase by 10% in accrued income to US\$ 8.7 million during the year, while expenditure remained the same as 1986. The net current assets of the Centre increased by US\$ 1.2 million, a result of an operating surplus of US\$ 1.1 million and interest on the Reserve Fund of US\$ 100,000.

During the year the Centre received US\$ 500,000 from DANIDA to support the cost of clinical services. This significant contribution helped the Centre to eliminate its operating deficit because the clinical services of the Centre were previously funded completely from the core budget.

There was no significant change in any major items of expenditure except in salaries: local staff received increases ranging from between 18% and 34% during the year, which added US\$ 140,000 to the salaries bill. A significant benefit was derived from a change in interest rates during the year which led to a reduction in interest payments of US\$ 170,000.

Despite inflation and increases in salaries, total expenditure during the year was reduced, particularly in the costs of management and central services. However the greater number of patients seen at ICDDR,B treatment centres resulted in an increased expenditure on clinical services.

By the end of 1987 the Centre's bank overdraft had been eliminated primarily as a result of having received substantial contributions in advance from donors. The Centre's cash balance was US\$ 2.3 million which included the Reserve Fund of US\$ 1.5 million. At the end of the year the Centre had obligations to complete projects for which funds equivalent to US\$ 2.2 million had been received while US\$ 800,000 was due for work already completed. Contributions from major donors during the last 3 years are shown in Table 6

System development

Significant improvements were made during the year in developing an asset register stored on computer and in improving the software used for the Centre's payroll (see CIS Report p 55). There are plans to develop a more efficient accounting system, improved inventory management and a better system of reporting to donors. These plans will involve external consultants and the United States AID has agreed to finance this expense.

Table 6
Contributions to the ICDDR,B during the last 3 years on the basis of cash received in US\$. From 1987 the accrual method of accounting for receipts was adopted (see Auditors Report on page 84)

	1987	1986	1985
Central Funds:			
Australia	126,325	123,237	143,365
Bangladesh		59,311	*
Saudia Arabia		70,000	100,000
Sweden		117,810	-
Switzerland		780,309	310,813
UNICEF	250,000	500,000	250,000
United Kingdom	230,302	206,448	171,741
United States AID	250,000	500,000	-
Others	1,217	10,000	139
Total	857,844	2,367,115	976,058
Project Funds:			
Aga Khan Foundation	45,585	17,951	52,260
Arab Gulf Fund	250,000	-	485,440
Belgium	243,045	114,739	68,115
BOSTID	28,425	22,170	13,312
Canada - CIDA	932,710	1,021,677	807,806
Case Western Reserve University	12,160	12,782	-
DANIDA	506,016	-	-
FAO	-	37,987	-
Ford Foundation	-	68,349	354,544
France	55,568	-	12,600
Germany, Federal Republic	-	-	13,671
IDRC	53,884	93,796	85,468
IBM	30,916	-	-
IBRD (World Bank)	174,753	78,863	85,986
Japan	295,176	320,000	260,000
Medecins Sans frontieres	-	24,063	-
Miles Pharmaceuticals	107,822	47,399	-
Nestle	2,793	9,205	-
Norway - NORAD	459,364	427,827	228,837
Norwich Eaton Pharmaceuticals	12,086	22,500	10,500
OPEC	-	30,000	-
Population Council	13,438	5,352	32,474
Saudi Arabia	530,708	536,596	275,053
SDC	136,920	-	-
UNDP/UNROB	-	43,571	43,570
UNDP - UVP	-	103,154	96,470
UNDP/WHO	300,000	388,000	187,000
UNFPA	-	-	75,375
UNICEF	193,665	335,480	253,645
United States AID	3,189,544	3,167,627	2,980,682
WHO	195,041	88,104	57,762
Wellcome Trust	29,019	-	-
Others	17,720	18,661	30,769
Total project funds	7,816,358	7,035,853	6,511,339
GRAND TOTAL US\$	8,674,202	9,402,968	7,487,397

ERRATUM § Funds received in 1988 * Funds received in 1986

Please read the following under heading "1987":

Project Funds:

Line 5: Canada - CIDA 953,979, instead of 932,710
 Line 31: WHO 195,040, instead of 195,041
 Total project funds 7,837,626, instead of 7,816,358
 GRAND TOTAL US\$ 8,695,470, instead of 8,674,202

Personnel Services (Chief Personnel Officers: Ronald Dery and W Ahmed)
During 1987 efforts continued to reassign staff paid by the core funds of the Centre to funded projects. In addition, many staff no longer needed by projects were reassigned to new projects or to departments in which staff were needed. Some positions were left vacant if no specific funding was available.

The structure of the personnel system came under detailed review during the year by a task force constituted by the Board of Trustees. Two consultants in Personnel Management financed by the UNDP visited the Centre for two weeks in March to review the personnel system, its recruitment, promotion and salary systems, and to suggest improvements. Some of their recommendations are still under review while some have already been implemented.

A review of the classification of Scientific staff was performed by a Scientific Ranking Committee. Their recommendations were implemented and this included promoting 19 National Scientific staff and redesignating 7.

The computer database of all Centre's staff is now in full operation using a PC linked to the IBM 4361 mainframe (see CIS Report, page 55).

Resources Development Division
Associate Director: MR Bashir

Realistic planning in 1986 produced positive results in 1987. Firm commitments from donors were received, emergency grants were secured to meet the additional demands on the Centre's services caused by the unprecedented floods in Bangladesh and, thanks to the donors' co-operation, sustained efforts to obtain prompt disbursements resulted in a greatly improved cash flow. A direct benefit of the improved cash flow was that for the first time for several years the Centre's bank account was in credit (see Finance Report above).

Donors

The United States Agency for International Development (US AID) continues to be a major donor. During the year, a Co-operative Agreement with United States AID was extended in Washington. With the help of US AID collaboration with two institutions, Johns Hopkins and Tufts Universities, was negotiated and formal agreements are expected to be signed soon. The US AID mission in Dhaka extended its support for the Centre's Urban Volunteer Program for an additional four years.

The Canadian International Development Agency (CIDA), continued to support the Centre's Demographic Surveillance System in 1987 and agreed to extend support for the next four years.

The Government of the People's Republic of Bangladesh, remains a generous supporter of the Centre and has agreed to provide central funds as well as material assistance to support the Centre's activities.

UNICEF, continued their institutional support for the Centre and to specific projects in 1987 while the United Nations Development Programme (UNDP) maintained its support for clinical research.

NORAD, the Norwegian agency for development, which began its support

of the MCH-FP services in 1985, has agreed to continue its support in 1988. The Belgian Administration for Development Co-operation (BADC) remains an active supporter of the Centre's Urban Volunteer Programme and provided emergency support during the floods.

Swiss Development Co-operation (SDC) made commitments in 1987 to continue their institutional support, and in addition to this contribution has agreed to begin providing programme support in 1988. The SDC also provided emergency support during the floods.

Saudi Arabia, also agreed during 1987 to continue their contributions to the Centre's core support.

The Danish aid agency DANIDA began in 1987 three years support for the Dhaka Treatment Centre. Japan has continued with valuable assistance for the Centre's research and training activities. The Aga Khan Foundation, the World Bank, the World Health Organisation and the International Development Research Centre (Canada) all provided funding for project support.

Collaborative activities

During 1987 the ICDDR,B continued to develop links with institutions and organisations from other countries.

Since signing a collaborative agreement with the Ministry of Public Health, People's Republic of China in 1985, the Centre has been exchanging scientists and several training courses have been held at the Centre for Chinese participants. This collaboration continued in 1987.

The Centre's current technical assistance to the Diarrhoeal Disease Treatment Centre in Dammam and Riyadh, Saudi Arabia, continued during the year. Collaboration with the Kenya Medical Research Institute (KEMRI) in studies on cereal based ORT was renewed for further two years. An agreement is expected to be signed in early 1988. This venture is sponsored in conjunction with the Aga Khan Foundation.

The Fourth Asian Conference on Diarrhoeal Diseases was held in Colombo, Sri Lanka in September, 1987. This conference was attended by 12 physicians and scientists from the Centre who used this opportunity to exchange views with other Asian scientists on the latest developments in diarrhoeal disease research.

Donors' Consortium

The ICDDR,B organised two meetings of its donors during 1987, the first in March in Dhaka and the second in June in Geneva. At the meetings donors reviewed the Centre's plans and prospects and discussed possible fund raising strategies.

Capital Development

The agreement with the United Nations Capital Development Fund (UNCDF) to construct a new building for Matlab Field Station was renegotiated and finalised with the Government of Bangladesh to incorporate the recommendations of the UNCDF consultants. Construction will begin in early 1988.

STATUTORY COMMITTEES

The Director of the Centre answers to the Board of Trustees: representatives of the Government of Bangladesh and eminent national and international scientists. The Board met twice during 1987: in Dhaka in June and in Bangkok in November. The members of the Board at the end of the year were:

- | | |
|--|---|
| Dr. AR Al-Sweilem (Saudi Arabia)
Mr. MK Anwar (Bangladesh)
* Dr. D Ashley (Jamaica)
Prof. David Bell (USA), Chairman
Dr. I Cornaz (Switzerland)
Prof. Roger Eeckels, Secretary
Prof. Richard Feachem (UK)
Prof. D Habte (Ethiopia)
* Prof. A Lindberg (Sweden) | * Prof. VI Mathan (India)
Dr. M Merson (WHO, Switzerland)
Dr. KA Monsur (Bangladesh)
Dr. Nyi Nyi (UNICEF, USA)
* Mr. T Rahman (Bangladesh)
Prof. D Rowley (Australia)
Dr. P Sumbung (Indonesia)
* Prof. H Tanaka (Japan) |
|--|---|

(* Appointed in 1987)

Seven members of the Board finished their term of office or left the Board during the year. They were:

- | | |
|--|---|
| Mr. AK Chowdhury (Bangladesh)
Prof. J Kostrzewski (Poland)
Dr. L Mata (Costa Rica)
Mr. KG Rahman (Bangladesh) | The late Mr. SA Rahman (Bangladesh)
Prof. V Ramalingaswami (India)
Prof. Y Takeda (Japan) |
|--|---|

The 43 member Programme Co-ordination Committee (PCC) met once during the year and its 20 member Executive Committee met twice. The full PCC includes 6 members of the ICDDR,B while the remainder come from government departments, universities and non-governmental organisations concerned with health, development, education and population studies. Six matters were dealt with:

- A book on herbal medicine compiled by Dr. M Salar Khan to be reviewed by 5 specialists and then considered for publication by the ICDDR,B
- A monograph on diarrhoeal diseases to be published by the ICDDR,B
- Encouraging the Centre's scientists to find collaborators for research among national institutions: there were 10 collaborative research projects during 1987
- The arrangement of a national workshop on water and sanitation in preventing diarrhoeal diseases in Bangladesh
- Strengthening interest in medical colleges in diarrhoeal disease with the assistance of the ICDDR,B
- Two collaborative research studies, one on treating shigellosis using substances extracted from garlic, asok and neem, and one on correlations between susceptibility to bacteriophages and the plasmids of enterotoxigenic E.coli; these studies have been funded from money provided by the ICDDR,B.

As an indication of the growing collaboration between national educational institutions and the Centre, 18 students conducted research for their dissertations at the Centre. Fifteen students from Dhaka University (DU) and the Bangladesh Agricultural University did research as part of MSC degrees and 3 students from DU worked for their MPhil degrees.

The Centre collaborated with the Directorate General of Health Services during the widespread and serious flooding by sending 28 Medical teams to 73 Upazilas in 23 districts. The Centre's medical teams treated 3735 cases of acute diarrhoea and over 3000 cases of respiratory tract infections, skin infections, conjunctivitis and parasitic infections. Of the 1033 deaths due to diarrhoea reported by the Government surveillance system, 807 were investigated by visits to the location to establish the causes of death.

The Centre assisted the following organisations during the year by helping to improve their services and research, by giving lectures, providing animals for experiments, giving or loaning books and journals, and by providing computer services and training: the Directorate General of Health Services, NIPORT, Dhaka University, the Institute of Public Health, the National Institute of Preventive and Social Medicine, the Institute of Postgraduate Medicine and Research, BIRDEM, BCSIR, Dhaka Medical College Hospital, the Bangladesh Rural Advancement Committee, Dhaka Shishu Hospital, BIDS, the Bangladesh Agricultural University, the Bangladesh University of Engineering & Technology.

During 1987 the PCC Chairman was Prof. MA Matin, the Vice-Chairman was Prof. Kamaluddin Ahmad and the Member-Secretary, Mr. MR Bashir.

Members of the PCC in 1987:

- Prof. MA Matin, Hon. Deputy Prime Minister, Government of Bangladesh (a)
- Prof. Kamaluddin Ahmad, Chairman, Standing Technical Committee, National Nutrition Council (a,c)
- Mr. MR Bashir, ICDDR,B (a,b)
- Prof. Nurul Islam, National Prof. (a,b,c)
- Maj. Gen. MR Chowdhury, Commandant AFIP&T, Dhaka Cantonment (a,c)
- Prof. AKM Aminul Haque, Vice Chancellor, Bangladesh Agricultural University, Mymensingh (a)
- Prof. MH Khan, Vice Chancellor, Bangladesh University of Engineering & Technology
- Prof. Abdul Mannan, Vice Chancellor, Dhaka University (a)
- Prof. Mohammad Ali, Vice Chancellor, Chittagong University
- Prof. MA Raquib, Vice Chancellor, Rajshahi University
- Prof. AFM Kamaluddin, Vice Chancellor, Jahangir Nagar University
- Mr. MK Anwar, Secretary, External Resources Division, Govt. of Bangladesh
- Mr. Taslimur Rahman, Joint Secretary, Ministry of Health & Family Planning, Government of Bangladesh
- Prof. KA Monsur, Member, Board of Trustees, ICDDR,B (a,c)
- Dr. SSMA Khorasani, Chairman, BCSIR Laboratories
- Dr. Matluber Rahman, Chairman, Bangladesh Agricultural Research Council
- Col. Abdul Latif Mallik, Director General, Family Planning Implementation, Government of Bangladesh (a)
- Mr. M Mahe Alam, Director General, NIPORT (a)

Dr. Munawara Binte Rahman, Director General, Health Services, Government of Bangladesh (a)
 Prof. TA Chowdhury, Director Inst. of Postgraduate Medicine & Research (a)
 Dr. Humayun KMA Hye, Director, Institute of Public Health (a)
 Prof. AJM Mijanur Rahman, Director, National Institute of Preventive & Social Medicine
 Dr. Shafiqur Rahman, Director, Bangladesh Medical Research Council (a,b,c)
 Dr. Sultana Khanum, Medical Director, Save the Children Fund, UK, Children's Nutrition Unit (a)
 Dr. MR Khan, Research Director, Bangladesh Inst. of Development Studies (a)
 Dr. Zafrullah Chowdhury, Project Coordinator, Gonoshaystha Kendro (a)
 Col. A Samad Khan, Director, Institute of Public Health Nutrition
 Dr. M A Malek, Director, Institute of Nutrition & Food Science, Dhaka University
 Dr. Salehuddin Ahmed, Programme Coordinator, Bangladesh Rural Advancement Committee
 Prof. MS Akbar, Joint Director, Bangladesh Institute of Child Health
 Dr. Muslimuddin Khan, Project Director, National Oral Rehydration Project
 Dr. Hajera Mahtab, Medical Director, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders
 Mr. Shafiqur Rahman Chowdhury, Director, MIS Unit, Directorate of Family Planning
 Dr. Halida Hanum Akhtar, Director, Bangladesh Fertility Research Programme
 Dr. SA Akanda, Director, Institute of Bangladesh Studies, Rajshahi University
 Brig.(Retd.) M Hedayetullah
 Dr. AK Khan
 Dr. Mobarak Hossain
 Prof. Roger Eeckels, ICDDR,B (a)
 Dr. Ivan Ciznar, ICDDR,B
 Dr. M Badrud Duza, ICDDR,B
 Dr. David A Sack, ICDDR,B (until 30th June 1987)
 Dr. M G M Rowland, ICDDR,B (until 31st August 1987)

- (a) Members of Standing Committee of Programme Coordination Committee
- (b) Members of the Management Sub-Committee of PCC
- (c) Members of the Scientific Review Sub-Committee of PCC.

The Ethical Review Committee (ERC) meets regularly to examine and monitor ethical issues in research at the ICDDR,B which involves humans. It has 15 members: four from the Centre, one from the PCC Standing Committee, one representative from the Bangladesh Medical Research Council, one representative from the WHO in Bangladesh, and eight people representing other disciplines or interests.

The ERC has a five-member sub-committee to ensure that research studies are being conducted ethically and according to the approved proposal. The committee ensures that patients know that the quality of medical care will not be affected if they decide not to participate in a study or to withdraw.

In 1987 the ERC met 13 times to consider 32 research proposals: 28 were approved, 2 proposals were turned down and a decision was deferred in the case of 2 proposals. In addition the ERC considered and approved two PCC-

Collaborative research proposals. The new rules of the ERC, approved by the Board of Trustees, which define its powers, functions and duties, came into effect on January 1st 1987.

Members of the ERC in 1987:

Prof. Kamaluddin Ahmad, Chairman and representative of the PCC Standing Committee; Biochemist and Nutritionist
Dr. Humayun KMA Hye, Alternative Chairman; Pharmacologist
Prof. TA Chowdhury, 2nd Alternative Chairman and representative of the Bangladesh Medical Research Council; Gynaecologist
Prof. KA Monsur; Scientist
Dr. Khaleda Banu; Paediatrician
Barrister KZ Alam; representative of the legal profession
Mrs Taherunnessa Abdullah; Behavioural Scientist
Mrs Husnara Kamal; Behavioural Scientist
Mr. Md. Mofazzal Hossain Khan; religious representative
Dr. Jamal Ara Rahman; non-scientific member
Mr. M El-Naggar; Representative of the WHO
Dr. MGM Rowland, Associate Director, Community Medicine Division ICDDR,B (until August 31 1987); Physician
Dr. AKM Siddique, Community Medicine Division, ICDDR,B (from 1.9.87 to 31.10.87); Physician
Prof. Roger Eeckels, Director, ICDDR,B (from 1.10.87 to 31.12.87); Paediatrician
Dr. Andre Briend, Community Medicine Division, ICDDR,B; Physician and Nutritionist
Dr. AN Alam, Clinical Sciences Division, ICDDR,B; Physician
Mrs Rahima Khatun, Clinical Sciences Division, ICDDR,B; Nursing profession

The Research Review Committee (RRC), although not a statutory committee, is included in this section. It is composed of scientists and physicians from the ICDDR,B and one representative of the PCC Standing Committee. The RRC reviews research protocols to evaluate their value, significance and feasibility according to the Centre's objectives and financial means. During 1987 the RRC met 11 times to consider 22 protocols: 21 were approved and one is awaiting approval.

Members of the RRC in 1987 :

Prof. Roger Eeckels, Chairman; Dr. Ivan Ciznar, Member-Secretary; Dr. David A Sack (until June 30th, 1987); Dr. MGM Rowland (until August 31st, 1987); Maj.Gen. MR Chowdhury (Member of PCC Standing Committee); Prof. Kamaluddin Ahmad (Chairman, ERC); Dr M Badrud Duza; Dr. Andre Briend; Dr. M Yunus; Dr. PK Bardhan; Dr. AN Alam; Dr. AKM Siddique; and Mrs Rahima Khatun.

The following people from outside the Centre kindly reviewed research protocols during the year:

Prof. TA Chowdhury	Dr. Humayun KMA Hye	Prof. MQ-K Talukder
Dr. Sultana Khanum	Dr. Syed Saleheen Qadri	Prof. MR Khan
Dr. Syed Waliullah	Dr. Monjur Hossain	Prof. SGM Chowdhury
Dr. Mosleh Uddin	Dr. Sadeqa Tahera Khanum	Prof. Harun KM Yusuf
Prof. Kamaluddin Ahmad		

PEOPLE

At the end of 1987 there were 1,450 members of staff at the ICDDR,B: 1,425 were national staff, a rise of almost 7% since the end of 1986; 25 were international staff, a further decline of 19% during the year and a fall of about 50% since 1985. The increase in the number of national staff is due to an increased amount of research and thus a greater demand on services.

Staff development

Three members of the national staff left the Centre last year to start research for doctorates in Japan, while one person completed a Ph.D. at the University of Dhaka and another at the University of London. Details of these and other staff who have left the Centre for training or who have returned are given here.

Khorshed Alam, a Section Chief in the Laboratory Services Department completed a year's training in Clinical Microbiology in the laboratory of Prof. JB Butzler at the St. Pierre Hospital, Free University of Brussels, Belgium.

Dr. Abul Kalam Azad, a Senior Medical Officer in the Dhaka Treatment Centre left in August to take up a Fellowship in Paediatric Gastroenterology at the State University of New York, Buffalo, USA.

Hosne Ara Begum, a Data Management Officer left the Centre in December to begin graduate studies in Demography at the Australian National University, Canberra.

Afzalur Rahim Chowdhury, a Research Officer, left for the Department of Environmental Hygiene at Okayama University, Japan to begin his Ph.D. research on Vibrio mimicus.

Dr. ASG Faruque, a Physician in the Training Branch, returned from Johns Hopkins University, USA after completing the course work for a Masters degree in Public Health.

Khaleda Haider was awarded a Ph.D. by the University of Dhaka for a dissertation entitled "Plasmid analysis of a Shigella strain isolated in Bangladesh with special reference to its drug resistance and invasive character".

Serajul Islam, an Assistant Scientist in the Laboratory Services Department returned to the Centre in October having successfully completed his Ph.D. in Environmental Microbiology at the London School of Hygiene & Tropical Medicine, U.K.

KM Faisal Khan, a Research Trainee in Biochemistry, left to study for a Ph.D. in the Department of Nutrition of the School of Medicine at Tokushima University in Japan.

Dr. RN Mazumder, a Senior Physician has left to spend a year at Shishu Hospital being trained by Professor M S Akbar.

Md. Kaiser Ali Talukder, a Research Officer in the Microbiology Branch, left in October to begin studies for a Ph.D. in Molecular Biology at the Institute of Medical Science, University of Tokyo, Japan.

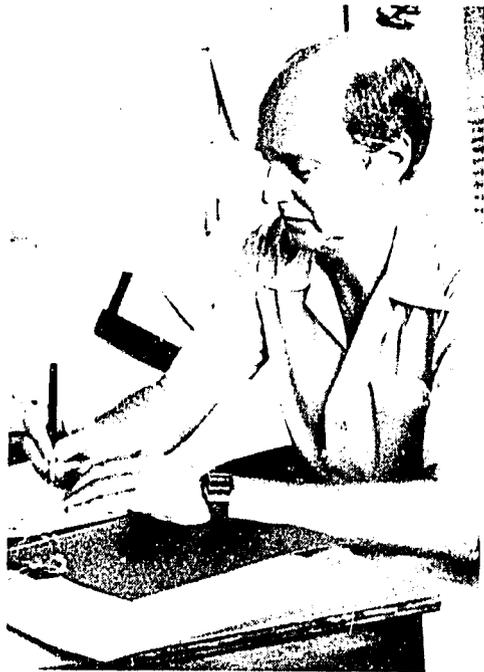
Departures

Dr. Michael Rowland (UK), Associate Director of the Community Medicine Division, left the Centre in September at the end of a three year contract. He has returned to Britain to take up a position at the Dunn Nutritional Laboratory of the University of Cambridge.

Dr. David Sack (USA), Associate Director of what is now the Laboratory Sciences Division, left at the end of 1987 to return to the post of Associate Professor in the Division of Geographic Medicine at Johns Hopkins University.



David Sack



Michael Rowland

The head of the Demographic Surveillance System for the last 4 years, Dr. Bogdan Wojtyniak (Poland), left at the end of 1987 to return to his post at the National Institute of Hygiene in Warsaw.

Three members of the Administration left during the year. Hartley Janssen (Canada) had been provided to the Centre as Chief Finance Office by the World University Service of Canada. He has returned to his post with the National Bank of Canada. Leonard Chang (Australia) was for 3 years the

Centre's Budget and Finance Officer: he has moved to Peshawar in Pakistan to work for United States AID on a project involving Afghan refugees. Ronald Dery (USA) has returned to the United States after three years at the Centre working mostly as the Chief Personnel Officer.

Two of three international staff of the Computer Information Services left during the year: Roma Ghosh (India) and Dr. V Sundararajan (Sri Lanka).

Ms Deborah Balk, a long term consultant in the MCH-FP Extension Project, left during the year and is now studying for a PhD at the University of California at Berkeley.

New staff and consultants

Six new international members of staff joined the Centre on secondment during the year.

Three of them were provided by the Belgian Administration for Development Cooperation: Albert Felsenstein, a biologist, is working with the Environmental Microbiology Unit; Dr. Carine Lenders, a physician, has joined the Urban Volunteer Programme; and Dr. Carine Ronsmans, also a physician, has joined the Community Medicine Division.

Two staff from the Division of Geographic Medicine at Johns Hopkins University also arrived during 1987: Dr. Gary Hlady (USA) a physician and epidemiologist has, appropriately, joined the new Epidemiology Department in the Centre, and Dr. Diana Silimperi (USA), a paediatrician and epidemiologist, has joined the Centre to become the new Director of the Urban Volunteer Programme.

Finally the Danish aid agency DANIDA has also provided Dr. Poul-Erik Kofoed, a paediatrician, for the Dhaka Treatment Centre.

Dr. Syed A.I. Ally (Bangladesh), a pathologist, joined the Centre at the beginning of the year to work as a Human Morbid Anatomist. Dr. Ally has also been appointed a guest lecturer in the Department of Pathology at the Institute of Postgraduate Medicine and Research.

Two new Bangladeshi members of the administration joined in 1987: MA Mahub took up the international grade position of Associate Director in charge of Administration, Personnel and Finance, while Wahabuzzaman Ahmed joined the national staff as Chief Personnel Officer.

The Travellers' Clinic was staffed by two North American nurses during the year: Ms. Donna Plunkert and Ms. Susan St. Aubin.

Retirements and Resignation

Four members of staff retired during 1987, all having served the ICDDR,B and its predecessor, the Cholera Research Laboratory, for a considerable length of time. Gilbert Costa, a Security Guard retired after 12 years; Munsur Ahmed Chowdhury, a driver at Matlab Station retired after 12 years; Md. Ali Hussain a Security Guard in Matlab retired after 20 years; and Md. Abdul Momen, a Senior Health Assistant also in Matlab retired after almost 23 years of service.

A Senior Technician in the Clinical Biochemistry Section, Md. Ayub Bhuiyan resigned from the Centre after 20 years service to take up a position with the Diabetic Institute.

Long service

During 1987, 14 members of the national staff of the Centre completed 25 years of service with the ICDDR,B and its predecessor, the Cholera Research Laboratory. They are :

Bernadette Barman	Aid Nurse
Abdul Gaffar Bhuiyan	Senior Lab. Technician
Joseph George Gomes	Senior Laboratory Technician
Abdul Mannan Howlader	Ward Attendant
Md. Shafiqul Islam	Assistant Scientist
Shushama Pashi	Research Officer
Sultan Ahmed Sarder	Supervisor I.V. Fluid Preparation
Subodh Sarker	Security Guard
Md. Shafuruddin	Head Gardener
Osman Ghani Siddiqui	Senior Research Technician
John Cicil Sikder	Aid Nurse
Abdus Sobhan	Laboratory Attendant
Suratunnessa	Assistant Matron
Mayeen Uddin	Animal Technician

Visitors

In 1987 the Centre had many visitors, from many countries, who came for many different reasons: to see the Centre's facilities, to set up techniques, to review research projects, and to see how money was being spent. A selection of these visitors is given here.

The Belgian Minister for Overseas Development, Mr. André Kempinaire visited in January with the Belgian Ambassador H.E. Mr H Vandreche (see picture on page 74) as did Dr. Cao Qing from the Ministry of Public Health of the People's Republic of China.

The Nayargaon Nutrition Rehabilitation Unit was opened by H.E. Mr. Stanislas Filliol the Ambassador of France in Bangladesh. Other visitors from the diplomatic community were H.E. Mr. Yoshitomo Tanaka, Ambassador of Japan, H.E. Mr. JHJ Jeurissen, Ambassador of the Netherlands, H.E. Ms. Susan Boyd, High Commissioner of Australia, and H.E. Mr. Anthony Vincent, High Commissioner of Canada.

Mr. Paul Boyd came from the UNDP in New York to help prepare documents and reports for the meeting of the Donors' Consortium. The review of the Personnel system of the Centre also brought three UNDP consultants during the year: Mr. Garry Rahn, Mr. Reginald Hiscock and Mr. William Grombley.

The United States AID sponsored three consultants to Matlab Field Station: Dr. Sung Hee Yun, Mr. Scott Wirtet and Dr. Rob Porter.

Two consultants came to discuss the DISC Project during the year: Mrs. Martha Stone, Director of Information Services, from the IDRC in Canada and Mr. Clive Wing from the IDRC in New Delhi. The DISC project was also formally evaluated by an independant external consultant, Mr. Paul Hodgson, a former Librarian of the National Library of Australia, Canberra.

Dr. John Rohde and Ms. Rina Gill led a team from UNICEF who were making a film on diarrhoeal diseases, while Mr. Jere van Dyk visited the Centre as a special correspondent for the National Geographic Magazine.

Three people from the Aga Khan University in Karachi visited the Centre in June: Professor Jack Bryant, Dr. Aziz Najjam and Dr. Hansen.

Mr. Salauddin Quader Chowdhury, Minister for Health and Family Planning, Government of the People's Republic of Bangladesh visited the Centre in September to see its activities.



The Director of the ICDDR,B, Dr R Eeckels, explaining the work of the Nutrition Rehabilitation Unit to Mr André Kempinaire, the Belgian Minister for Overseas Development.

Two consultants from the Department of Tropical Hygiene at the London School of Hygiene and Tropical Medicine visited the Centre to help with the analysis of data from the Mirzapur Handpump Projects: Prof. Richard Feachem and Ms. Sharon Huttly. Other visitors from the London School were Dr. Andrew Tomkins and Dr. Ron Behrens who both came to work in the Dhaka Treatment Centre on a study of intestinal permeability.

Regular visitors to the Centre, Prof. Jane Menken and Mr. Andrew Foster came to set up a DSS workshop. Prof. Richard Osborn came from the University of Toronto as a CIDA consultant to the Population Science Division, as did Mr. DJ Pieper and Mr. Alan Sunter.

The Laboratory Sciences Division had many expert visitors. Ms. Frances Downes came from the Centers for Disease Control in Atlanta, USA to set up an assay for verotoxins; Dr. Jim Hackett came from the Department of Microbiology and Immunology in the University of Adelaide, Australia as a consultant on the Shigella project; Dr. Patricia Charache, Director of the Microbiology Laboratory at Johns Hopkins Hospital came to set up methods to diagnose virus infection of the respiratory tract; Dr. Lauren Pierik from the Boston Childrens' Hospital also came to help in diagnosing respiratory tract viruses; Dr. Nils Carlin came from Stockholm to set up techniques to serotype Shigella flexneri using monoclonal antibodies; three consultants in Environmental Microbiology, Dr. Mark Tamplin, Ms. Ann Gauzens and Prof. Sam Joseph, came from the University of Maryland, USA; another visitor from Maryland, Prof. Rita Colwell came as a consultant; Dr. Christine Wanke came from Charlottesville, USA as a consultant on chronic diarrhoea; finally, a regular visitor to the ICDRR, B, Dr. Anne Mari Svennerholm of the University of Goteborg, Sweden came as a consultant on serology.

Dr Klaus Gyr visited the Dhaka Treatment Centre once again from the University Hospital, Basel in Switzerland to work on a study of pancreatic function, while Dr J-F Desjeux from INSERM U.290, Hôpital Saint-Lazare in Paris, came to prepare a study of methylated casein as an antisecretory agent.

ICDDR,B PUBLICATIONS 1987

A INTERNAL PUBLICATION SERIES:

- A.1 ICDDR,B Annual Report, 1986. June 1987. 123 p.

Technical Documentation Series

- A.2 Rahman M, Wojtyniak B, Chowdhury SA, Saha SK, Anwar S. Demographic Surveillance System-Teknaf: code plan, 1976-85. Dhaka: International Centre for Diarrhoeal Disease Research, Bangladesh, Mar 1987. 69 p.
- A.3 Rahman M, Nahar N, Ahmed RU, Umra M, Wojtyniak B. Demographic Surveillance System-Teknaf: instruction manual for data collection. Dhaka: International Centre for Diarrhoeal Disease Research, Bangladesh, Aug 1987. 80 p. (Text in Bengali)

Journal and Newsletter

- A.4 Journal of Diarrhoeal Diseases Research (also includes: Annotated Bibliography of Asian Literature on Diarrhoeal Diseases). v. 4, nos. 2-4, 1986 and v. 5, no. 1, 1987.
- A.5 Glimpse. v. 8, nos. 5-6, 1986 and v. 9, nos. 1-5, 1987.

B ORIGINAL SCIENTIFIC PAPERS (Including Short Communications):

- B.1 Ahsan CR, Ciznar I. Release of endotoxin by toxigenic and non-toxigenic *Vibrio cholerae* 01. *J Diarrhoeal Dis Res* 1987 Mar;5(1):7-15
- B.2 Akhtar SQ. Isolation of *Clostridium difficile* from diarrhoea patients in Bangladesh. *J Trop Med Hyg* 1987 Aug;90(4):189-92
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- B.6 Bairagi R, Edmonston B, Khan AD. Effects of age misstatement on the utility of age-dependent anthropometric indicators of nutritional status in rural Bangladesh. *Am J Public Health* 1987 Mar;77(3):280-2

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- B.8 Banu H, Phillips JF, Degraff DS, Koenig MA. Baseline social, economic and demographic differentials in contraceptive behaviour in intervention and comparison areas of the MCH-FP Extension Project. Dhaka: International Centre for Diarrhoeal Disease Research, Bangladesh, 1987. 249 p.
- B.9 Bhatia S, Becker S, Kim YJ. The effect of oral contraceptive acceptance on fertility in the postpartum period. *Int J Gynaecol Obstet* 1987;25 (suppl):1-11
- B.10 Bhuiya A, Wojtyniak B, D'Souza S, Nahar L, Shaikh K. Measles case fatality among the under-fives: a multivariate analysis of risk factors in a rural area of Bangladesh. *Soc Sci Med* 1987;24(5):439-43
- B.11 Brayton PR, Tamplin ML, Huq A, Colwell RR. Enumeration of *Vibrio cholerae* 01 in Bangladesh waters by fluorescent-antibody direct viable count. *Appl Environ Microbiol* 1987 Dec;53(12):2862-5
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- B.59 Shahid NS, Rahman ASM, Sanyal SC. Cryptosporidium as a pathogen for diarrhoea in Bangladesh. Trop Geogr Med 1987 Jul;39(3):265-70
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- B.70 Stanton BF, Clemens JD, Aziz KMA, Rahman M. Twenty-four-hour recall, knowledge-attitude-practice questionnaires, and direct observations of sanitary practices: a comparative study. *Bull WHO* 1987 65(2):217-22
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- C.2 Ahmed ZU, Sack DA, Sarker MR, Haider K. Possible approaches to the development of a vaccine against shigellosis. In: Ahmed ZU, Choudhury N, eds. *Proceedings of the International Seminar on Biotechnology and Genetic Engineering, Dhaka, 25-27 Jan 1986*. Dhaka: Bangladesh Academy of Sciences, 1987:195-204
- C.3 Ahmed ZU, Choudhury N, eds. *Proceedings of the International Seminar on Biotechnology and Genetic Engineering, Dhaka, 25-27 Jan 1986*. Dhaka: Bangladesh Academy of Sciences, 1987. 218 p.

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- D.1 Briend A, Rowland MGM, Wojtyniak B. Measures of nutritional status [letter]. Lancet 1987 May 9;1(8541):1098-9
- D.2 Butler T, Aikawa M, Azad AK. Erythrocyte vacuolation in haemolytic anaemia during shigellosis [letter]. Lancet 1987 Jul 11;2(8550):111
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APPENDIX A

AUDITORS' REPORT
TO THE BOARD OF TRUSTEES OF
INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH

We report that we have audited the Balance Sheet of International Centre for Diarrhoeal Disease Research, Bangladesh as at December 31, 1987, signed by us under reference to this report and the relative Income and Expenditure Account for the year ended on that date which are in agreement with the books of account maintained by the Centre and produced to us. Our examination was made in accordance with generally accepted auditing standards and, accordingly, included such tests of the accounting records and such other auditing procedures as we considered necessary in the circumstances.

In our opinion and to the best of our information and according to the explanations given to us, the Balance Sheet and Income and Expenditure Account together with the Notes attached thereto, give respectively a true and fair view of the state of affairs of the Centre as at December 31, 1987 and its surplus for the year ended on that date.



PRICE WATERHOUSE
Chartered Accountants



RAHMAN RAHMAN HUQ & CO.
Chartered Accountants

Dhaka, April 5, 1988

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH
BALANCE SHEET AS AT DECEMBER 31, 1987

	<u>Notes</u>		<u>1986</u>
Fixed Assets : Cost less depreciation	2	3,714,934	4,291,600
Employees' Retirement Fund Deposits	3	2,245,880	1,757,013
Current Assets			
Stock of stores and spares	4	458,803	432,089
Contributions receivable from donors	13	805,011	575,682
Advances, deposits and prepayments	5	360,192	382,862
Cash and bank balances	6	2,294,699	1,828,251
		<u>3,918,705</u>	<u>3,218,884</u>
Less: Current Liabilities			
Bank overdraft	7	70	927,313
Interest free loan	8	1,186,080	1,186,080
Contributions paid in advance by donors	13	2,212,698	2,085,959
Other current liabilities	9	670,999	328,857
		<u>4,069,847</u>	<u>4,528,209</u>
Net Current Assets		<u>(151,142)</u>	<u>(1,309,325)</u>
		US \$ <u>5,809,672</u>	<u>4,739,288</u>
Financed By :			
Capital Development Fund	10	6,071,072	5,692,533
Operating Fund	11	(4,060,200)	(4,181,449)
Reserve Fund	12	1,552,920	1,471,191
Employees' Retirement Fund		2,245,880	1,757,013
		<u>US \$ 5,809,672</u>	<u>4,739,288</u>

Notes form part of the accounts

huss.

Director
ICDDR,B

[Signature]
Member
Board of Trustees

This is the Balance Sheet referred to in our report of same date.

[Signature]
Price Waterhouse
Chartered Accountants

[Signature]
Rahman Rahman Huq & Co.
Chartered Accountants

Dhaka, April 5, 1988

INCOME AND EXPENDITURE ACCOUNT (OPERATING FUND)
FOR THE YEAR ENDED DECEMBER 31, 1987

	<u>Notes</u>		<u>1986</u>
Income			
Contributions	13	8,798,060	7,892,691
Less:			
Transferred to Capital Development Fund to the extent of capital expenditure/contribution		378,539	475,720
		8,419,521	7,416,971
Other receipts		345,011	430,458
Exchange gain		40,672	31,449
		8,805,204	7,878,378
Expenditure			
Personnel services and benefits	14	5,379,595	5,181,005
Supplies and materials		973,622	1,112,985
Travel expenses		429,951	436,664
Transportation of materials		129,962	83,525
Rent, communication and utilities		239,469	184,150
Printing and reproduction		112,776	111,603
Other contractual services		465,101	619,318
Depreciation		953,479	462,291
		8,683,955	8,191,541
Surplus/(Deficit)	US \$	121,249	(312,663)

Notes form part of the accounts

[Handwritten Signature]

Director
ICDDR,B

[Handwritten Signature]
Member
Board of Trustees

This is the Income and Expenditure Account referred to in our report of same date.

[Handwritten Signature]
Price Waterhouse
Chartered Accountants

[Handwritten Signature]
Rahman Rahman Huq & Co.
Chartered Accountants

Dhaka, April 5, 1988

SOURCES AND APPLICATIONS OF FUNDS
FOR THE YEAR ENDED DECEMBER 31, 1987

1986

Sources

Donors' contributions for capital expenditure	378,539	475,720
Bank interest on deposit of reserve fund	81,729	70,241
Retirement Fund receipts (net)	488,867	341,363
Sale of assets	1,717	8,686
Cash surplus from operation	1,074,737	153,423
	<u>US \$ 2,025,589</u>	<u>1,049,433</u>

Applications

Addition to fixed assets	378,539	475,720
Increase in net current assets	1,158,183	232,350
Investment of Retirement Fund (net)	488,867	341,363
	<u>US \$ 2,025,589</u>	<u>1,049,433</u>

NOTES TO ACCOUNTS FOR THE YEAR ENDED DECEMBER 31, 1987

1. SIGNIFICANT ACCOUNTING POLICIES

- i) Income and Expenditure Account and Balance Sheet of the Centre are prepared in the manner as prescribed and approved by the Board of Trustees.
- ii) Fixed assets had been brought to account at material cost up to August 1981. Subsequent to that date incidental expenses such as labour, freight, insurance etc. (excluding clearing charges) have also been included in arriving at the cost of fixed assets.
- iii) Stock of stores and spares are valued at material cost only.
- iv) "Income" & "Expenditure" of the Centre for the year have been accounted for on an "accrual" basis in accordance with past practice.
- v) Depreciation on fixed assets has been charged on a "straight line" basis.
- vi) The accounts have been prepared on a 'historical cost' convention. For advances, liabilities (except interest free loan), cash and bank balances the year end exchange rate was used for converting non-US currencies to US Dollars. For other transactions, average monthly exchange rates were used for conversion purposes.
- vii) All assets costing Tk. 1,000 or less are expensed.

2. FIXED ASSETS

ASSETS	COST				DEPRECIATION					NET BOOK VALUE AS AT DEC. 31 1987
	As at January 1 1987	Additions this year	Sales/ Adjustments this year	Total	Rate	As at Jan. 1, 1987	Charge for the year	Adjustments	Total	
Land	71,362			71,362						71,362
Building	1,834,699	31,386		1,866,085	5%	139,342	93,304		232,646	1,633,439
Vehicles	476,943	22,275	7,917	491,301	25%	316,237	122,825	6,332	432,730	58,571
Furniture	372,640	12,487	234	384,893	20%	132,829	76,979	93	209,715	175,178
Equipment	2,869,434	311,249		3,180,683	20%	867,062	636,137		1,503,199	1,677,484
Others	120,026	1,142		121,168	20%	22,960	24,234		47,194	73,974
Work in progress	24,926			24,926						24,926
US \$	5,770,030	378,539	8,151	6,140,418		1,478,430	953,479	6,425	2,425,484	3,714,934

- i) Land measuring 4.10 and 0.51 acres situated at Mohakhali (Dhaka) and Matlab (Comilla) received as donations from the Government of Bangladesh and a private party respectively have not been included in this account.
- ii) Cost of buildings includes an amount of US\$ 102,910 spent on the extension of the Institute of Public Health building, owned by the Government of Bangladesh and at present partly accommodating the Centre. The extension was done for use by the ICDDR,B.
- iii) Work in progress represents the cost of a transformer, installed in 1984, which could not be made operational due to unavailability of a required lubricant.
- iv) No provision for depreciation had been made upto December 31, 1982. Further, depreciation rates were increased effective January 1, 1987 resulting in an additional charge of US\$ 455,282 in this regard for 1987.

3. EMPLOYEES' RETIREMENT' FUND DEPOSITS

These deposits represent employees' and Centre's contributions lodged with "Generali Group" under a group annuity contract through the Institute of International Education, New York, to provide for retirement benefits to local employees who are in the WHO scale. Since the fund is not maintained by the Centre, these deposits do not form part of its assets but have been incorporated into the books of account by a contra credit to "Employees' Retirement Fund" on the basis of memorandum records maintained by the Centre in this respect. Accretions to the deposits by way of interest as may be allowed by "Generali" are not recognised in the Centre's records.

4. STOCK OF STORES AND SPARES

	<u>1987</u>	<u>1986</u>
Supply stores (including stores in transit US\$ 46,919; 1986 US\$ 37,555)	294,800	255,770
Maintenance stores	<u>122,141</u>	<u>121,867</u>
	416,941	377,637
Capital assets in transit	<u>41,862</u>	<u>54,452</u>
	<u>US \$ 458,803</u>	<u>432,089</u>

5. ADVANCES, DEPOSITS AND PREPAYMENTS

	<u>1987</u>	<u>1986</u>
Advances:		
Against - supplies and services	146,958	209,935
- expenses	198,694	144,213
- Others	10,694	24,936
	<hr/>	<hr/>
Deposits	356,346	379,084
	3,846	3,778
	<hr/>	<hr/>
US \$	<u>360,192</u>	<u>382,862</u>

6. CASH AND BANK BALANCES

	<u>1987</u>	<u>1986</u>
Cash on hand	3,327	1,469
Cash at banks:		
US\$ Accounts		
American Express Bank Ltd. -		
New York		
- Reserve Account	11,509	38,372
- Demand Account	508,073	
- Call Deposit	500,000	500,000
Switzerland		7,935
Dhaka		21,819
- Reserve Account	5,411	131,084
- Current Account	68,495	524
- BOSTID Account	147	526
- USAID - MCH	217	
- USAID - UVP	2,563	
- Call Deposit	1,036,000	911,000
Janata Bank - Dhaka	2,132,415	1,612,534
UK £ Account		
American Express Bank Ltd., London	22,581	8,478
SFR Account		
American Express Bank Ltd., Switzerland		7,394
SR Account		
Saudi American Bank, Dammam		1,468
Taka Account		
American Express Bank Ltd., Dhaka		
- NORAD Fund	109,489	6,555
- Current Account	1,436	25,643
- Call Deposit		116,764
Agrani Bank	25,451	46,577
Janata Bank		1,369
	<hr/>	<hr/>
	136,376	196,908
	<hr/>	<hr/>
US \$	<u>2,294,699</u>	<u>1,828,251</u>

7. BANK OVERDRAFT

	<u>1987</u>	<u>1986</u>
US\$ Account		
American Express Bank Ltd., New York		367,596
Taka Account		
American Express Bank Ltd., Dhaka	70	559,717
	<u>70</u>	<u>559,717</u>
US \$	<u>70</u>	<u>927,313</u>

8. INTEREST FREE LOAN

- In May 1983, the Centre was provided by the Government of Bangladesh with an interest free loan of Tk. 28,928,775 (US\$ 1,186,080) initially for a period of one year. After several extensions by the Government of Bangladesh, the repayment date expired on June 30, 1986. As per the terms of the loan, the Centre is liable to pay interest at the prevailing commercial lending rate if the loan remains unpaid beyond the expiry of the period of repayment. No provision for interest has been made in the accounts in this regard as the Centre holds the view that the loan should be converted into a grant on the grounds that this loan was originally a grant to the Centre by UNROB and was utilized for providing free medical treatment to patients in Bangladesh as well as to provide free training to Bangladeshis.

9. OTHER CURRENT LIABILITIES

	<u>1987</u>	<u>1986</u>
For supplies and materials	113,865	83,526
For expenses	515,659	211,869
Security and other deposits	41,475	33,462
	<u>670,999</u>	<u>328,857</u>
US \$	<u>670,999</u>	<u>328,857</u>

10. CAPITAL DEVELOPMENT FUND

Balance as at January 1	5,692,533	5,216,813
Add: Transferred during the year from Income and Expenditure Account	378,539	475,720
	<u>6,071,072</u>	<u>5,692,533</u>
US \$	<u>6,071,072</u>	<u>5,692,533</u>

11. OPERATING FUND

Balance as at January 1	(4,181,449)	(3,868,786)
Surplus/(Deficit) for the year ended December 31	121,249	(312,663)
	<u>(4,060,200)</u>	<u>(4,181,449)</u>
US \$	<u>(4,060,200)</u>	<u>(4,181,449)</u>

12. RESERVE FUND

Balance as at January 1	1,471,191	1,400,950
Add: Interest earned on deposits	81,729	70,241
	<u>1,552,920</u>	<u>1,471,191</u>
US \$	<u>1,552,920</u>	<u>1,471,191</u>

13. CONTRIBUTIONS

	Advance/ (Accrual) 31 Decem- ber 1986	1987				1986
		Received	Accrued year end	Carried over	Income	Income
Central Funds:						
Australia	61,619	126,325		45,462	142,482	61,618
Bangladesh	15,627		15,181		30,808	43,684
China						10,000
Saudi Arabia			70,000		70,000	70,000
Sweden						117,810
United States-AID		250,000			250,000	500,000
Switzerland	648,203				648,203	132,106
United Kingdom	103,224	230,302		115,151	218,375	103,224
UNICEF		250,000			250,000	500,000
Others		1,217			1,217	
Total Central Funds	828,673	857,844	85,181	160,613	1,611,085	1,538,442
Project Funds:						
Aga Khan Foundation	16,886	45,585		46,500	15,971	1,065
Arab Gulf Fund		250,000	202,221		452,221	
Australia (Nandipara)	1,122			577	545	1,102
Australian National University	2,397				2,397	3,376
Belgium	(74,113)	243,045		112,603	56,329	188,852
BOSTID	(5,443)	28,425		5,816	17,166	27,613
Canada						
- CIDA (Training)	72,662	156,607		169,782	59,487	181,975
- CIDA (DSS)	200,318	797,372		349,200	648,490	566,722
- IDRC (DISC)	6,712	53,884	18,400		78,996	76,429
- IDRC (Infant Mortality)	2,202		851		3,053	7,191
- IDRC (Video)						1,262
Case Western Reserve University	3,101	12,160	7,679		22,940	9,681
DANIDA		506,016			506,016	
FAO	37,129				37,129	858
France	(13,873)	55,568		29,976	11,719	13,873
Ford Foundation	86,114		13,092	3,773	95,433	(17,765)
Holland		7,335		5,191	2,144	
IBRD	(99,078)	174,753	59,297		134,972	177,941
Japan	18,501	295,176			313,677	401,499

Continued on next page

Continued from previous page

	Advance/ (Accrual) to Decem- ber 1986	1987				1986
		Received	Accrued year end	Carried over	Income	Income
Management Science for Health						4,500
Medicins Sans Frontieres						24,063
Miles Pharmaceuticals	(28,633)	107,822		12,918	66,271	76,032
Nestle	3,379	2,793		1,125	5,047	5,826
NORWAY-NORAD	101,920	459,364		178,048	383,236	325,907
Norwich Eaton Pharmaceutical	3,924	12,086		4,940	11,070	18,576
Others		13,463		7,398	6,065	30,000
Population Council	(13,438)	13,438				18,790
SDC-Emergency Relief -Training		136,920		4,738	132,182	
Rockefeller Foundation	3,414	(3,078)			14,579	
Saudi Arabia (DCC)	(88,500)	530,708	123,778		336	2,750
UNDP/UNROB					565,986	625,096
UNDP - UVP						43,571
UNDP - WHO	147,982	300,000		263,811	184,171	103,154
UNICEF (ORT, Training)	(88,518)	193,665	25,415		130,562	240,018
						423,998
UNITED STATES - AI						
- Cholera Vaccine Trial						380,000
- Cooperative Agreement	497,571	1,868,075		794,427	1,571,219	1,202,429
- Urban Volunteer Programme	(77,994)	340,664	100,347		363,017	77,994
- Dhaka, MCH-FP	(72,945)	948,165	154,171		1,029,391	1,056,757
- NIROG						14,731
- Training		32,640			32,640	89,084
IBM		30,916			30,916	
Welcome Trust		29,019		2,820	26,199	
WHO	38,805	195,040		58,442	175,403	49,299
Total Project Funds	681,604	7,837,626	719,830	2,052,085	7,186,975	6,354,249
Grand Total US\$	1,510,277	8,695,470	805,011	2,212,698	8,798,060	7,892,691

...ants by way of various services rendered by the donor agencies to the
entre have not been considered in the accounts.

14. PERSONNEL SERVICES AND BENEFITS

This includes an aggregate amount of US\$ 18,437 paid as honorarium to the Members of the Board of Trustees who had waived their entitlement to such payment in 1986.

15. CURRENCY TRANSLATION

<u>Currency</u>	<u>Average monthly exchange rates</u>	<u>Year-end exchange rate</u>
	US\$	US\$
Tk. 1.00	0.0327	0.0324
UK £ 1.00	1.5942	1.8610
SFR 1.00	0.6406	0.7746
SR 1.00	0.2666	0.2667
S\$ 1.00	0.4759	0.5016

16. OTHERS

Previous year's figures have been rearranged and regrouped to conform to current year's presentation.

Figures have been rounded off to nearest US dollar.

APPENDIX B

ACRONYMS AND ABBREVIATIONS

AFIP&T	Armed Forces Institute of Pathology and Transfusion
BCSIR	Bangladesh Council of Scientific and Industrial Research
BIDS	Bangladesh Institute of Development Studies
BIRDEM	Bangladesh Institute of Research & Rehabilitation in Diabetes, Endocrine & Metabolic Disorders
BOSTID	Board on Science and Technology for International Development
BRAC	Bangladesh Rural Advancement Committee
CIDA	Canadian International Development Agency
CIS	Computer Information Services
CMD	Community Medicine Division
CSD	Clinical Sciences Division
DANIDA	Danish International Development Agency
DMCH	Dhaka Medical College Hospital
DISC	International Diarrhoeal Disease Information Service and Documentation Centre
DMB	Data Management Branch
DSS	Demographic Surveillance System
ELISA	Enzyme-linked immunosorbent assay
EPI	Expanded Programme of Immunization
ERC	Ethical Review Committee
FAO	Food and Agriculture Organisation
IBRD	International Bank for Reconstruction and Development
ICDDR,B	International Centre for Diarrhoeal Disease Research, Bangladesh
IDRC	International Development Research Centre
INSERM	Institut National de la Santé et de la Recherche Médicale
IPH	Institute of Public Health
JDDR	Journal of Diarrhoeal Diseases Research
LSD	Laboratory Sciences Division
MCH-FP	Maternal and Child Health - Family Planning
NIPORT	National Institute of Population Research and Training
NORAD	Norwegian Agency for Development
OPEC	Oil Producing and Exporting Countries
ORS	Oral rehydration salts; oral rehydration solution
ORSTOM	Institut Français de Recherche Scientifique pour le Développement en Coopération
ORT	Oral rehydration therapy
PCC	Programme Coordination Committee
PSED	Population Science and Extension Division
SAREC	Swedish Agency for Research Cooperation with Developing Countries
SDC	Swiss Development Co-operation
RRC	Research Review Committee
UNCDF	United Nations Capital Development Fund
UNDP	United Nations Development Programme
UNFPA	United Nations Fund for Population Activities
UNICEF	United Nations Children's Fund
UNROB	United Nations Relief Organisation in Bangladesh
US AID	United States Agency for International Development
UVP	Urban Volunteers Programme
WHO	World Health Organization

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