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The second meeting of the Consultative Group for ICDDR,B was held in New York

CONSULTATIVE GROUP MEETS

The second meeting of the Consultative Group for the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) was held in New York in June 1981. This meeting was sponsored by UNDP, New York and was chaired by Mr. William T. Mashler, Senior Director, Division for Global and Inter-Regional Projects, UNDP. The progress report, future programme and financial requirements of ICDDR,B were presented at this meeting.

Australia, Bangladesh, Belgium, Canada, Egypt, Federal Republic of Germany, India, Indonesia, Japan, Switzerland, USA, UNDP, UNFPA, World Bank, World Health Organization, Ford Foundation, INCAP and Rockefeller Foundation participated in the meeting and showed keen interest in the activities of the Centre and extended full support.

SCIENTIFIC ACTIVITIES REVIEWED

A three member External Review Committee consisting of Dr. Orjan Ouchterloney,[1] Dr. Alexander Muller[2] and Dr. Dilip Mahalanabis[3] examined in detail the research activities of the Centre and submitted its report to the Board of Trustees at its IVth meeting.

The Committee felt that the activities are directed towards the goals and aims set forth for the Centre and was satisfied with the output. However, the Committee felt that there was a potential danger of spreading the efforts too thin and recommended a sharper focus in selected areas of interest.

The Committee emphasized the need to have more studies on water ecology, and more emphasis should be placed on sociological and anthropological studies. It was recommended that the general equipment in the Microbiology Department be upgraded. More collaborative work with microbiologists from other countries was suggested. The surveillance work carried out in Matlab and Teknaf in

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PRIORITY AREAS FOR RESEARCH IN SHIGELLOSIS :
Recommendations of an international conference

Shigellosis has been and still remains a significant cause of morbidity and mortality in developing countries, particularly in preschool children. From published data and those presented at the Conference held in Cox's Bazar, Bangladesh between June 15-19, 1981 under the auspices of the ICDDR,B, it was clear that a high proportion of preschool children who die between the ages 2-4 years have a history of dysenteric illness. In most developed countries of the world, there had been several consistent changes in the epidemiologic characteristics of shigellosis which were also accompanied by a great reduction of its endemicity.

These include :

* Disappearance of both endemic and epidemic strains of *S. dysenteriae* type 1
* Progressive reduction of *S. flexneri* cases
* Progressive increase of *S. sonnei* cases
* Reduction of mortality associated with dysentery

Though serious illness can result from infection with any *Shigella* strain, the most serious cases of shigellosis result from infection with *S. dysenteriae* type 1, often in epidemics (at present mainly prevalent) in the developing countries.

Aetiologic confirmation of (the species and serotypes of) *Shigella* is difficult even in laboratories with good facilities. Therefore the importance of shigellosis as a cause of morbidity and mortality is not often realized in areas where it is a serious public health problem. For example a serious epidemic of shigellosis in 1969-1971 caused by a multiresistant strain of *S. dysenteriae* type 1 affecting five countries in Central America was initially thought to be due to *E. histolytica,* a parasitic illness, almost never seen as epidemic.

Epidemiology and Microbiology

* Several hypotheses advanced to explain the changes in the epidemiology of *Shigella* observed in developed countries should be tested in developing countries so that these changes may result from designed control efforts. These should include studies of duration of excretion, duration of viability in the environments, including food and water, determination of vehicles of transmission, secondary infection rates and disease to infection ratios, new reinfection rates and disease to infection ratios. With these data in hand rational use of intervention measures including vaccines, can be planned.

* Better media should be developed for the enrichment, isolation and transportation (storage) of *Shigella* organisms present in faeces and environmental samples. A selective enrichment medium that can be used to detect small numbers of *Shigella* organisms in contaminated enrichments is of first priority. Media and isolation procedures that can be readily adapted for use in laboratories in field situations should be given priority.

* Surveillance centres should be established in strategic geographic locations throughout the less-developed world to identify, quantitate and determine the antibiotic sensitivity of *Shigella* organisms and the global data compared.

* Dysentery like symptoms not caused by *Shigella* require microbiological investigation. The role of *Campylobacter* in causing dysentery like illness requires further clinical studies.

Pathophysiology

* The mechanism of invasion of the epithelial cells by *Shigella* is not yet fully understood. There are simple models to study this problem in cell culture which may be effectively investigated now; however, new systems must also be devised for future investigations in the gastrointestinal tract itself.

* The nature of the glycocalyx (glycoprotein coating of cell) and the way in which the organism penetrates it to reach the brush border is yet to be established. This is a difficult problem and depends on prior work of biochemists on purification and characterization of material from the glycocalyx.

* The role of specific surface or secreted factors responsible for invasion are not known. Are these plasmid controlled ? Sophisticated genetic techniques should be applied to characterize organisms in various *in vitro* and *in vivo* models.

* How many toxins do the *Shigellas* produce ? Are these the same in non-Shiga species ? There are some evidences that one toxin may possess neurotoxic, enterotoxic and cytotoxic properties. Is this due to the same portion of the molecule ? Is the mechanism of these effects in different cell systems the same and dependent on the attributes of the cell, or are there different biochemical processes involved ? Studies to answer these questions should be undertaken.

* Is there a small bowel phase in human shigellosis ? Is there colonization and invasion of jejunum and production of toxin(s) by *Shigellas ?* Clinical investigations to answer these questions including intubation, perfusion and biopsy techniques are both feasible and safe. The necessary laboratory methodology to suggest these investigations are available or in developmental stages.

* The possibility of the presence of a toxin receptor on the jejunal brush border membrane and the colonic cells need to be investigated. Such studies can be anticipated in the future when *in vitro* and *in vivo* experimental models have been further explored.

* The effect of experimental antisecretory drugs such as chlorpromazine, indomethacin, aspirin etc. on the watery diarrhoea phase of shigellosis deserves evaluation.

* The role of toxin(s) in the pathogenesis of the complications of shigellosis such as the leukaemoid reaction, haemolytic-uraemic-syndrome or convulsions needs to be studied and their possible presence in the leukocytes, kidney or in the CNS should be looked into. Immunological studies with purified reagents (e.g. monoclonal antibodies) can be planned for future. Biological specimens (e.g. CSF) can also be obtained when clinically appropriate and for future evaluation.

* Existing knowledge on nutritional status and effect on dietary intake of chronic shigellosis (symptomatic and asymptomatic) in small children is inadequate.

* Existing knowledge on the relationship of chronic shigellosis to changes in gut flora, absorption, protein-losing enteropathy, nutrient diversion, tissue destruction and catabolism is not enough.

* Protein-losing enteropathy in "asymptomatic carriers" should be investigated further to determine their role in stunting growth and wastage of nutrients, particularly in children.

Complications and Management

* The search for new and effective antibiotics against shigellosis should be continued along with a programme for the prevention of their abuse.

The role of appropriate antibiotics in mild and moderately severe cases and on development of the carrier state require further studies. Factors responsible for early emergence of antibiotic resistance in shigellosis require identification.

* In haemolytic-uraemic-syndrome (HUS) caused by shigellosis the following studies are needed to reduce mortality in hospitalized cases :

Role of severe colitis and endotoxaemia in the initiation of HUS.

- Role of prostacycline in the aetiology and management of HUS.
- Effects of early infusion of fresh or frozen plasma or fresh blood in preventing the onset or shortening the course of HUS.

* Early introduction of food in severe shigellosis with colitis is thought to be responsible for causing toxic megacolon and needs investigation.

* The effect of malnutrition on susceptibility to infection and continuation of the carrier state require further studies.

* The possibility of exclusive breast feeding in conferring immunity to shigellosis should be studied.

* The extent and duration of protein-loss in shigellosis of varying serotype and severity requires investigation.

* Pathogenesis of convulsion in children with shigellosis requires investigation.

* Hospital data (autopsy) combined with those collected through community surveillance ("verbal autopsy") should provide valuable information in determining the factors responsible for death due to shigellosis, so that appropriate measures could be taken to reduce loss of lives.

Immunology, Vaccine Development and Intervention Measures

* Immediate steps should be taken to encourage studies directed towards development of vaccine(s) against shigellosis. The streptomycin-dependent *Shigella* vaccines despite their draw-backs had shown demonstrable efficacy. Based on these earlier observations, development of new vaccines against shigellosis utilizing recent technology like the attenuated *Salmonella typhi* vaccine should be taken up immediately.

* Early safety and immunogenicity tests of the potential candidate vaccine(s) should perhaps be carried out in healthy adult volunteers in the developed countries followed by field studies in adults and children in endemic areas.

* Once an effective vaccine is developed immunization of high-risk individuals with oral attenuated *Shigella* directed against the prevalent serotype(s) should receive priority.

* Little is known on the role of local and cellular immunity in malnourished children with shigellosis.

* No knowledge is available on *Shigella* susceptibility of pre-term infants as compared to infants of full-term, small for gestational age and term adequate for gestational age.

* Anthropological studies should be undertaken to specifically identify habits and practices responsible for transmission of *Shigella* organisms within and between the families in the developing countries.

* To reduce (interpersonal) transmission of *Shigella* simple, practical, culturally acceptable intervention measures must be designed to modify personal behaviours and cultural practices. The efficacy, practicability and compatibility of the behavioural modifications should be evaluated within the specific cultural context.

* Identifying simple, practical, culturally-acceptable practices which if dutifully undertaken will result in decreased acquisition and diminished transmission of *Shigella* e.g. washing hand with soap or a suitable substitute.

* There is need for more knowledge on the mechanisms of transmission in regard to maternal technology and environmental factors particularly among the rural and urban poor of the developing countries.

* Evaluation is needed to determine the role of improved hygiene technology in the home and treatment of cases for limiting the carrier state.

SCIENTIFIC ACTIVITIES

(Continued from page 1)

the opinion of the Committee members were of very high quality, however, the Committee recommended research directed at reducing the cost of surveillance, e.g. to simplify the monitoring systems in order to provide it as a model for other developing countries. The Committee recognized the tremendous amount of successful improvisation by the Centre to function within the limited resources but felt it was time to seek the resources needed to decrease the pressure for improvisation in certain areas. The Committee also commented on the excellent Animal Research facilities available at the Centre which was also serving the needs of the host country.

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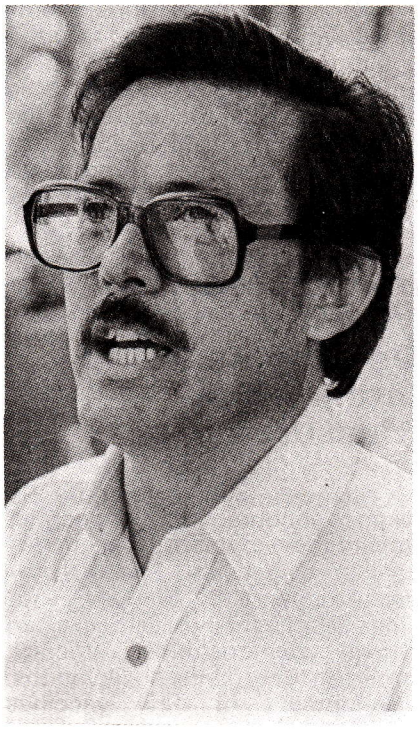
TRUSTEE BOARD MEMBER HONOURED

Dr. Leonardo J Mata, member of the Board of Trustees, ICDDR,B was awarded the UNESCO Science Prize 1980 jointly with a group of four scientists from Ireland. UNESCO Science Prize is awarded every year for outstanding contribution to scientific and technological development in developing countries. Dr. Mata received the prize for his malnutrition infection studies in Central America, first in Guatemala from 1962-1974, later in Costa Rica. The study conducted in the village of Santa Maria Cauque (Guatemala) prospectively studied children and mothers for ten years. Throughout the study a socially fruitful and close relationship was maintained between the workers of the Research Project and the indigenous population.

The findings of the study on foetal growth, child birth, neonatal infection, infant survival, child nutrition, growth and development are applicable to other regions of Latin America and elsewhere with similar ecosystems. It was found that in this village there was a high incidence of foetal growth retardation which diminished the chances of survival and effective performance. Despite earlier doubts the study helped to establish that infection and infectious diseases cause malnutrition. This finding on the role of infection on malnutrition (especially diarrhoea) has influenced health policy in many countries, emphasizing the need for preventing diarrhoea and other communicable diseases of the child hood as the logical path to avoid nutrient wastage and deterioration of the nutritional conditions. Once this is achieved the Cauque study found that children could do with much less food than what was recommended by international organizations. This has enormous implications given todays shortage of food throughout the world.



Dr Leonardo J Mata

An important revelation of the Cauque study was that health components have an educational and social component that must be taken into account if solutions are to be provided. The logical approach should be holistic since it would encompass and attack many variables. The implementation of a single measure may result more often than not in alteration in other variables, with negative effect on nutrition, health or social well-being.

The Cauque study recommends that the holistic approach to public health should begin with pregnant mothers, and give highest priority to children.

The more recent study (also a long term one) started in Puriscal, a large rural area in Costa Rica. This study of mothers and children contrast with the Cauque study, it is an intervention in itself. It is conducted by a team of Costa Ricans primarily by coordinating efforts with the Ministry of Health and with Social Security system and starts from an already improved health situation. The study capitalizes on the findings in Cauque.

In Puriscal, the population is in transition from a traditional to a modern way of life-with decline in breast-feeding and marked alteration in natural childbirth (promoted by medical profession in the last decade). To counter these, an aggressive intervention in the hospital where most of the Puriscal infants are born, resulted in a marked reversion towards breast-feeding in the last two years, the infant mortality rate came down to an incredible 5 per 1,000 (even less than many European countries). Nutrition and growth have been adequate in 95% of the infants born during the period of study.

Dr. Mata in his speech accepting the award said that his personal experience from the study taught him that "Imagination was needed to apply sophisticated knowledge to village situation, also needed were perseverance and endurance on the part of the researcher especially in the field and a deep growing humanity among all involved.....psycho-socio-anthropological determinants could be more important than other factors in determining disease, and the obvious paramount importance of maternal technologies in conditioning the health and survival of infants and young children, are two major avenues for further exploration of the aspects originally identified in the studies."

TRUSTEE BOARD MEETS IN DACCA

The 4th meeting of the Board of Trustees was held in Dacca from 11-12th June, 1981. Professor M.A. Matin, at present Minister for Health and Population Control, Government of the People's Republic of Bangladesh and a member of the Board of Trustees, has been unanimously elected as the new Chairman for a period of one year.

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