



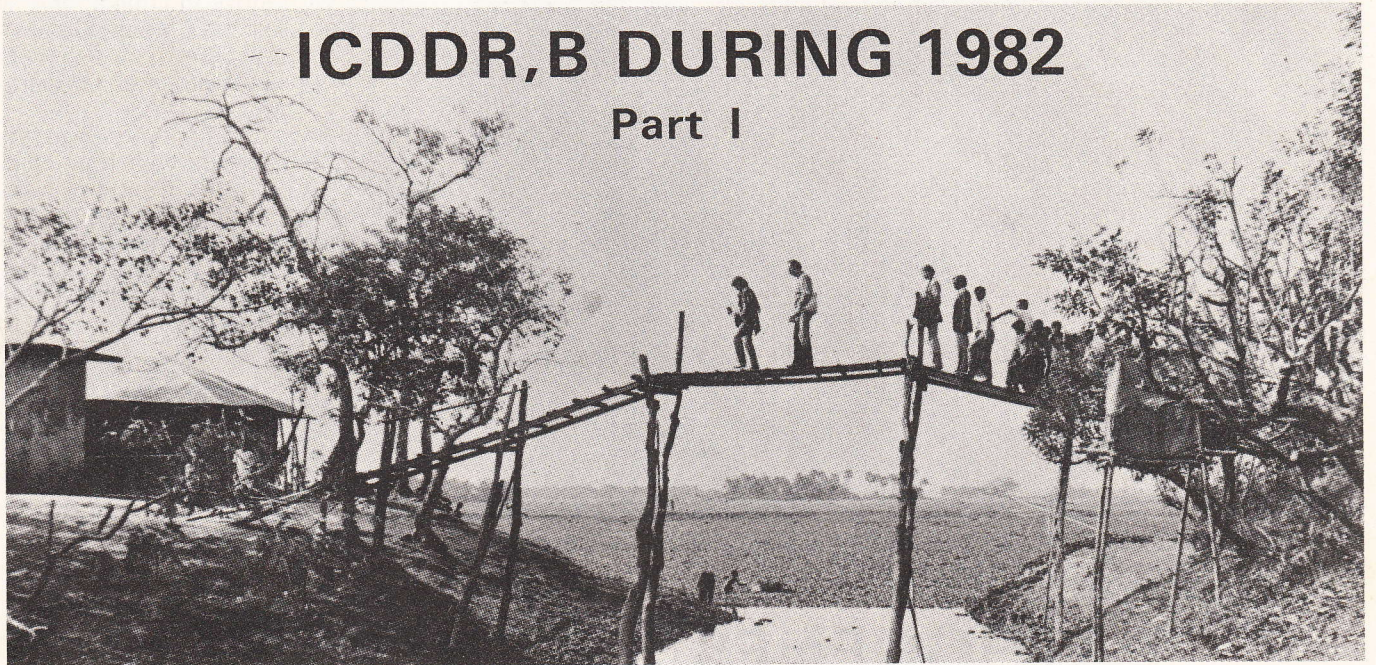
Glimpse

international centre for
diarrhoeal disease research, bangladesh
NEWSLETTER

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ICDDR,B DURING 1982

Part I



TAKING RESEARCH AND TREATMENT to where the problems are most prevalent, the ICDDR,B maintains four sub-centres strategically located throughout its 25 square-mile Matlab Demographic Surveillance Area. This bridge crossing leading to a sub-centre exemplifies the realities that help perpetuate the spread of diarrhoeal diseases: a latrine empties into water used for bathing, drinking etc.

Building on a growing body of knowledge and past successes, ICDDR,B researchers in 1982 significantly broadened the world's scientific understanding of diarrhoeal disease realities—in a series of discoveries and insights that already are influencing the diagnosis, treatment and prevention of diarrhoeal diseases, and have set the stage for future Centre research.

Maintaining the rigorous standards and hard work that have placed the Centre at the forefront of diarrhoeal disease research, the ICDDR,B's five research working groups made several important and/or intriguing findings in 1982. These are detailed on the following pages.

Among other things, such findings dictate the quality of research articles that can be offered for publication in refereed scientific journals worldwide. And, while numbers do not attest to quality and are only one index of productivity, the Centre is happy to report a steady improvement in successful presentation of its scientists' work. Thus, in 1982, 60 articles, editorials and related papers were published in refereed journals, and 16 book chapters and conference papers came out, compared to 42 and 22 in 1981.

Moreover, the Centre improved its internal publication process, targeting on significant work, and up-grading its reports to the level of

full publications. Also, in a major innovation supported by IDRC of Canada, the Centre established DISC (the International Diarrhoeal Disease Information Service and Documentation Centre), and began publishing a unique quarterly diarrhoeal diseases journal (see Training, Extension and Communications).

At the same time, research founded on sound technology resulted from physical improvements in our facilities and equipment, improvements that, in turn, will enhance our research efforts in 1983 and beyond.

The new North Wing of our hospital was completed; and, on November 29th, patients were

moved from the temporary tin shed to a modern, proper treatment facility. This event occurred exactly 20 years to the day from the time the first patient was admitted to the old Cholera Research Laboratory. The space vacated will allow expansion of the library, publication and computer facilities; and will provide breathing space for other overcrowded activities.

Philosophically speaking, the ICDDR,B believes that the reason it has made useful contributions to its research field, is that the Centre's most important priority has been to make certain that all work strives for the highest quality, while addressing critical issues. This

often is difficult in the setting of epidemic illness in a developing country; but, at the same time, the opportunities for discovery are far greater.

Beyond this, the single most important influence on what we choose to study relates to whether the answers will help solve the diarrhoeal disease and related problems that plague the people of our host country. For not only do we have a special commitment to Bangladesh, but the critical health issues we face here and many of the solutions we can provide, are directly applicable throughout the developing world.

Recognizing this point, the Centre in 1982 initiated its first major international outreach effort, by getting involved in major projects in other developing countries. First, an ICDDR,B team spent two months in Aceh, Indonesia, helping government health workers establish a system for identifying and controlling cholera epidemics. Second, the Centre and the Kingdom of Saudi Arabia finalized a technical collaboration agreement, whereby the ICDDR,B is helping establish a centre for clinical, laboratory and field activities aimed at diagnosing and treating diarrhoeal diseases. Finally, cooperating with Kenya, an ICDDR,B team compared rotavirus types existing there with those in Dhaka; and, at the request of the Chinese Government, another team visited there to define possible areas of cooperation.

Finally, turning its eyes to the future as it enters year four of its five-year plan, the Centre is carefully examining the findings and suggestions of a 7-member External Scientific Review Committee, that performed in 1982 the first of what will be bi-annual critiques of the Centre; and the subsequent suggestions of the ICDDR,B Board of Trustees, which conducted its own in-depth review, using the External Reviewers' comments. Their valuable recommendations provide a platform for formulation of a new five-year Plan.



PRECISE, PATIENT, highly skilled microscopy lies at the heart of ICDDR,B research efforts.

PATHOGENESIS & THERAPY

The principal concern of the Pathogenesis and Therapy Working Group (PTWG) is to gain knowledge about the mechanisms of diarrhoea; and to use this knowledge to prevent and treat diarrhoea.

The emphasis during 1982 was on the invasive diarrhoeal diseases: shigellosis, amebiasis and other forms of dysentery.

Pathogenesis

Autopsy Studies

In an autopsy study of 50 diarrhoeal disease victims, the PTWG researchers found that *Shigella* and *E. histolytica* were the most

common pathogens related to the fatalities, followed by *Campylobacter* and *V. cholerae*. Moreover, *Yersinia intermedia*, so far not known to cause diarrhoea, was detected for the first time in diarrhoea-related fatalities. Other *Yersinia* has been known to be invasive, and to burrow into or through the intestinal wall, reaching the lymph nodes and hence the bloodstream, where it causes severe abdominal pain and fever, mimicking appendicitis. In the two cases from which *Yersinia* was isolated, one had fatal pneumonia, the other fatal sepsis. This raises the question, "What connection is there between *Yersinia* and other killer diseases?"

It was also found that most of the diarrhoea-related fatalities were

complicated by non-intestinal diseases—pneumonia, septicemia, hypoglycemia, Rye's syndrome, and necrotic enteritis following circulatory failure. In previous autopsy studies of victims of *Shigella* and some other invasive diarrhoeas, the researchers had found severe lung and liver damage. It is possible, the scientists say, that a severe invasive diarrhoea infection predisposes patients to pneumonia—or the other way around.

Parenteral Diarrhoea

Because for as many as one-third of diarrhoeas no pathogen can be discerned in the stool, PTWG scientists speculate that, while a majority of such cases are caused by intestinal agents, parenteral

diarrhoea may be the culprit in some cases where another major disease is present.

Moreover, a related disease mechanism may be involved in some serious diarrhoea cases where a pathogen has been found—which relates to the research noted above.

disease, almost one-third of typhoid victims do suffer from a type of diarrhoea somewhere in-between invasive and non-invasive. Their stool has some blood and mucous, and it is watery. Experience in many developing countries shows that, especially in childhood typhoid, diarrhoea can be dangerous. This work is continuing.

Antisecretory Drugs

Having shown in 1979 that chlorpromazine is an anti-secretory agent for cholera, ICDDR,B researchers began testing in 1982 three similar drugs. Nicotinic acid, a B vitamin, was found to be useful in reducing fluid loss. However, those drugs so far tested showed



DIARRHOEAL DISEASE MECHANISMS must be understood before successful vaccines and other treatments can be developed. Animal tests are crucial; and the ICDDR,B's Animal Laboratory has been cited as one of the world's finest.

Shigellosis

In the first major study of colonic dysfunction in shigellosis, PTWG scientists, using fiberoptic endoscopes donated by the Japanese Government, found that the extent and severity of colonic ulceration depends on the duration of shigellosis. By studying the colon's functions with dyes and by sampling colonic fluids, the researchers hope to improve shigellosis treatment.

In related work, PTWG scientists studied the often fatal shigellosis complication "hemolytic-uremic syndrome." Seeking to learn what host factors contribute to development of the disease, the scientists produced the kidney syndrome in rabbits infected with a *Shigella* bacteria extract. This work is continuing.

Typhoid Connection

While typhoid has not been widely considered a diarrhoeal

Therapy

Improved ORS

A new ORS, made with rice instead of sugar, was developed and field-tested in 1982. The results show that the rice-based ORS not only replaces body fluids efficiently, but also reduces vomiting, thereby requiring less fluid replacement. Moreover, it helps maintain and even improve nutrition (for more about the rice-ORS, see the Nutrition Working Group).

During 1983, research will focus on the possibility of further improving ORS by using citrates to replace bicarbonates. Citrates are alkaline and more readily available in developing countries; and also may be more stable than bicarbonates when placed in ORS packets.

significant side-effects, including drowsiness or flushing of the skin. This research is continuing.

The Hospital

The case fatality rate at the ICDDR,B's Dhaka Treatment Centre dropped to 0.44 percent from 0.51 percent in 1981. The number of patients also declined, from 78,822 in 1981 to 73,924 in 1982, most likely reflecting wider community use of ORS—partly due to the Centre's Urban Volunteers Programme (see separate listing for this programme).

A new Dietary Care Unit started functioning during 1982, providing intensive feeding regimens: frequent feeding of milk and diets rich in protein and calories to undernourished children coming to the hospital.

An Intensive Care Unit, equipped with resuscitative equipment, was set up in the hospital.

DISEASE TRANSMISSION

Much more needs to be learned about known diarrhoea-causing pathogens. Moreover, the organism causing disease in roughly one-fifth of diarrhoea cases cannot be identified. Disease Transmission Working Group (DTWG) scientists are seeking to understand how diarrhoeal disease is transmitted, and how the disease agents interact with human hosts and the environment in which they survive and thrive; and to find the best ways of combatting diarrhoeal disease pathogens.

Causes

For the first time it was found in 1982 that a bacterium, *Vibrio mimicus*, is responsible for causing diarrhoea in Bangladesh. Moreover, *Aeromonas hydrophilia* and *Plesiomonas shigelloides*, two known groups of bacteria, were found to be responsible for about two percent of the country's previously undiagnosed diarrhoea cases.

In another study, DT scientists in 1982 isolated *Campylobacter* from 14 percent of the patients coming to the ICDDR,B's treatment centres and seven percent of healthy people examined. To learn why *Campylobacter* produces disease in some people but not in others, infant chicks were challenged with the bacteria. Eighty-one percent of the chicks receiving *Campylobacter* from diarrhoea patients developed the disease; while a negligible percent of chicks receiving the bacteria

from healthy carriers developed the symptoms. A high rise in antibodies to *Campylobacter* was seen in recovered diarrhoea victims, but not in healthy carriers.

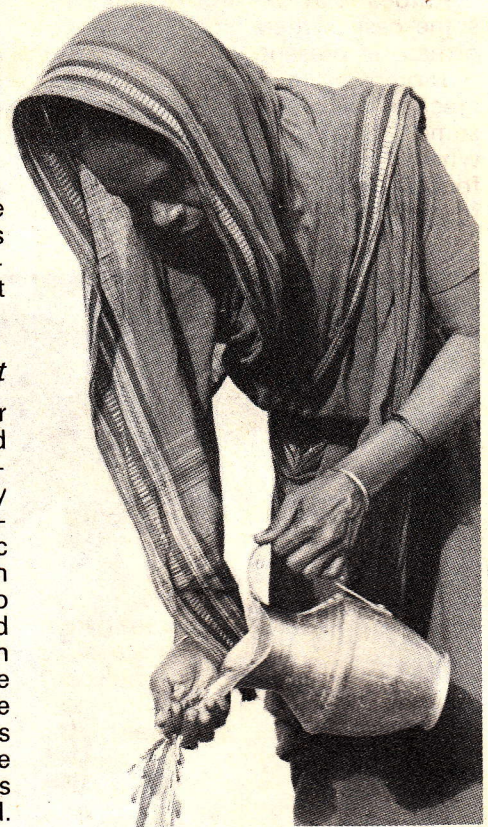
Disease, Host and Environment

Nearly 10 years after an El Tor cholera strain had totally replaced classical *V. cholerae* in Bangladesh, the classical strain suddenly resurfaced with a vengeance, during a large 1982 cholera epidemic in Bangladesh. While elsewhere in the past El Tor was known to replace classical, the reverse had never occurred. And though both cholera strains are dangerous, the newly-emergent classical type causes more severe illness. For this and other reasons, the unique occurrence raises vital questions about how and why it happened. Of utmost interest is whether classical bacteria have changed, acquiring new, crucial biological characteristics that give it advantages over the El Tor variety that once pushed it into oblivion.

ICDDR,B scientists, who detected the phenomenon, are examining its implications.

Disease Intervention

The Centre's scientists will continue to collaborate through 1983 with Harvard University researchers, to develop an effective live, oral cholera vaccine, using a non-toxic cholera strain. The researchers are testing phage-altered live strains that result in the immuniz-



DIARRHOEAL DISEASES ARE spread by failure to wash hands after "answering nature's call," before eating or handling food, etc.

ing, non-toxic cholera toxin "B-subunit."

Seeking to prevent or minimize the spread of cholera among family contacts of cholera index patients, the researchers, in preliminary findings, showed that :

- People with blood group O are at increased risk of getting cholera;
- The risk of contracting cholera is unrelated to malnutrition;
- Breast-fed babies are protected against contracting the disease, but not against becoming carriers, due to colonization.

In another study, *Vibrio parahaemolyticus* was found to be present in a certain combination of water temperature and amount of salt, dissolved oxygen and aquatic plants. This collaborative study with the University of Maryland may have important implications in understanding the survival of *V. cholerae* in the environment.

In a third study, ICDDR,B researchers found that the use of latrines did not reduce incidences of diarrhoea. The conclusion: much broader hygienic measures are necessary, including education about personal hygiene, etc.



HYGIENE EDUCATION, conducted by Centre field workers, is a crucial factor in the campaign against diarrhoeal diseases.

preceded by diarrhoea. The investigators found 548 per 100,000 people either blind or going blind, due to vitamin A deficiency. About 90 percent of those with severe eye disease apparently had suffered from diarrhoea during the early stages of their eye problems. In a trial feeding of vitamin A, the researchers found that after ingesting an oral dose of vitamin A, people showed significantly higher levels of vitamin A in the blood, even during the acute and recovery stages of diarrhoea.

Studies now are underway to attempt to fortify ORS with vitamin A, in order to prevent eye damage due to vitamin A deficiency.

In a study with significant implication for health planners, nutrition scientists found that nutritional rehabilitation is vital for malnourished children suffering from diarrhoea. After following up 551 three-month-to-three-year-old children for one year after they had been hospitalized with diarrhoea, the researchers found that the first three months were very crucial. For 90 percent of the deaths among these children occurred during the first three months after they left the treatment centre.

Nutrition Education

Aiming to improve young children's diets by effectively educating mothers, NWG scientists began

a research-cum-action program. The goal is to learn what cultural factors limit the food intake of 5-24-month-old children; and then to devise effective nutrition messages to counter these factors in the study community.

Teknaf

The ICDDR,B maintains a nine-year-old research-cum-diarrhoeal-treatment centre in Teknaf, at the southeastern tip of Bangladesh. Initially funded by UNICEF, this facility, run by the NWG, is now partly funded by the IDRC of Canada.

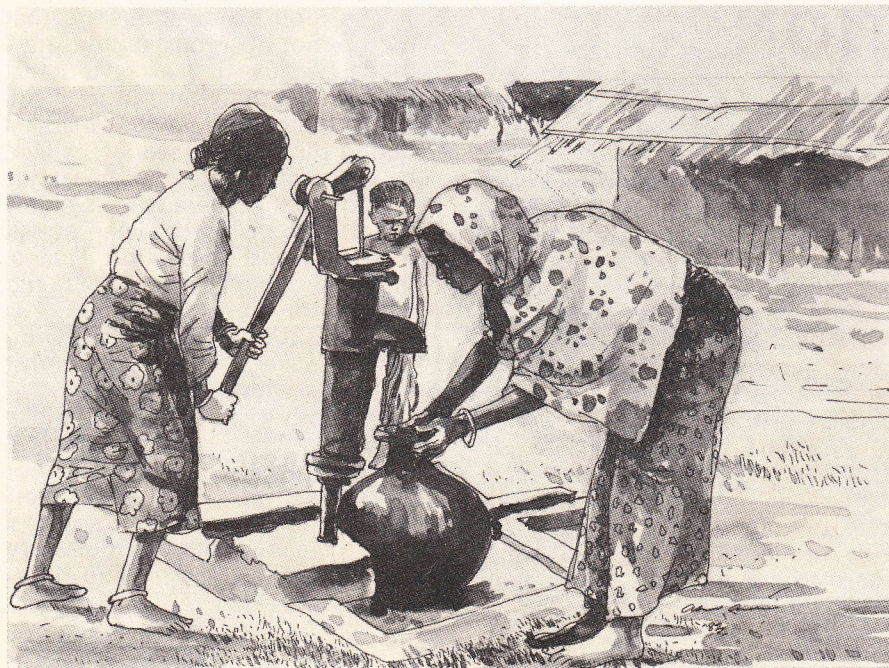
Teknaf was adopted by the ICDDR,B as one of its field-research areas, after a widespread epidemic of a virulent and often drug-resistant dysentery. Even today, dysentery is a major problem in the area, as opposed to cholera, the diarrhoeal disease frequently seen in Matlab, the ICDDR,B's other field-research area.

The birth and infant mortality rates in Teknaf are among the highest in Bangladesh, and the population consists of very conservative Muslims.

The ICDDR,B believes there is potential to improve the health of Teknaf residents—by monitoring disease and death rates; providing diarrhoea diagnosis and treatment;



USING RICE OR ANY CEREAL to replace the sugar in ORS not only reduces stool output, but also provides more calories—a crucial combination for rehydrating and rehabilitating malnourished, diarrhoea-stricken children, such as this one.



CAN CHILDREN'S NUTRITIONAL AND DISEASE status be improved by providing clean tubewell water and education about sanitation and health? This question is under study at the Centre's Teknaf field station.

introducing education about nutrition, water use and hygiene; providing some sanitation facilities; and encouraging family planning.

To implement these aims, the researchers are using invaluable data collected for nine years, and are studying the effects of tubewells and latrines.

Continuing their studies in 1982, trained Community Health Workers (CHWs) every week or two visited each household in a 50,000 population area. They collect demographic information, as well as data on the prevalence of diarrhoea and other infectious diseases.

Moreover, two clinics, at Teknaf and an out-station, provide free treatment for diarrhoea; and, backed by a small microbiology laboratory, diagnose diarrhoea causes.

COMMUNITY SERVICES RESEARCH

The backbone of the Community Services Research Working Group (CSRWG) is the Demographic Surveillance System (DSS)—a unique demographic resource in Asia, and the most comprehensive developing country profile of its kind. The goals of the CSRWG are:

- To do basic research on the bio-social determinants of health, disease and fertility.
- To improve the health of big populations, by instituting large-scale community projects.

The DSS

Starting with a small-scale DSS in 1963 (23 villages with a total population of 28,000), the DSS eventually expanded so that, by the 1982 census, it encompassed about 149 villages, with 180,000 people, located near Matlab district, about 45 miles southeast of Dhaka.

The system combines periodic censuses with continuous registration of such "vital events" as births, deaths, marriages, divorces, and migrations. In view of its data base, unique in developing countries, the Matlab DSS has been selected by the UN Population Division and the WHO Global Epidemiological Surveillance and Health Situation Assessment Section as one of five areas in the world where extensive mortality studies will be done.

The Matlab Experiment

The Matlab research area is divided into two equal population areas for treatment and control. In the treatment area, community health workers (CHWs) dispense a wide range of family planning devices, provide primary maternal and child care, as well as contraceptive follow-up, and distribute ORS for diarrhoea victims.

In both areas, extensive and intensive collection of vital registration data is continually done. A 50-bed hospital operates at the Matlab Bazaar, which also serves as headquarters for the research area. The Matlab hospital, which treats the diarrhoeal disease problems of treatment, control and adjoining areas, mainly is designed

to monitor the incidences and pinpoint the causes of diverse diarrhoeal diseases.

Treatment Area

At the heart of the treatment area lies the hospital, staffed by five full-time doctors, five nurses and a few aides.

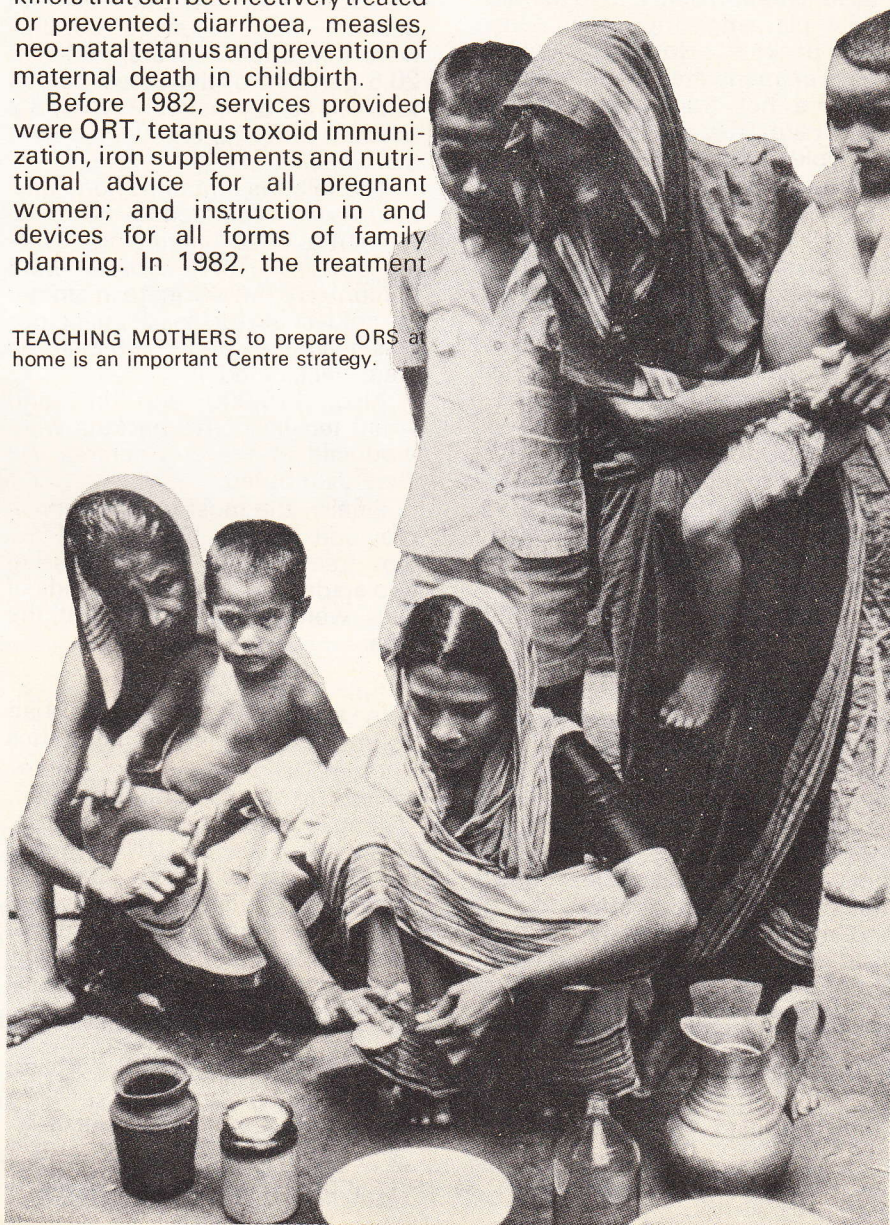
In addition to its main mission, the hospital also provides a Maternal-Child Health/Family Planning Program. The purpose is to concentrate on the major child killers that can be effectively treated or prevented: diarrhoea, measles, neo-natal tetanus and prevention of maternal death in childbirth.

Before 1982, services provided were ORT, tetanus toxoid immunization, iron supplements and nutritional advice for all pregnant women; and instruction in and devices for all forms of family planning. In 1982, the treatment

area was subdivided in two, to test the effectiveness of expanded treatment. In one half there was added tetanus immunization for all women of reproductive age; measles immunization for under-five children; high risk pregnancy screening; distribution of safe birth kits; and training of traditional midwives to enhance their skills.

Also important is the fact that within the treatment area there are four sub-centres, which provide basic health care treatment and family planning help to all comers. A government accredited woman

TEACHING MOTHERS to prepare ORS at home is an important Centre strategy.



paramedic, with 18 months training, runs each sub-centre. Attendance is good. Thus, from March to December 1982, the four sub-centres treated a total of 1,363 children under five, as well as 243 pregnant or lactating women. Moreover, 2,026 women came for contraceptive-related reasons.

Working under the paramedic at each centre are about 20 women community health workers (CHWs) who are constantly trained and re-trained until they have a repertoire of health and family planning activities.

Comparison Area

Thirty CHWs, who have at least an 8th grade education, each visit 500 households weekly. While their main duties are to collect vital registration data and to handle family planning, they also carry ORT packets. However, unlike their treatment area counterparts, they are not trained in primary health care. They can refer seriously ill people to the Matlab hospital.

Other Activities

The DSS data were upgraded and computerized in 1982. A socio-economic survey was completed in the DSS area of the important health-related variables—such as use of water and latrines; educational levels; housing types; and number of possessions, including land. Using previous similar surveys of the same large groups of people, efforts now are being made to determine how diverse changes—including health intervention efforts—have affected illnesses and deaths over time.

In another effort, CSRWG researchers began an in-depth study of variations by area in contraceptive practices, as well as beliefs and practices related to the care and feeding of pregnant women and newborn babies. Using field workers, not questionnaires, the study aims to assess what socio-economic and other factors affect health and mortality. Ultimately, the researchers would like to learn what factors work for and against a

community's willingness to accept MCH/FP components.

On another front, the researchers pinpointed some of the Matlab treatment area successes. Clearly seen was a significant drop in newborn and infant deaths after 1978; as well as lower birth and death rates for the Matlab area as a whole. Thus, the crude birth rate per 1,000 declined over 15 years from 47 to just below 40 (being 35.3 and 43.8 for treatment and comparison areas, respectively). The corresponding death rates for 1981 were 11.9 and 14.4, compared to 12.1 and 15.6 in 1979.

Matlab Treatment / Research Centre

During 1982, the treatment centre at Matlab treated 11,054 patients, 34 percent from within the DSS area, and the rest from outside. Routine stool cultures were done on all DSS-area patients: 26.5 per cent of the cases yielded *V. cholerae*, 5.1 per cent NAG, 8.2 per cent *Shigella*, and 0.4 per cent *Salmonella*.

The tetanus immunization campaign was expanded to cover all women of child-bearing age. During the year, 7,092 women were immunized. An effort to maintain the cold-chain for measles vaccines was geared up, and 5,765 children were vaccinated in 1982.

Also, 170,000 one-litre, and 4,940 ten-litre ORS packets were produced at the sub-centres. All were distributed.

Finally, the most crucial service provided by the Centre in 1982 was treatment of cholera during two epidemics, when thousands of lives were saved throughout the area.

ERRATUM

In an article entitled "Urban Volunteers: Helping Communities Combat Diarrhoea by Themselves," in the March/April 1983, "Glimpse," an inadvertent error was made. The ICDDR,B should have been described as "the only *international* institution devoted solely to finding the causes, preventives, treatments and cures for a host of diarrheal diseases..."

Community-Based Treatment Centres

In a related effort to improve community health care, the Matlab Centre helped two communities establish small, community-run diarrhoea treatment centres, and continued to support and assist another one begun in 1980. Such centres are an ICDDR,B goal, since experience shows that it's more effective to have simple, easy access treatment centres dispersed over a large area, than a sophisticated hospital in a single place.

One of the new centres, at a place called Kalir Bazaar about 20 km north of Matlab station, was opened in June 1982. Locally administered and run by six community volunteers, the centre treated 1,285 diarrhoea patients in its first six months; and, during a fall cholera outbreak, saved hundreds of lives.

Finally, in another health-related effort, the ICDDR,B, responding to a Bangladesh Government request, prepared to extend part of the MCH/FP program so successful at Matlab to two other areas of Bangladesh.

Other CSRWG Activities

The CSRWG also runs two scientific support branches: Data Management and Computer Information. During 1982, the computer facilities expanded, and the IBM System 34 now is being used round-the-clock. On-the-job assistance and staff development was provided by the U.N. Statistical Office and the University of Namur, Belgium. Important software, including statistical packages, was installed, and others were developed for future use.

The ICDDR,B's Computer Branch also helps many Bangladeshi agencies develop their computer capacities.

Part I, on the ICDDR,B's scientific activities, ends here. Part II, which accompanies this for our readers' convenience, highlights the Centre's other activities.

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