



Glimpse

international centre for
diarrhoeal disease research, bangladesh
NEWSLETTER

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ICDDR,B DURING 1980

There was increased momentum in the activities of ICDDR,B during 1980. This was particularly visible in new areas of effort such as the Training and Extension Programme and the Computer Branch. During this year ICDDR,B was recognised as a collaborating institution for diarrhoeal diseases by the World Health Organization and held the first inter-regional course on the clinical management of diarrhoea in collaboration with the Diarrhoeal Disease Control (CDD) Global Programme of WHO and the inter-regional programme of UNDP. An IBM Systems 34 computer was delivered, installed and became operational shortly after the middle of the year. It has been in increasingly active use ever since, not only by ICDDR,B scientists but by other users in the Dacca community. Besides new activities the research programmes have been productive publishing 51 original scientific papers, 11 reviews, and have manifested an active participation by 101 presentations, abstracts and letters to local, regional and international meetings and journals.

Community Services Research Programme

The Community Services Research Programme completed several important projects this year. A comparison of the standard WHO recommended oral rehydration solution with a simple solution made with salt-molasses (*loban-gur*) available in all villages in rural

Bangladesh in a population of 80,000 was completed. An analysis of deaths in relation to socio-economic status and education showed that the mortality rate is inversely related to socioeconomic status. However, the education of the mothers is a variable which correlates even more closely with decreased risk of childhood death irrespective of the socioeconomic status of a family. The findings of these analyses will provide a matrix from which specific hypotheses may be tested to determine how education or wealth may prevent childhood disease and death in rural Bangladesh. In addition the mortality figures were higher among females from shortly after birth through childbearing age, than males.

This year initial studies on measles were carried out in Matlab. The epidemic pattern was defined and a case control study demonstrated that measles predisposes to shigellosis and is related to a higher incidence of conjunctival dryness or putative vitamin A deficiency. This seems to link diarrhoea with measles, and measles with blindness due to vitamin A deficiency.

Studies on sex socialisation and philosophies of life in relation to fertility behaviours showed many misconceptions which influence fertility behaviour. These must be taken into account in developing fertility control programmes.

Basic studies were also carried

out to define the endocrinologic characteristics of women in Bangladesh. These indicate a marked departure from data on women in developed countries.

The second three-year period of a six-year intervention trial, first using fertility control methods alone and then adding health measures was completed. Although detailed analysis is in progress, it is apparent that the results of the second three-year cycle, where a better educated field worker was recruited to provide health measures with fertility control devices, show impressive effects on both fertility and mortality.

In addition to these studies there was an analysis of the data collection systems and plans were established to streamline the demographic surveillance system (DSS) to make it more applicable in settings where the intensive surveillance employed in Matlab may not be feasible. Studies in this direction will be carefully designed to ensure the high quality of data gathered.

A new Computer Branch was established with an IBM Systems 34 computer; a staff was hired and is in the training process. At present the computer has a disk storage capacity of 128 megabytes. It has a diskette magazine drive, a printer, three single station terminals and two dual station terminals. The IBM utilities installed include FORTRAN, COBOL, RPGII and BASIC compilers. Programme packages include UNEDIT, UNXTALY, MINITAB, MINI-LIFE and WHO

ADDRESS under installation. There has been a steady increase in the use of the computer by the scientists.

Nutrition Programme

The Nutrition Programme completed studies on food absorption in diarrhoea of various aetiologies showing that the invasive diarrhoeas, particularly rotavirus, have a marked and lasting effect on the absorption of protein and fat. Despite this, further studies showed that food intake can be maintained, albeit at a level 20 to 30 percent below normal, and that with this level of the absorptive capacity a child experiencing diarrhoea can maintain nutrition even during the acute phases. Compounding the problem of malabsorption and reduction of food intake, presumably due to anorexia, is the newly recognised protein loss in the stool of patients with *Shigella*, rotavirus and other toxigenic *E. coli* diseases. The importance of this finding is yet to be assessed on a quantitative basis. In addition, the study of distribution of food within families in rural Bangladesh showed that males received a higher proportion of available food.

The Teknaf Field Station has been the responsibility of the Nutrition Programme. The programme initiated an intervention study designed to assess the impact of a good water supply, water sealed latrines and health education on the nutritional and health status of the community as compared to communities not experiencing these inputs. Although this study is only in its early stages it is anticipated that should a beneficial effect occur on the rate of diarrhoea, improvement of the nutritional status of the children in the study areas will also be seen compared to children in areas without interventions.

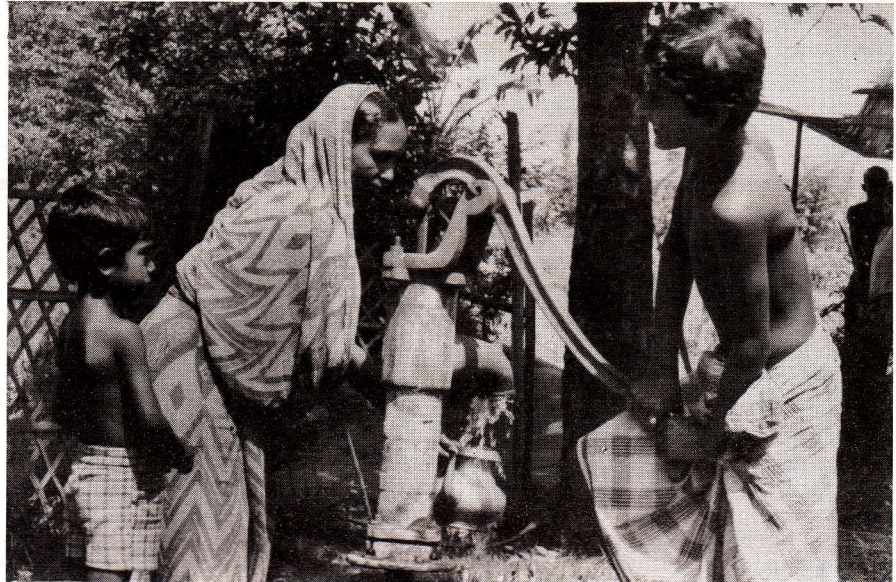
Disease Transmission Programme

The Disease Transmission Programme established that the simple intervention of hand washing with soap and water can sharply affect secondary transmission of shigellosis even in the worst of urban slum areas. New agents associated with diarrhoea were sought and, in the case of *Campylobacter*, found in surfeit. In this instance since *Campylobacter* could be isolated from more than one-third of all

children, often without diarrhoea, many questions are raised about these organisms; this must be investigated to make further advances in the epidemiology of diarrhoeal disease related to this important group of organisms. *Yersinia enterocolitica* was sought and not found in cases of abdominal pain, fever and diarrhoea. Findings on the epidemiology of multiple antibiotic resistant *V. cholerae* were

associated with more than one genotype and only about two-thirds of them were recognised with the ST probe used.

In a study of *V. cholerae* biotype El tor, the surprising result was found that in the Dacca urban area this variant of cholera equalled the infection rates, illness rates and severity of illness of the classical biotypes. This change indicated that in Bangladesh El tor is no



Interventions like tubewells and water sealed latrines were introduced to promote use of safe water and to prevent pollution of surface water. The impact of these interventions on the nutritional status would be measured.

reported but significant new epidemics did not occur during 1980. A close relationship between lack of latrine or piped water with the spread of *Shigella* in young children was found.

During 1980 a major technological breakthrough was validated in the laboratory. A chemical probe was employed with a radioactive label to specifically identify on culture plates colonies of *E. coli* which produce the diarrhoea-causing toxins (heat labile LT and/or heat stable ST). The DNA of the genes which code for the production of LT or ST were isolated and made single-stranded. An isotope ^{32}P was introduced to label these DNA "gene probes." Cultures from patients with diarrhoea were prepared on membrane filters. These were treated in such a way that when exposed to the labelled DNA LT and/or ST gene probe, colonies of toxin-producing *E. coli* could be easily recognised.

This procedure allows rapid identification of smaller numbers of toxigenic *E. coli* in the midst of other stool flora. All LT organisms may be recognised by this method; ST is

longer a milder and less virulent variant of *V. cholerae*. This change must be anticipated elsewhere as well.

Several phages were isolated from the environment from strains of *V. cholerae* and were investigated at Harvard University. These phages are unique in their characteristics and although not yet demonstrated to carry DNA from one bacteria to another, they have been of sufficient interest to justify extending the studies into 1981. The differences between the new cholera phage and phages isolated from all other bacteria to date are several unusual structural features and unique patterns of their DNA structure.

Host Defense Programme

The Host Defense Programme developed new methods to determine immunoglobulin type specific antibodies to cholera toxins, and *V. cholerae* lipopolysaccharides and to determine low concentrations of secretory IgA in body fluids. The development of these methods has made it possible to study the antigenicity of

newer experimental oral vaccines and to find ways of stimulating the local enteric immune system in humans.

Studies showed that measurement of antibody in saliva may reflect the production of local antibody further down in the intestinal tract. This is important since studies of local immunity in the gut have been handicapped for many years by lack of a good proxy measure of response to antigens.

Further work on the B subunit of cholera toxin was completed showing that local immune response can be elicited either by antigen provided orally or parenterally. This data was collected by the cumbersome method of having to lavage the intestinal tracts of subjects with large volumes of saline. During this process relationships between gut antibody and salivary antibody were studied. These seem to indicate a correlation between salivary IgA antibody against B subunit and IgA antibody measured in the intestinal lavage. Such a correlation was, however, not seen between the IgA responses in milk and intestine.

Important information was gathered on other surface antigens *V. cholerae* demonstrating differences in the endotoxin of this organism compared to those of other gram-negative organisms. A nontoxic protein from the outer cell membrane was isolated which may have promise as an immunising agent. In addition to these two antigens, investigations of colonising factors of both *V. cholerae* and *E. coli* were undertaken. The basic technology for their measurement was established and increasing attention will be given to bacterial antigens which are associated with attachment to and colonisation of the gut and invasion into its lining.

Pathogenesis and Therapy Programme

The Pathogenesis and Therapy Programme completed a full study which confirmed the effectiveness and defined the limitations of chlorpromazine in reducing fluid output during cholera, and initiated a study on salicylates. A case control study on the substitution of rich for glucose as the basis of an oral rehydration solution was completed which opens a pathway for the integration of the treatment of diarrhoea by oral rehydration with an increased caloric density to be presented to children, particularly



Though breast-feeding is almost universal in the rural areas, health workers are trying to educate mothers on the importance of breast-feeding during diarrhoea.

during acute diarrhoea. The next steps in this study will be to determine to what level the caloric density may be increased and still not have an increase in the stool volume.

A study on the usefulness of the specific receptor for cholera toxin GM1 ganglioside bound to charcoal showed a significant but small alteration in the severity of disease. This establishes the theoretical point that complete binding of toxin in the gut lumen reduces the severity of diarrhoea. It also establishes the fact that the principal site of release of cholera toxin is close to the gut lining, thus not accessible to agents which bind free toxins in the gut lumen.

Reviews of the incidence and characteristics of hypoglycaemia as a complication of diarrhoea were completed together with information on the incidence of hypernatraemia in diarrhoea patients seen at ICDDR,B.

In some basic studies in collaboration with Dr. Morishita, Keio University, Tokyo, Japan, it was determined at the Dacca Treatment Centre that there may be some mucosal damage in patients during cholera; in addition, a series of derangements of gut hormones was also defined.

Full reports were published on the effectiveness of oral rehydration in rotavirus patients and comparison of glucose- and sucrose-based solutions in children with cholera.

A comparison of accuracy and sensitivity of methods for recognising *E. histolytica* was reported.

This allows a choice of tests with knowledge of these sensitivities in hospital and field settings.

A higher death rate in diarrhoea due to invasive organisms such as *Shigella*, even with ORS therapy, has led to an increase in research emphasis on these more refractory diseases.

Training and Extension Branch

The Training and Extension Branch expanded its activities in 1980. ICDDR,B staff members studied in Bangladesh and abroad to bring new information and skills back to the Centre which in turn trained others through courses, seminars, lectures and training programmes. These were attended by national and international participants and led by people from Bangladesh and other countries. Collaborative research programmes have grown as well, with ICDDR,B researchers studying abroad, and international researchers studying at ICDDR,B. Several programmes were set up to facilitate this information exchange.

During 1980, three existing fellowships at ICDDR,B were extended: one in Microbiology and two in Nutrition. Two one-year fellowships were granted: one each in Clinical Epidemiology and Clinical Research. One Nutrition fellowship was completed and one Clinical Research fellowship was terminated.

Twenty-two post-doctoral trainees came to ICDDR,B from nine countries: six from India, four from Thailand, three from Egypt and Japan, two from Indonesia and one each from Philippines, Sudan, United States and Vietnam. The trainees attended 14 courses: eight on the management of diarrhoea including cases which occur in institutions and at home, two on cholera immunology and epidemiological trends, two on paediatrics, one on urban epidemiology and diagnostic procedures involving virology and viral diarrhoea, and one on social medicine, biostatistics and community health.

Pre-doctoral trainees numbered 18 and came from Sri Lanka (12), Maldives Islands (3), United States (2) and United Kingdom (1). Six training sessions were held: three on clinical, community and rural health diarrhoeal disease control programmes, one on socio-economic and cultural factors in transmission and contraction of diseases in Bangladesh, one on the

use of vital records in field studies, and one on epidemiology and microbiological aspects of different diarrhoeal diseases.

ICDDR,B's national training programme consisted of eight courses: four on management and control of diarrhoea; two on the aetiology, pathophysiology, treatment and epidemiology of diarrhoeal diseases; one on paediatric diarrhoea, elementary chemistry and oral therapy, pathophysiology of diarrhoeal diseases, *E. coli* diarrhoea and microbiological aspects of diarrhoeal diseases; and one orientation course for Female Village Workers (FVWs) from Matlab. Two hundred ninety-one people participated from six sources: FVWs from Matlab (110), Dacca Medical College students (90), FVWs from Comilla (59), staff from BRAC (14) and NIPSOM (12), and doctors from IPGM&R (6).

Two hundred paramedics from 12 organisations attended 17 courses on the treatment of cholera. Nineteen courses on cholera treatment were held to train 938 medical students from six medical colleges.

The ICDDR,B staff development programme sent 18 staff members to several countries for various programmes for one-month to four-years duration. Nine of these staff members were funded by ICDDR,B grants, four received funds from the British Council, and five benefitted from scholarships or fellowships from other sources. Five trainees went to the United Kingdom, four to Thailand, three each to Australia and the United States, and one each to Belgium, Denmark and Yugoslavia.

Twenty-nine ICDDR,B staff members attended courses at six Bangladeshi institutions in accounting, anthropology, computer programming, housekeeping, inventory control, office management, personnel management, plumbing and air conditioning, and secretarial science.

A study completed in Chandpur indicated that a training programme for village practitioners with family members/mothers using pamphlets, posters, and measuring spoons, achieved highly satis-

factory results in a community-based diarrhoea management programme. Use of locally available ORS ingredients, independent of an outside supply system is useful. Extension activities are now focusing on further work with the village practitioners in conjunction with the Government *Palli Chikit-*



A net-work of speed boats and motor vehicles provide valuable services for the transfer of serious patients from the remote areas to the treatment centre in Matlab.

shak programme with a commitment to implement some of the most effective interventions from Matlab studies in four of the Government-served areas of Bangladesh.

Finance

As a result of new commitments, ICDDR,B's FY 1980 budget was \$4.11 million, which was approximately 15 percent larger than that of 1979. A large number of donors are contributing various amounts to the budget. In order to meet their different reporting requirements, the Board of Trustees approved changing the Center's fiscal year from July-June to January-December, beginning January 1981. The accounts of the first 18 months, July 1979-June 1980 and July-December 1980 have been closed and audited.

The budget for FY 1981 is \$6.1

million of which approximately \$4.5 million has thus far been committed. The Centre's Five Year Programme budget from 1981 to 1985 is \$44 million, which includes both a continuing inflation rate and a real increase in the Centre's activities. ICDDR,B has also undertaken a Capital Development programme to relieve the acute shortage of space and enable it to move into its own building. The Government of Bangladesh has recently donated four acres of land for the new facilities. The programme will be taken up in two phases; the first phase of construction includes the ground floor of the main building and facilities at the two field stations. Estimated cost for completion of the first phase is approximately \$2 million, of which \$80,000 has thus far been made available by the OPEC Fund and the Government of Saudi Arabia. Phase two will include completion of the final six storeys of the main building at Dacca, and the completion of buildings at the two field stations. The total cost of the second phase will be roughly \$10 million.

Board of Trustees

The Board of Trustees met twice in 1980 in February and December. They established a fully operational set of guidelines on which effective scientific, administrative and financial management can be performed. The Search Committee for a new Director completed its task when Dr. Greenough agreed to serve a three-year term beginning in June of 1980. The Board ranked all scientific and senior management staff and appointed 12 to the international level in both science and management, most of whom are from developing countries. It also formed a Selection Sub-committee for evaluating and recommending future candidates for international-level positions.

The first Consultative Group meeting of donors and interested countries and agencies was sponsored by UNDP and held during its governing Council in June in Geneva. Due to the success of the first Consultative Group meeting, the Board decided to hold a second meeting in New York in 1981 during the UNDP Governing Council.

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