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Scientific Achievements
of the ICDDR,B
1979-1990

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INTRODUCTION

Evaluation of institutional strengths and accomplishments take many forms. Compiling and measuring output, as this document attempts to do, creates one important and enlightening scene, but it does not represent the whole picture. In fact, the period of time these publications cover (1979-1990) does not even give a comprehensive view of the entire history of research at the ICDDR,B.

The interest in studying diarrhoeal diseases in Dhaka (then Dacca) began more than 30 years ago in the SEATO Cholera Research Laboratory, which was the forerunner of today's Centre. For 18 years the CRL pioneered cholera research, making important discoveries, among which were the benefits of antibiotics in shortening the course of illness, the use of intravenous fluids to prevent death from dehydration, the ineffectiveness of the commonly used injectable cholera vaccine, and the early clinical success of oral rehydration therapy. These findings and others are the basis for many of the works reported in the publications listed herein.

Since 1979, the major differences of the Centre, along with the name, have been its international thrust and a diversification of interests. Whereas the main focus was once cholera, the scope has now broadened to include other causes of diarrhoea and disease-related studies, such as those involving nutrition and family planning. The internationalisation was a result of the institution's need for a worldwide interest in its work, to attract the expertise and funding required to operate with expedience and accomplishment.

These changes reflect the growth of the institution, but no institution grows in isolation.

Just as the ICDDR,B depends upon cooperation with other organisations in Bangladesh and throughout the world, so do the researchers depend on the findings of other studies and collaboration with others in their respective fields. Therefore, these accomplishments cannot be claimed by the Centre alone; they belong to the scientific community at large.

This introduction began by stating that this bibliography only begins to define the accomplishments of the Centre. Indeed, merely listing the scientific achievements of an institution in no way accounts for the day to day benefits to the people who are involved in various aspects of research, training, and service, nor the long-range impact that these involvements have on the community, the country, and the world. It does, however, tell an important part of the story of the ICDDR,B.

When the idea to prepare such a document was conceived, Dr. Michael Bennish was asked to attempt the impossible task of writing a summary of the works. At the risk of not being comprehensive, or of being too voluminous, he has prepared what he calls "Scientific Accomplishments of the ICDDR,B, 1979-1990". As a result of his struggle with this assignment, it has been subsequently decided that the Centre will compile a bibliography more frequently, perhaps every five years, thus facilitating the highlighting of important developments.

The Centre's gratitude is extended to Dr. Bennish and to all those whose efforts made this work possible, including the scientists whose names appear herein.

Demissie Habte, MD
Director

HIGHLIGHTS OF PUBLISHED STUDIES

By ordinance of the Government of the People's Republic of Bangladesh, the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) was established as an autonomous, international institution on the 9th of December 1978. The ICDDR,B was the successive institution to the Cholera Research Laboratory, which had been jointly founded by the Government of the United States and the then Government of Pakistan, in 1960. The Cholera Research Laboratory (CRL) had been continued by agreement of the Government of the People's Republic of Bangladesh and the Government of the United States in 1974.

One of two objectives of the ICDDR,B, as stated in the Ordinance under which it was created, was "To function as an institution to undertake and promote study, research and dissemination of knowledge in diarrhoeal diseases and directly related subjects of nutrition and fertility with a view to developing improved methods of health care for the prevention and control of diarrhoeal diseases and improvement of public health programmes with special relevance to developing countries". How well has the Centre fulfilled its charge of conducting research in the fields of diarrhoea, nutrition, and fertility?

Scientific accomplishment is difficult to measure, and no one single measure is adequate. One measure of accomplishment, as stated in the Ordinance, is the contribution research has made to the health of persons living in developing countries. By and large, in the last 12 years, rates of infant and maternal mortality have decreased in developing countries. Diarrhoeal morbidity and mortality have been substantially reduced, and contraceptive use has increased, with an attendant decline in fertility. Improvements in public health are, however, usually the result of changes in socioeconomic conditions. Therefore, discerning the relative contribution of health research, health care delivery, and improved socioeconomic conditions to improved health conditions is difficult.

An alternative measure of scientific accomplishment is scientific publication. This measure of research accomplishment is one that is used at research institutions -- for assessment of both individual and institutional accomplishments. This measure has the advantage of being easy to compute. It has a number of disadvantages as well. First, the number of publications says nothing about the quality of work that is being done. Second, the number of research publications is not necessarily a good indicator of the impact of research work within either the scientific community or on health status in developing countries.

Despite these limitations, a compilation of all scientific publications by the Centre scientists since its inception in 1979 is useful in assessing the contributions the Centre has made to the understanding of health problems in developing countries. The bibliography in this report lists scientific publications originating from the Centre, and divides them into four categories: A) Original articles, review articles, short communications, and brief reports in scientific journals; B) Letters and notes in scientific journals; C) Books and book chapters; and D) ICDDR,B publications. One hundred twenty-five papers and chapters in published proceedings, and 21 monographs, reports, and theses are not included in this bibliography. A listing of these latter publications is available on request from the ICDDR,B.

When one counts the publications, the numbers are impressive. There have been 1,152 publications during these 12 years; 731 (63.40%) of these have been original scientific articles written by 230 different first authors. These 731 original articles have appeared in 159 different scientific journals, including some of the most prestigious journals in the fields of medicine, epidemiology, microbiology, social science, and demography and family planning (Table 1). Journals that have published 15 articles or more by the Centre scientists are: *American Journal of Clinical Nutrition*, 25 publications; *British Medical*

Journal, 17 publications; *Bulletin of the World Health Organization*, 19 publications; *Indian Journal of Medical Research*, 16 publications; *Infection and Immunity*, 17 publications; *International Journal of Epidemiology*, 19 publications; *Journal of Biosocial Science*, 20 publications; *Journal of Clinical Microbiology*, 23 publications; *Journal of Diarrhoeal Diseases Research* (published since 1983), 36 publications; *The Journal of Infectious Diseases*, 31 publications; *Journal of Tropical Medicine and Hygiene*, 20 publications; *The Lancet*, 22 publications; *Studies in Family Planning*, 27 publications; *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 31 publications; and *Tropical and Geographical Medicine*, 19 publications.

As shown in Fig. 1, the 731 original scientific articles have been well distributed between journals in the general medical sciences (389 articles); microbiology and other laboratory sciences (99 articles); demography and family planning (69 articles); nutrition (68 articles); epidemiology (48 articles); and anthropology and political and social sciences (47 articles). This division of articles by disciplines, however, is inherently arbitrary. For instance, many of the articles published in general medical journals address a wide variety of topics – including nutrition, microbiology, and epidemiology. In addition, many of the published studies involve more than one discipline. The best example of this are the studies that address the relationship between infection, disease, and nutritional status. Overall, the mixture of journals in which the Centre scientists have published suggests that the Centre has been successful in directing its research efforts at the three areas of research mandated by the Ordinance – namely diarrhoea, nutrition, and fertility.

The 731 original scientific articles were published in journals from diverse geographic locations (Fig. 2). Two hundred forty-six (33.65%) articles were published in journals from North America, 224 (30.64%) in journals from Great Britain, 109 (14.91%) in journals from Bangladesh (36 of these in the *Journal of Diarrhoeal Diseases Research*), 39 (5.34%) in Indian journals, 37 (5.06%) articles published in journals from elsewhere in Asia or from Africa,

and 76 (10.40%) articles published in non-British European journals. This rather wide geographic distribution of publications fulfils, at least to some degree, the Centre's mandate under the Ordinance to achieve the widest possible dissemination of its research findings.

The research productivity of the Centre has been relatively constant (Fig. 3). Since 1984, more than 60 original articles have been published every year, with a maximum in 1989 of 81 publications.

The publications from the last 12 years that are based on work done at the ICDDR,B are diverse in subject matter. No one can claim an expert's understanding of all of this work. The following discussion is intended to highlight some of the more important and intriguing research findings. For convenience, the research findings have been somewhat arbitrarily classified into 15 different categories.

1. Cholera Epidemiology.

More than 125 years after John Snow's seminal work, there are still large gaps in the knowledge of the epidemiology of cholera. Work done at the Centre is helping to fill in some of those gaps. Over 20 publications during the last 12 years have directly addressed unresolved questions of the epidemiology of cholera.

The central role of an aquatic reservoir in sustaining endemic cholera was emphasised in a number of papers. The use of phage typing has shown that many different phage types circulate in the community, a finding consistent with an environmental reservoir of the organism. The use of newer techniques, such as the fluorescent-antibody direct viable count, has demonstrated that viable organisms exist in surface waters even when *Vibrio cholerae* is not cultivatable. This finding helps explain one of the conundrums of cholera epidemiology, namely the inability to culture *V. cholerae* from waters that were implicated as being a reservoir of the organism.

Studies of disease patterns in Matlab over a 15-year period allow for a number of important conclusions. One is that second attacks of clinically apparent cholera are relatively rare.

Thus, there is reason to believe that long-term natural immunity to cholera does exist, and that vaccines that mimic natural infection may result in long-standing immunity. A second observation was that severe disease is relatively uncommon in children aged less than two years. This observation was followed up by a study which found that breast milk antibodies against cholera toxin and *V. cholerae* lipopolysaccharide protected against severe disease. These findings provide an explanation for the decreased incidence of clinically apparent cholera in children aged less than two years. They also provide additional support for policies that stress the crucial role of breast-feeding in protecting against infection.

The change in biotype of the endemic strain of cholera from El Tor back to classical in Matlab during the late 1970s provided the opportunity to examine differences in the epidemiology of these two strains, and to attempt to resolve the question of differences in the severity of disease between the two biotypes.

2. Cholera Vaccines.

The Centre's efforts to identify effective enteric vaccines have, to date, focussed primarily on the development of a cholera vaccine. The initial clinical trials, and then the large-scale field trial of a cholera toxin B-subunit-killed whole cell vaccine, are among the best known of the Centre's efforts.

The field trial was the result of extensive smaller clinical trials which showed that the purified B-subunit of cholera toxin, when administered orally, elicited both a local and systemic immune response. Additional epidemiologic studies showed the relative protective effects of pre-existing antibody of different types.

Based upon these studies, a field trial of two different oral vaccines -- one composed of the purified B-subunit of cholera toxin and killed whole cholera vibrios, and the other of killed whole vibrios alone -- was carried out. After three years the protective efficacy of either vaccine was approximately 50%. Efficacy waned more quickly in children aged 2-5 years, and protection against disease due to infection with the El Tor biotype of cholera was less than

against disease caused by the classical biotype of cholera.

Important lessons have been learned from this trial. These include the surprising relative efficacy of the killed vaccine, the problems with sustaining immunity in children who are immunised at a young age, the limited cross protection that a cholera vaccine provides against disease due to labile toxin producing *Escherichia coli*, and the technical and political issues involved in carrying out a large-scale vaccine trial.

3. Clinical Complications and Pathophysiology of Diarrhoea.

During the period of the CRL, especially in its heyday of the 1960s, the focus of pathophysiology studies was on the mechanisms of watery diarrhoea and dehydration. In contrast, the focus during the 12 years of the ICDDR,B has been on the descriptive epidemiology and pathophysiology of systemic complications of diarrhoea other than dehydration, especially those complications occurring during shigella infection.

Published studies in this field include descriptions of the clinical features and risk factors for intestinal perforation during typhoid fever, a description of the diarrhoea that occurs with typhoid fever, a description of necrotising enterocolitis in young patients severely ill with diarrhoea, a description of autopsy findings in selected patients who died with diarrhoea at the ICDDR,B, and studies of the incidence, risk factors and clinical features of patients with shigellosis and the leukaemoid reaction, or those with shigellosis and the haemolytic-uraemic syndrome. Other studies have looked at the incidence and risk factors for death in all patients admitted to the inpatient unit of the treatment centre in Dhaka, or risk factors for death in those patients admitted with shigellosis. There have also been a number of papers that describe electrolyte abnormalities in patients seen at the ICDDR,B Treatment Centres, and correlate these abnormalities with clinical outcome.

Actual pathophysiologic studies have been few. One study of pathophysiology examined the causes of acidosis during cholera, and found that the acidosis was not simply attributable to a loss

of bicarbonate. Another study examined the incidence and pathophysiology of hypoglycaemia during diarrhoea, a problem that was first identified at the CRL in 1965. Other pathophysiologic studies have examined colonic function during cholera and shigellosis, pancreatic function during cholera, the role of prostaglandins during cholera, and the relationship between gastric acidity, nutritional status and intestinal bacterial colonisation. Studies done during the last days of the CRL, but published in the early days of the ICDDR,B examined immune function of patients of differing nutritional status with a variety of enteric infections. Such studies of immune function were not subsequently pursued, and have only recently been resumed.

4. Treatment of Watery Diarrhoea.

Studies on the management and treatment of watery diarrhoea have focused on four major areas: (1) refinements of the standard oral rehydration solution; (2) development of solutions using oligosaccharides or amino acids for cotransport of sodium; (3) the use of antisecretory agents; and (4) field implementation and evaluation of oral rehydration solutions. Among the first category are studies examining the replacement of glucose with sucrose (more easily available in households), the replacement of bicarbonate by citrate (longer shelf life), lowering the concentration of sodium in the solution (concerns with hypernatraemia), and the early introduction of feeding, including milk (concerns about nutritional support of the child with diarrhoea).

The second category of studies, those addressing the use of oral rehydration based upon a cereal substrate or an amino acid for the cotransport of sodium, are at the same time among the most promising and the most provocative and controversial studies. A number of studies have been published showing that a cereal-based oral rehydration preparation is effective in replacing stool losses during diarrhoea, that such a preparation reduces stool volume, and that it can be prepared under field conditions. Such cereal-based solutions are now routinely being used in the ICDDR,B, Diarrhoea Treatment Centres in Dhaka and Matlab. These studies are provocative, because they suggest that oral therapy may not be able only to treat

diarrhoea, but to "cure" it as well. They are controversial, because their role as a public health measure is uncertain -- governments and international agencies have invested considerable time and effort in spreading the gospel of oral rehydration therapy based upon sachets of salts and dextrose, or home-made therapy using sugar and salt. Whether the advantages of cereal-based therapy are sufficient to warrant a restructuring of the oral rehydration therapy campaigns is now under study.

The other approach to making fundamental improvements to the time tested glucose-based oral rehydration solution is to add an amino acid substrate to enhance absorption. Such solutions underwent preliminary evaluation in the CRL period, and a solution containing alanine has been evaluated at the ICDDR,B. It was found to reduce total stool output in comparison to standard oral rehydration solution containing only glucose as a carrier molecule.

Antisecretory agents evaluated include aspirin, chlorpromazine, indomethacin, chloroquine, somatostatin, clonidine, nicotinic acid, and the herbal agent berberine. Some of these agents have been found effective in reducing stool output during diarrhoea. None have been found effective enough to gain a foothold in clinical practice. A novel approach to reducing intestinal secretion has been the administration of GM-1 ganglioside adsorbed onto charcoal to patients with cholera in an attempt to block the effects of cholera toxin (GM-1 ganglioside is the putative membrane receptor for cholera toxin). A similar approach has been the administration of the B-subunit of cholera toxin to family contacts of patients with cholera. Both trials showed interesting results, but this line of investigation has not been pursued.

The last set of issues, that of evaluating strategies for implementing oral rehydration therapy in communities, is both the most challenging and the least studied. In view of the fact that the proportion of deaths attributable to diarrhoea in Matlab is similar today to what it was 15 years ago, there clearly is a need for more effective strategies for implementing the appropriate use of oral rehydration therapy.

A number of studies from the early 1980s examined the efficacy and safety of home administration of oral rehydration solution. Electrolyte disturbances resulting from inappropriate mixing of the home-administered solutions were not found to be a major problem. Bacterial contamination of the home-prepared solutions was a problem however, the "solution" to which has not been identified.

5. Treatment of Invasive Diarrhoea.

The treatment of invasive diarrhoeas is largely synonymous with the treatment of shigellosis. Studies at the ICDDR,B have documented the increasing resistance to previously used antimicrobial agents. The large number of patients with shigellosis (approximately 12,000) who yearly come to the Treatment Centre in Dhaka for care, along with the research facilities available there, has permitted the Centre to carry out seven published treatment studies of shigellosis, with two additional studies currently underway. Drugs found effective include ampicillin, co-trimoxazole, pivamdinocillin (pivmecillinam was the previous name for this drug), nalidixic acid, and ciprofloxacin. The Centre has played an important role in bringing attention to the major public health implications of multi-resistant shigellosis, a problem that also affects other countries in Asia and Africa. The Centre has also conducted at least one study of the treatment of typhoid fever, in which a third generation cephalosporin administered parenterally for seven days was shown to be somewhat less effective than a standard 14-day course of chloramphenicol.

6. Clinical Features and Epidemiology of Enteric Infections Other Than Cholera.

The Centre scientists have been instrumental in describing the clinical features and epidemiology of a number of different enteric pathogens. Descriptions of clinical illness were greatly facilitated by the establishment of a systematic surveillance system at the Treatment Centre in Dhaka in 1979, as well as by the ongoing collection of data on patients coming to the Treatment Centre in Matlab. Based on data from those two patient populations, descriptions of the clinical and epidemiologic characteristics of

patients with non-typhoidal salmonellosis, typhoid fever, shigellosis, giardiasis, amoebiasis, *Campylobacter jejuni* infection, rotavirus and toxin-producing *Escherichia coli*-associated diarrhoea, yersiniosis, and cryptosporidiosis have been published. While most of these organisms were well established pathogens by the time these studies were done, the impressively large number of patients with diarrhoea who attend the Treatment Centres of the ICDDR,B allowed for more complete clinical descriptions of these infections than had previously been available.

The epidemiologic studies conducted at the Centre's field sites in urban Dhaka (Rayer Bazaar and the catchment area of the Urban Volunteer Program), peri-urban Dhaka (Nandipara) and in rural Bangladesh (Matlab) have been the community counterpart of the Treatment Centre-based studies. These latter sets of studies have helped explain the importance of enteric infections in the community - what organisms are responsible for infection, who is infected, how often do infections occur, what is the nature of the immune response, how does the immune response affect susceptibility to future infections, what is the impact of infection on nutritional status, how are these infections spread, and how might they be prevented. More recently, the epidemiology and clinical features of persistent diarrhoea in these populations have been studied, and this will be an area of increasing interest.

These studies of the epidemiology of diarrhoeal illness have been some of the most influential and widely quoted of the studies conducted at the Centre. There are a number of reasons for this. One is that these studies were predicated on having both excellent community surveillance as well as excellent laboratory support, an infrequent combination in field situations in developing countries. Two, they addressed a subject that was of immense public health importance - what is the "behaviour" of these enteric infections in rather typical communities, and what is the impact of these infections on the health of children. The information they provide is, thus, crucial for designing and "targeting" health care interventions. Three, they were published in well respected journals with high visibility in their respective fields.

7. Mortality: Causes and Associations.

Too many infants and children still die in Bangladesh. Why this is so has been the subject of perhaps the largest number of studies conducted at the ICDDR,B -- studies that try to identify the causes, and more frequently the factors associated with, childhood mortality in Bangladesh.

Studies examining the causes of mortality come from two main sources -- the ICDDR,B Treatment Centre in Dhaka where approximately 600 children die from diarrhoeal illness every year, and the Matlab Demographic Surveillance Area, where approximately 900 infant deaths and about 750 deaths in children aged 1 to 5 years occur yearly. Additional studies of mortality patterns have been conducted in Burmese refugee camps along the southern border of Bangladesh and in urban areas of Dhaka.

The studies examining causes of mortality in children with diarrhoea presenting to the Treatment Centre in Dhaka have been described in the section on clinical studies. The field-based studies have focused on four main subject areas: 1) socioeconomic correlates of mortality; 2) the relationship between gender and mortality; 3) nutritional "predictors" of mortality, primarily using anthropometry; and 4) specific causes of death using a "verbal" autopsy system. In addition to the studies examining the correlates of infant and child mortality, recent studies have addressed the issue of maternal mortality, which previously had received very little attention.

There are no big surprises in the findings from these studies. Diarrhoea (primarily dysentery, not watery diarrhoea) and respiratory tract infections account for the majority of childhood deaths. Now that maternal tetanus immunisation is common, most neonatal deaths are attributable to complications of prematurity. Declining infant mortality rates are mainly attributable to the fall in neonatal, as opposed to post-neonatal, mortality rates. Girls continue to die more often than boys. Poorly nourished children (as measured by any of the available anthropometric indices) die more often than do better nourished children.

As with studies on the epidemiology of

enteric infections, the studies of the causes and correlates of infant and childhood mortality have been among the Centre's most prominent work. The reasons for this are similar for the two subject areas -- relatively solid data on a subject of immense public health importance. Although the findings during the ICDDR,B period have not brought about fundamentally new insights, they are comprehensive, and thus extremely valuable.

8. Nutrition -- diarrhoea Interactions.

Too many Bangladeshi children are malnourished. Malnutrition is so ubiquitous, and of such importance, that the majority of articles published from the ICDDR,B have addressed this problem in some manner. Those studies with nutrition as their main focus have addressed the following issues: 1) food intake and absorption during diarrhoea; 2) the effect of diarrhoea and other infections on growth; 3) breast-feeding patterns and the adequacy of breast-milk production in malnourished mothers; 4) the relationship between maternal nutritional status and fertility; and 5) diseases attributable to trace element deficiency, focusing primarily on vitamin A and zinc deficiencies.

A number of important findings have resulted from these studies. One is that patients with diarrhoea absorb most of the nutrients that they ingest. This finding has helped shape the policies advocating continued feeding during diarrhoea. A second is that dysentery appears to have a more profound impact on the growth of children than does watery diarrhoea. A third is that children who are malnourished tend to have more prolonged episodes of diarrhoea than do better nourished children. Lastly, a number of studies have documented the poor growth of children in Bangladesh, as well as their inadequate caloric and protein intake.

9. Laboratory Studies.

Laboratory-based investigations have focused on 6 main areas: 1) evaluation of newer, often simpler, diagnostic methods for detecting enteric pathogens, or toxin production by enteric pathogens; 2) virulence attributes of *V. cholerae*, *Shigella*, and other enteric pathogens; 3) defining epitopes of enteric pathogens that elicit an

immune response and therefore may be useful in vaccine development; 4) sero-epidemiologic studies; 5) epidemiologic studies using plasmid profiles, and correlations between plasmid profiles and resistance to antimicrobial agents; and 6) the development of animal models of enteric infection or disease complications.

The development of diagnostic tests has made use of reagents developed in laboratories in industrialised countries, and evaluated here at the ICDDR,B. The ICDDR,B is in the somewhat unique position of seeing more patients with the gamut of enteric pathogens than most any other institution in the world. Therefore, tests of the utility of newer diagnostic methods can be most efficiently (and effectively) carried out here. Tests evaluated in the early 1980s focused on identifying heat-labile or heat-stable toxins produced by *E. coli*. These tests included adrenal-cell, infant mouse and enzyme-linked immunosorbent assay (ELISA) systems for detection of these toxins in stools; evaluation of antisera and DNA colony hybridisation for identifying *E. coli* that produce toxin; and evaluation of the Biken immunoprecipitation test. The ELISA method has been extensively evaluated for the detection of other important pathogens, toxins, or biological substances, including Shiga toxin, *Giardia lamblia*, *Entamoeba histolytica*, and secretory and serum IgA. Tests that have been validated have then been used in sero-epidemiologic studies of rotavirus and other enteric viruses, *C. jejuni*, and *V. cholerae*.

Since the utility of these diagnostic tools could only be evaluated in areas where the disease they are intended to diagnose is endemic, the Centre, because of its large patient population, and adequate, if not state of the art laboratories and laboratory staff, was the ideal location to evaluate many of these tests.

Studies on virulence mechanisms have focused on the relationship between toxin production and clinical illness, or the production of other known or putative virulence factors, such as neuraminidase or haemolysin in clinical strains of enteric organisms. Identification of antigens evoking an immune response has focused on outer-membrane proteins and the lipopoly-saccharide of *V. cholerae* and *Shigella*.

Despite the availability of an excellent animal facility, there have been very few studies on animal models of disease. Published studies include one on a model of *C. jejuni* in infant chickens, a rabbit model for shigellosis, and another on an endotoxin-induced renal lesion in rabbits. The latter was an attempt to mimic the haemolytic-uraemic syndrome.

10. Family Planning and Population Studies.

There is general agreement that improvements in socioeconomic conditions (and therefore improvements in health) will require reductions in the rate of increase of the population. The Matlab Family Planning and Health Services Project is recognised as a model for the delivery of family planning services. Since the project was initiated in 1977, the prevalence of contraceptive users among women in the programme area has risen from 7% to over 45% in 1985. In a comparison area comprised of neighbouring villages, contraceptive usage was only 17% in 1985.

Research is an integral component of the programme, and has been used to critically examine a host of operational issues in family planning delivery. Critical determinants for improving contraceptive acceptance that have been identified in these studies include the nature of the relationship between family planning provider and family planning user; the availability of different types of contraceptives; and the importance of an effective management structure. Lessons learned from this operations research have been used to improve the quality of service delivered, with the resultant increase in contraceptive usage. These lessons have also been implemented in the Government of Bangladesh Family Planning Programme, via the mechanism of the Maternal-Child Health Family Planning Extension Programme. This programme works with the Government to implement changes in delivery that have been found effective in the Matlab programme.

Other research studies in the field of family planning have examined the relative effectiveness of different types of contraceptive devices, as well as complications associated with the use of contraceptives. Issues relating to fertility, including

family size, nutritional and socioeconomic status, and parental perceptions, have also been examined. Most of these studies have been carried out using data collected by the Demographic Surveillance System, which for the last 25 years has continuously recorded vital events for a population of \approx 200,000 persons living in Matlab.

11. Water and Sanitation Interventions.

The studies in the field of water and sanitation have mainly dealt with the health impact of water supply, sanitation, and hygiene education. Some of the findings have important policy implications.

The general theme of these studies has been to examine the relationship between personal hygiene practices and diarrhoea incidence. In studies conducted in rural areas and urban slums, hand-washing practices are the personal hygiene practice that correlate most closely with diarrhoea incidence rates - inadequate hand-washing results in higher rates. Bacterial counts on hands have been found to be a good marker for increased risk of infection. In a much-quoted study conducted in the Rayer Bazaar slum in Dhaka, the introduction of effective hand-washing practices was able to reduce the incidence of shigellosis. Studies in rural communities, where soap is often not available, have found that the scrubbing of hands with other agents, such as mud, is almost as effective as scrubbing with soap in removing faecal coliforms from hands.

Studies in the rural communities of Mirzapur and Teknaf of programmes integrating improved water supply and sanitation, and hygiene education have provided important information on methods to reduce the incidence of diarrhoea. Studies in both areas found a significant reduction in the incidence rate of diarrhoea in children who lived in communities where the integrated programme was implemented, in comparison to other communities without the intervention. Those living closest to hand-pumps had the lowest incidence of diarrhoea. This finding of the importance of accessibility, whether it be to a hand-pump or to other health interventions, such as an oral rehydration therapy distribution centre,

is a consistent one in many studies. Other determinants of hand-pump use, beside accessibility, were family size, number of young children in the household, and social status.

As part of the Mirzapur project, the feasibility of newer hand-pump models, such as the Tara hand-pump, has also been studied. These studies showed that the pump (and double-pit sanitary latrines) could be effectively maintained by villagers without special skills.

12. Vaccines Other Than Cholera Vaccine.

The cholera toxin B-subunit-killed whole cell vaccine has been the only vaccine tested at the ICDDR,B; publications on other vaccines are fewer in number. Tetanus and measles immunisations are the only vaccines other than cholera to receive much attention. The focus of these studies has been the impact of these vaccines (which are now routinely given as part of the maternal child health programme) on mortality. In two studies, children born to mothers who had received tetanus immunisation had a 35% lower mortality. Children who have received measles immunisation also had reduced mortality compared to children who did not receive the vaccine. This reduction in mortality persisted for at least five years after the immunisation was given.

13. Health Care Delivery.

Publications on health care delivery have covered a broad range of issues. A number of studies have documented indiscriminate use of antimicrobial agents and other drugs. Other studies have examined the type of health care-providers practising in rural communities. Although physicians are few in number, the per capita number of health care-providers is similar to what is found in industrialised countries. Several studies have examined the preference given to sons when health care is sought. A number of studies have examined innovative health care delivery systems, including the MCH-FP programme in Matlab (discussed in part in the section on family planning) and the urban community-based programme in Dhaka. Lastly, cost-effectiveness studies have been surprisingly few in number.

14. Field Methodologies.

A few publications have directly addressed the issue of how studies are conducted – namely how reliable is the data that we obtain? These studies have examined the problem of age misstatement for young children as it affects determination of nutritional status, the comparability of questionnaires and direct observations of sanitary practices, and reporting errors in diarrhoea recall surveys.

15. Odds and Ends.

There always has to be a few items that don't fit in anywhere else. The ICDDR,B has also conducted studies on enterovirus 70 conjunctivitis, the prevalence of residual paralysis from poliomyelitis (1 per 1,000 children), risk factors for death during the devastating coastal cyclone in 1985, and ethnic differences in the metabolism of digoxin.

CONCLUSION.

These 1,152 publications from the ICDDR,B during its first 12 years are undoubtedly the largest contribution that any institution has made to the research of diarrhoeal diseases and the related subjects of nutrition and fertility during this period. At least in numbers of publications, the Centre appears to have fulfilled its mandate to conduct research in these areas, research that is appropriate to these problems as they exist in developing countries. The quality, impact, and value for money of this research work is more difficult to judge. Perhaps the best way to form an informed opinion on the value and importance of the research that has been conducted at the ICDDR,B is to obtain for yourself publications of interest. All are available upon request from the library of the ICDDR,B.

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TABLE 1 -- ICDDR,B PUBLICATIONS, BY JOURNALS 1979-1990

Journal Title	No. of Publications	Journal Title	No. of Publications
1. Acta Paediatrica Scandinavica	3	18. Archives of Disease in Childhood	8
2. Advances in Experimental Medicine and Biology	1	19. Asian Medical Journal	5
3. Al-Faisal Medical Journal	1	20. Asia-Pacific Population Journal	3
4. American Journal of Clinical Nutrition	25	21. Australian Journal of Experimental Biology and Medical Science	1
5. American Journal of Diseases of Children	2	22. Baillieres Clinical Gastroenterology	1
6. American Journal of Epidemiology	12	23. Bangladesh Development Studies	1
7. American Journal of Medicine	1	24. Bangladesh Journal of Botany	3
8. American Journal of Physical Anthropology	1	25. Bangladesh Journal of Child Health	7
9. American Journal of Public Health	3	26. Bangladesh Journal of Fisheries	1
10. American Journal of Roentgenology	1	27. Bangladesh Journal of Microbiology	13
11. American Journal of Tropical Medicine and Hygiene	8	28. Bangladesh Journal of Nutrition	4
12. Annals of Human Biology	1	29. Bangladesh Journal of Zoology	2
13. Annals of Internal Medicine	1	30. Bangladesh Medical Journal	9
14. Annals of Tropical Medicine and Parasitology	1	31. Bangladesh Medical Research Council Bulletin	6
15. Annals of Tropical Paediatrics	2	32. Bangladesh Paediatrics	2
16. Antimicrobial Agents and Chemotherapy	9	33. Bangladesh Private Medical Practitioners Journal	2
17. Applied and Environmental Microbiology	10	34. Bangladesh Veterinary Journal	2
		35. Biken Journal	1
		36. British Journal of Experimental Pathology	1
		37. British Journal of Nutrition	2

38. British Medical Journal	17	61. Experientia	1
39. Bulletin of the Medical Library Association	1	62. Experimental Parasitology	1
40. Bulletin of the World Health Organization	19	63. Food and Nutrition Bulletin	8
41. Canadian Journal of Microbiology	3	64. Gastroenterology	10
42. Chemotherapy	1	65. Gut	5
43. Clinical Nephrology	1	66. Health Policy and Education	1
44. Clinical Therapeutics	1	67. Health Policy and Planning	4
45. Comprehensive Therapy	1	68. Human Biology	1
46. Contributions to Microbiology and Immunology	1	69. Human Nutrition and Clinical Nutrition	3
47. Current Topics in Microbiology and Immunology	1	70. Hygeia (Dhaka)	2
48. Demography	3	71. Indian Journal of Animal Sciences	1
49. Demography India	4	72. Indian Journal of Experimental Biology	1
50. Dhaka Shishu (Children's) Hospital Journal	2	73. Indian Journal of Medical Microbiology	3
51. Dhaka University Studies	1	74. Indian Journal of Medical Research	16
52. Diagnostica	1	75. Indian Journal of Pathology and Microbiology	1
53. Drugs	1	76. Indian Journal of Pediatrics	5
54. East African Medical Journal	1	77. Indian Pediatrics	4
55. Eastern Librarian	2	78. Infection	1
56. Ecology of Food and Nutrition	6	79. Infection and Immunity	17
57. Environmental Pollution	1	80. Information and Development	1
58. Epidemiology and Infection	6	81. International Family Planning Perspectives	2
59. European Journal of Clinical Microbiology and Infectious Diseases	1	82. International Journal of Epidemiology	19
60. European Journal of Clinical Nutrition	5	83. International Journal of Gynaecology and Obstetrics	6
		84. International Journal of Health Services	1

Achievements

85. International Journal of Pancreatology	1	106. Journal of Pediatric Gastroenterology and Nutrition	2
86. Japanese Journal of Tropical Medicine and Hygiene	2	107. Journal of Pediatrics	8
87. Journal of American Statistical Association	1	108. Journal of Preventive and Social Medicine	2
88. Journal of Antimicrobial Chemotherapy	1	109. Journal of Royal Statistical Society	1
89. Journal of Bacteriology	1	110. Journal of Social Studies (Dhaka)	2
90. Journal of Bangladesh Association of Women Scientists	2	111. Journal of Tropical Medicine and Hygiene	20
91. Journal of Bangladesh College of Physicians and Surgeons	1	112. Journal of Tropical Pediatrics	9
92. Journal of Biological Standardization	1	113. Journal of Virology	1
93. Journal of Biosocial Science	20	114. Lancet	22
94. Journal of Clinical Epidemiology	2	115. New England Journal of Medicine	3
95. Journal of Clinical and Laboratory Immunology	1	116. Management Development (Dhaka)	1
96. Journal of Clinical Microbiology	23	117. Media Asia	1
97. Journal of Diarrhoeal Diseases Research	36	118. Medical Laboratory Sciences	2
98. Journal of Disaster Study and Management	1	119. Microbial Ecology	1
99. Journal of Family Welfare	1	120. Microbiology and Immunology	1
100. Journal of Food Composition and Analysis	1	121. Nutrition Reports International	7
101. Journal of General Microbiology	2	122. Nutrition Research	4
102. Journal of Hospital Infection	1	123. Nutrition Reviews	1
103. Journal of Infectious Diseases	31	124. Pakistan Pediatric Journal	1
104. Journal of Medical Microbiology	4	125. Pathology	1
105. Journal of Microbiological Methods	1	126. Pediatric Infectious Disease Journal	4
		127. Pediatrics	4
		128. Population	2
		129. Population and Development Review	6

130. Population Studies	7	146. Social Biology	2
131. Post Graduate Doctor – Middle East	1	147. Social Science and Medicine	9
132. Progress in Allergy and Immunology	1	148. South Asian Anthropologist	1
133. Progress in Food and Nutrition Science	1	149. South Asian Bulletin	1
134. Progress in Water Technology	3	150. Southeast Asian Journal of Tropical Medicine and Public Health	3
135. Public Health	1	151. Studies in Family Planning	27
136. Queensland Nursing	2	152. Transactions of the Royal Society of Tropical Medicine and Hygiene	31
137. Reviews of Infectious Diseases	4	153. Tropical Doctor	4
138. Rural Demography (Dhaka)	4	154. Tropical and Geographical Medicine	19
139. Sankhya	2	155. Tropical Medicine and Parasitology	1
140. Saudi Medical Journal	1	156. Vaccine	6
141. Scandinavian Journal of Gastroenterology	2	157. Water Supply Management	1
142. Scandinavian Journal of Infectious Diseases	2	158. Zentralblatt Fur Bakteriologie, Mikrobiologie, und Hygiene	1
143. Sekitar Perpustakaan	1	159. Zentralblatt Bakteriologie International Journal of Medical Microbiology	1
144. Science	1		
145. Singapore Journal of Obstetrics and Gynaecology	1		
		Total	731

Fig. 1 – Number of original journal articles, by
type of journal, 1979 – 1990

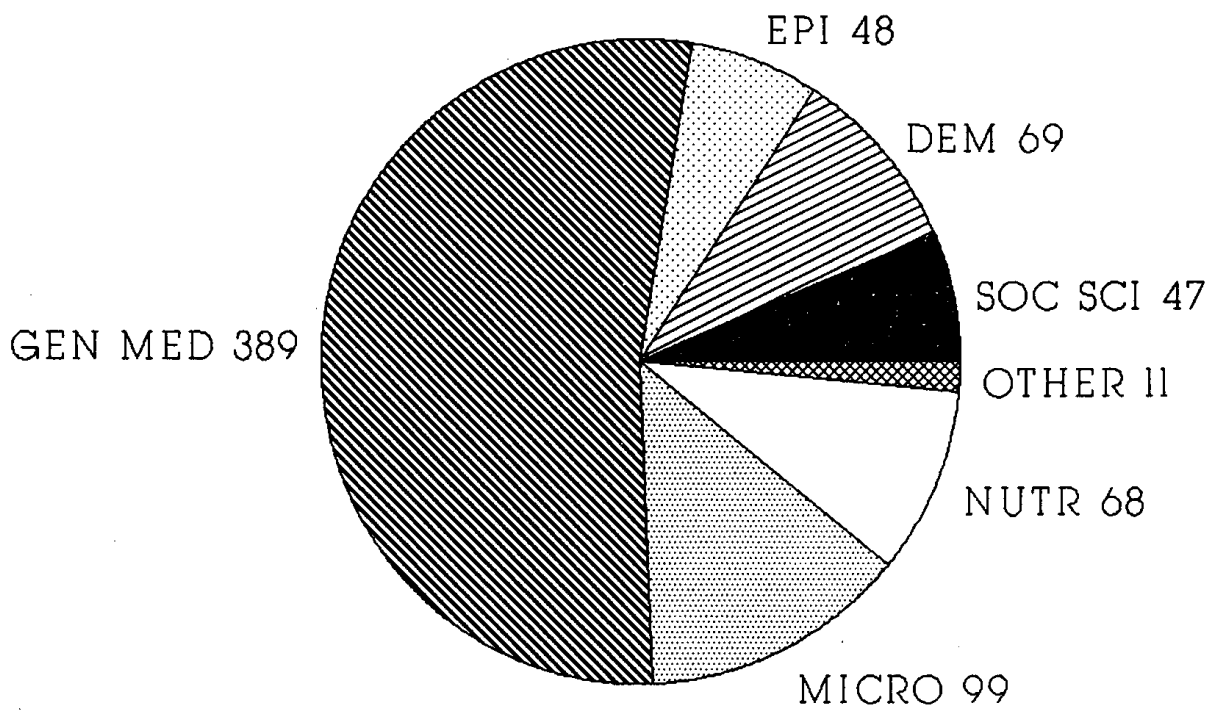


Fig. 2 – Number of original journal articles, by
geographic origin of journal, 1979 – 1990

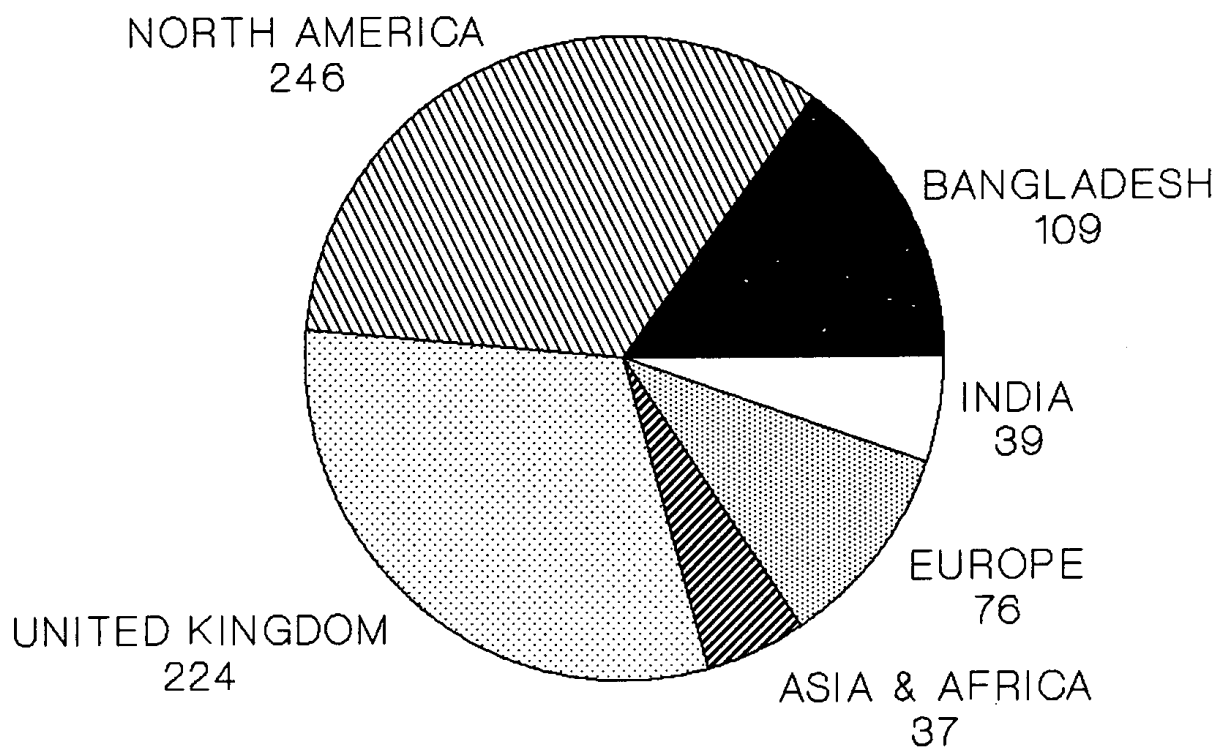
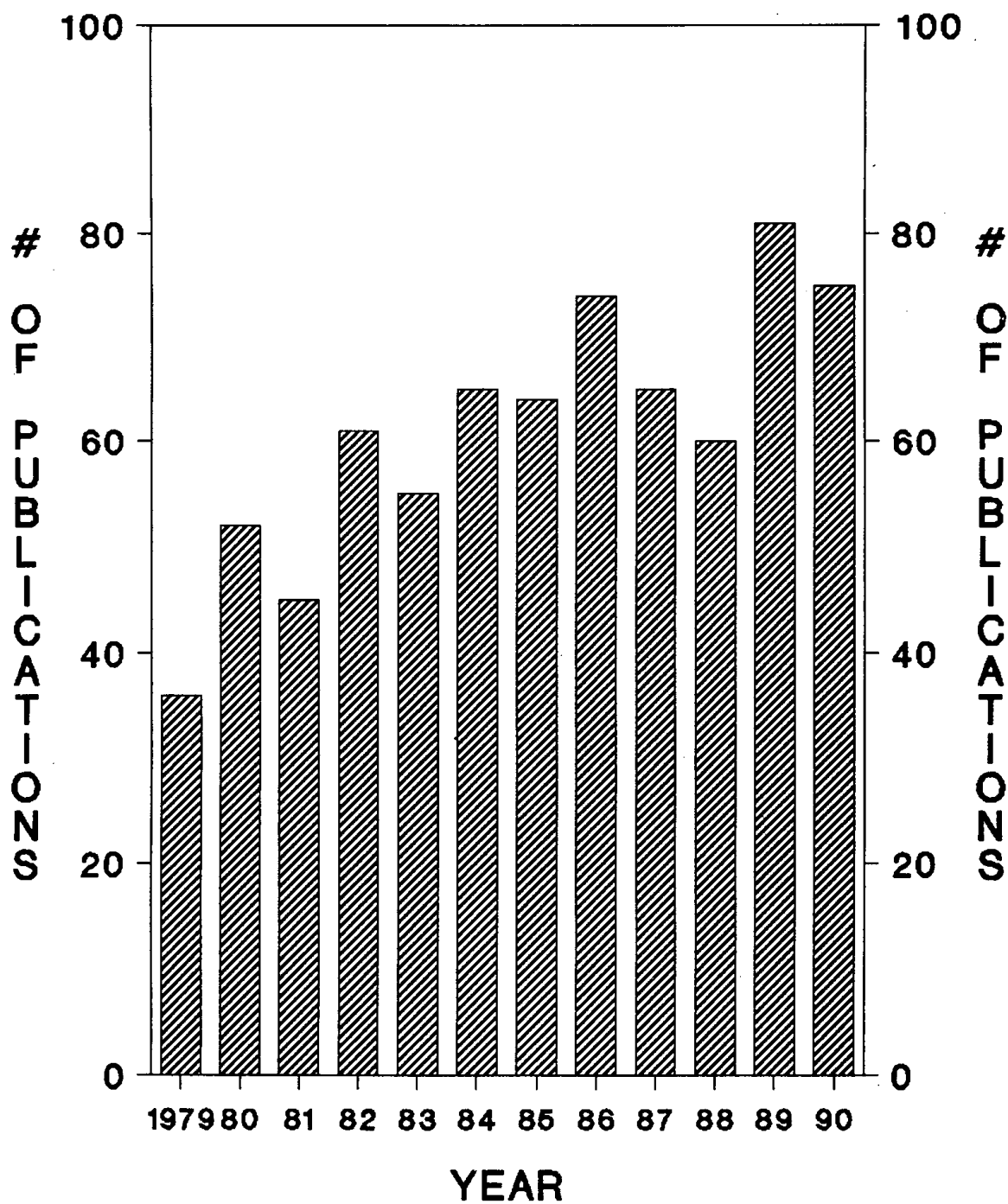


Fig. 3 – Number of original journal articles, by year of publication, 1979 – 1990



 ICDDR,B PUBLICATIONS, 1979 – 1990

A ORIGINAL ARTICLES, REVIEW ARTICLES, SHORT COMMUNICATIONS, AND BRIEF REPORTS IN SCIENTIFIC JOURNALS

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a	SAARC countries, except Bangladesh (Bhutan, India, Maldives, Nepal, Pakistan, Sri Lanka) and Myanmar (Burma)	US\$ 20.-
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c	Other countries	US\$ 30.-

* Price includes air mail postage cost.
