

PAHO ACME 18/6 (6)

GASTROENTERITIS WORKSHOP

16-19 October, 1978

PAHO/WHO
Caribbean Epidemiology Centre
Port of Spain
TRINIDAD

TABLE OF CONTENTS

	<u>PAGE</u>
Introduction	1
1. List of Participants	2
2. Agenda	4
3. Abstracts from Presentations - Session 1 - 16 October	7
3.1 Overview of Gastroenteritis Surveillance In the Caribbean - Dr. Peter Diggory, CAREC	7
3.2 Discussion of 3.1	7
3.3 Current Studies in Trinidad and Tobago, Guyana, and St Vincent - Ms Barbara Hull, CAREC	7
3.4 Discussion of 3.3	9
3.5 Diarrheal Disease Research at The University of the West Indies, Jamaica - Prof. P.S.E.G. Harland, UWI	9
3.6 Discussion of 3.5	10
3.7 The Caribbean Food and Nutrition Institute (CFNI) and Diarrheal Disease Research - Dr M Gueri, CFNI	10
3.8 Natural History of Rotavirus Infections in a Guatemalan Rural Community - Dr J J Urrutia, INCAP	11
3.9 The Institute of Nutrition for Central America and Panama (INCAP) and Diarrheal Disease Research - Dr R Schneider, INCAP	12
3.10 Discussion of 3.9	13
3.11 Diarrheal Disease Research Activities in Argentina - Dr J Barrera-Oro, Instituto Nacional de Argentina	13
3.12 Discussion of 3.11	15
3.13 Diarrheal Disease Research in Costa Rica and Modern Views on Diarrheal Disease and Its Relation to Nutrition - Dr L Mata, University of Costa Rica	15
3.14 Discussion of 3.13	16

Cont'd.....

	<u>Page</u>
4. Abstracts from Presentations - Session 2 - 17 October	17
4.1 Etiology of Acute Pediatric Diarrhea in Mexico City - Dr. Onofre Munoz, Instituto Mexicano del Seguro Social	17
4.2 Infantile Diarrhea Research Activities in Venezuela - Dr. J Flores, University of Venezuela	17
4.3 Discussion of 4.1 and 4.2	18
4.4 Serological Studies and Needs - Dr L Spence, University of Toronto	19
4.5 Discussion of 4.4	20
4.6 Oral Redhydration Studies and Needs - Dr M Levine, University of Maryland	20
4.7 Discussion of 4.6	21
4.8 WHO Activities and Interest - Dr D Barua, WHO Geneva	22
4.9 International Development Research Centre Activities and Interest - Dr J Garcia, IDRC	22
4.10 Discussion of 4.9	23
5. Outline of Planned Activities	24
5.1 Argentina - Dr J Barrera-Oro	24
5.2 Costa Rica - Dr L Mata	24
5.3 Guatemala - Dr J Urrutia	24
5.4 Mexico - Dr O Munoz	25
5.5 Venezuela - Dr J Flores	25
5.6 Caribbean Epidemiology Centre - Ms B. Hull	26
5.7 Caribbean Food and Nutrition Institute - Dr M Gueri	26
5.8 Institute of Nutrition for Central America and Panama - Dr R Schneider	27
5.9 University of Maryland, Centre for Vaccine Development - Dr M Levine	27

6.	Reports from Working Groups	29
6.1	Identified Needs Etiology/Epidemiology	29
6.2	Identified Needs Clinical	30
6.3	Identified Priorities Research	30
7.	General Recommendations of the Workshop	31
7.1	Application of Current Knowledge to Disease Diarrheal Disease	31
7.2	Uses of Oral Therapy	32
7.3	Coordination of Research Efforts	32

INTRODUCTION

The Gastroenteritis Workshop held at the PAHO/WHO Caribbean Epidemiology Centre in Port of Spain, Trinidad, was intended to bring researchers together from the Caribbean and the Americas. Six major objectives had been agreed on prior to the Workshop:-

1. To promote the exchange of information on gastroenteritis studies in the area;
2. To examine problems encountered in conducting studies in the areas of methodology, statistical models, laboratory work, field follow-up, and overall analysis;
3. To discuss solutions to these problems;
4. To exchange views on surveillance activities;
5. To discuss future research activities;
6. To decide on a time for a follow-up meeting in 1979.

Abstracts from the individual presentations and recommendations of the Workshop suggest that these objectives have been met.

The Canadian International Development Research Centre (IDRC) provided support for this Workshop as part of a grant to gastroenteritis research in Trinidad and Tobago. The support of international agencies is essential for the continued research into gastroenteritis and the participants would like to thank the IDRC for its interest in this Workshop.

PARTICIPANTS

<u>NAME</u>	<u>ADDRESS</u>
ALEXIS, Sunney	Nutrition Laboratory, Ministry of Health, Wrightson Road, P.O.S. <u>TRINIDAD</u>
BARUA, Dhiman	World Health Organisation, Geneva, <u>SWITZERLAND</u>
BARRERA ORO, Julio G	National Institute of Microbiology Av. Velez Sarsfield 563 Buenos Aires, Argentina, <u>S.A.</u>
BRATT, David	U.W.I. Office, ECMS, Port of Spain General Hospital, P.O.S., <u>TRINIDAD</u>
CHIN, Walter	Georgetown Hospital, Ministry of Health, Georgetown, <u>GUYANA</u>
DYER, Alma E.M.	Ministry of Health & Environmental Control, 10 Caledonia Ave, Kingston 6 <u>JAMAICA</u>
FLORES, Jorge	Instituto Nacional de Dermatologia, U.C.V., Apartado 4043, Caracas 101 <u>VENEZUELA</u>
GARCIA, Silva Jorge	Health Division, International Development Research Centre, 60 Queen St., Ottawa, <u>CANADA</u>
GUERI, Miguel	PAHO/WHO (CFNI), U.W.I. St. Augustine <u>TRINIDAD</u>
HARLAND, Philip	U.W.I., Mona, Kingston, <u>JAMAICA</u>
KINTANAR, Carmelita	General Hospital, <u>ST. VINCENT</u>
LEVINE, Myron	Centre for Vaccine Development, University of Maryland School of Medicine, 29 S. Greene St., Baltimore, Maryland, <u>U.S.A.</u>
MATA, Leonardo	Universidad de Costa Rica, San Pedro <u>COSTA RICA</u>
MOHAMMED, Isahak	General Hospital, San Fernando <u>TRINIDAD</u>
MUNOZ, Hernandez Onofre	Hospital de Pediatria, Instituto Mexicano del Seguro Social, Av. Cuauhtemoc, 330, <u>MEXICO 7.</u>

<u>NAME</u>	<u>ADDRESS</u>
RAMSEY, Frank	U.W.I. National Nutrition Centre, Bridgetown, <u>BARBADOS</u> .
RUST, James H.	Pan American Health Organisation, 525 23rd St., N.W., Washington, 20037, <u>U.S.A.</u>
SPENCE, Leslie	University of Toronto, Toronto General Hospital, 101 College St. Toronto, Ontario, <u>CANADA</u> .
SINHA, Dinesh	Caribbean Food & Nutrition Institute, Kingston, <u>JAMAICA</u> .
URRUTIA, Juan	Institute of Nutrition of Central America and Panama (INCAP), Carretera Roosevelt, Zone 11, <u>GUATEMALA</u> .
WEBB, June	Ministry of Health, Port of Spain General Hospital, P.O.S., <u>TRINIDAD</u> .
BASSETT, David	CAREC, Lab. Service
CHU FOON, Jocelyn	CAREC, Course Secretary
COX, Ross	CAREC, Training
DIGGORY, Peter	CAREC, Epidemiologist
HAMILTON, Patrick	CAREC, Director
HULL, Barbara	CAREC, Virology
LAMBOURNE, Adrian	CAREC, Statistician
QUAMINA, E.	Trinidad & Tobago
QUAMINA, D.	" "
CAMERON, R.	" "
CARRS, A.	" "
MAYNARD, B.	" "
RAHROOP, B.C.	" "
SHITH, D.	" "

GASTROENTERITIS WORKSHOP

16-19 October, 1978

PAHO/WHO CARIBBEAN EPIDEMIOLOGY CENTRE
PORT OF SPAIN, TRINIDADAGENDAMONDAY 16 OCTOBERChairman - Dr P Hamilton
Rapporteur - Dr D Bratt

- | | | |
|------------|--|--|
| 8.30 a.m. | Registration | |
| 9.00 a.m. | Welcome | Dr Elizabeth Quamina,
Chief Medical Officer,
Trinidad and Tobago.

Dr Barry Whalley,
PAHO Country Representative

Dr Patrick Hamilton,
Director, CAREC |
| 9.30 a.m. | Overview of Gastroenteritis
Surveillance in the Caribbean | Dr P Diggory
CAREC |
| 10.00 a.m. | COFFEE BREAK | |
| 10.30 a.m. | General Introduction | Dr J Rust
PAHO/WHO Washington |
| 10.40 a.m. | Current Studies in Trinidad and
Tobago, Guyana, and St Vincent | Ms Barbara Hull
CAREC Virologist |
| 11.30 a.m. | Diarrheal Disease Research at the
University of the West Indies,
Jamaica | Dr P S E G Harland
UWI, Jamaica |
| 12.00 | LUNCH | |
| 1.00 p.m. | Chairman - Prof L Spence
Rapporteur - Dr F Ramsey | |
| | The Caribbean Food and Nutrition
Institute and Diarrheal Disease
Research | Dr M Gueri
CFNI |
| 1.30 p.m. | Natural History of Rotavirus
Infection | Dr J Urrutia
INCAP |
| 2.00 p.m. | The Institute of Nutrition for
Central America and Panama and
Diarrheal Disease Research | Dr R Schneider
INCAP |
| 2.30 p.m. | COFFEE BREAK | |

MONDAY 16 OCTOBER cont'd ...

3.00 p.m.	Diarrheal Disease Research Activities in Argentina	Dr J Barrera-Oro Instituto Nacional de Microbiologia
3.30 p.m.	Diarrhoeal Disease Research Activities in Costa Rica	Dr Leonardo Mata
4.00 p.m.	General Discussion	
5.00 p.m.	CLOSE OF SESSION	
6.00 p.m.	Reception for Participants	Director CAREC and Mrs P J S Hamilton Flat 1 CAREC

TUESDAY 17 OCTOBER

Chairman - Dr L Mata
Rapporteur - Dr J Flores

8.30 a.m.	Diarrheal Disease Research in Mexico	Dr O Munoz - Instituto Mexicano del Seguro Social
9.00 a.m.	Diarrheal Disease Research in Venezuela	Dr J Flores - University of Venezuela
9.30 a.m.	Discussion	
10.00 a.m.	COFFEE BREAK	
10.30 a.m.	Serological Studies and Needs	Dr L Spence, IDRC
10.45 a.m.	Discussion	
11.00 a.m.	Oral Rehydration Studies and Needs	Dr M Levine University of Maryland
11.15 a.m.	Discussion	
11.30 a.m.	IDRC Activities and Interest	Dr J Garcia, IDRC
11.45 a.m.	WHO Activities and Interest	Dr D Barua/Dr J Rust
12.00	LUNCH	
1.00 p.m.	Work Groups: (1) Epidemiology/Aetiology (2) Clerical (Coffee available during sessions)	
5.00 p.m.	CLOSE	

OVERVIEW OF GASTROENTERITIS SURVEILLANCE IN THE CARIBBEAN
- Dr P Diggory, CAREC

The PAHO/WHO Caribbean Epidemiology Centre was established in January 1975 and early attention was given to the development of national and Caribbean surveillance for gastroenteritis and other important diseases. The third issue of the CAREC Surveillance Report (May 1975) contained the epidemiological implications of the "Strategy and Plan of Action for Combating Gastroenteritis and Malnutrition" which had been prepared by a Caribbean technical group and co-ordinated by the Caribbean Food Food and Nutrition Institute in 1974.

Each Government supporting CAREC had been requested to nominate a physician as a designated epidemiologist with whom CAREC could have a direct working relationship. These national epidemiologists first met as a group in May 1975 at CAREC and included in the discussions was a review of the priorities for reporting diseases. It was agreed for the first time that nursing personnel had an important role in reporting syndromes including gastroenteritis.

In the same year, in conjunction with the health statistical section at the PAHO Regional Office, a modified form (192E) was introduced for the reporting of diseases to PAHO with a copy to CAREC from the English-speaking Caribbean countries.

As part of the programme of technical co-operation CAREC has been assisting countries with the development of national surveillance systems. Several examples were shown of forms now in use in Grenada and other countries.

As a consequence of these activities, it was possible from 1976 to obtain reports on gastroenteritis from member countries as well as other countries in the Caribbean Basin, and to distribute them monthly through the CAREC Surveillance Report which, in 1978, has a circulation of 2,000.

Both for 1976 and 1977 it has been possible to prepare an annual communicable disease report, including information on gastroenteritis.

It is, however, generally recognised that there are great differences in the comprehensiveness of the national reporting systems. While this makes inter-country comparisons of limited value, nevertheless, trend analysis has been undertaken using intracountry reports.

Some countries, for example Jamaica, have so improved their reporting system for gastroenteritis through the use of sentinel hospitals and clinics in each parish that by the beginning of July, 1978, over 12,000 cases cumulative had been reported for 1978 compared with 60 cases for the same period in 1977. Even with an epidemic in 1978, this vast increase is largely due to improved reporting.

3.2 DISCUSSION

In the discussion that followed Dr Diggory's Overview of Gastroenteritis in the Caribbean, Dr W Chin commented that in Guyana one offshoot of the CAREC study was improvement in local bacteriological techniques, so that they were now detecting the relevant organisms in the stools of patients but had not carried out in-depth studies. Dr L Spence remarked that rotavirus was very important but it had a low excretion rate. He was looking forward to relevant hospital studies especially because of the apparent absence of rotavirus in the adult population. Dr N Andrews drew the attention of the group to the Trinidad Ministry of Health's follow-up system utilising public health inspectors and nurses, but complained of incomplete reporting of children discharged from hospital and recuperating from gastroenteritis.

3.3 CURRENT STUDIES IN TRINIDAD AND TOBAGO, GUYANA, AND ST VINCENT
- Ms B Hull, CAREC

This is a study of gastroenteritis in infants and children 0-3 years admitted to the major hospitals in Trinidad, St Vincent, and Guyana. Controls are selected from homes in the country and are matched by age, sex, and home district. Microbiological examination was done on faecal samples from both groups and evidence sought for association of organisms with illness. The three major pathogens to emerge from these studies were:-

- (1) The rotaviruses which occurred in 25% of children with Gastroenteritis in both Trinidad and St Vincent but were not found in 14 cases from Guyana;
- (2) The Salmonellae which occurred in approximately 8% of cases in Trinidad and St Vincent, and 20% in Guyana;
- (3) The Shigellae which were found in 4% of children in Trinidad and St Vincent, and in 20% of cases in Guyana. Enteropathogens E.coli and Toxin producing E.coli were isolated frequently from control children.

There were slight differences in the pattern of clinical infection with these three agents but these were not sufficiently marked to be used diagnostically.

Factors indicating or affecting the physical state of the child were compared in cases and controls.

Breast-feeding for 3 or more months occurred more frequently in healthy controls than in cases; low birth weights (less than 2.5 kg) were found in a higher percentage of cases; children of Gomez II or III degree of malnourishment suffered more frequently from gastroenteritis and had more prolonged illness.

Environmental factors which were not associated were family size and composition and care of the child by persons other than the mother. Associated factors were the availability of adequate water supply and sanitary sewage disposal.

The ...

The group of children at highest risk of death were those under 2 months of age, with low birthweights and nutritional status, dehydration on admission to the hospital, and the recurrence of diarrhea after discharge from hospital. Close follow-ups and maternal education was recommended for these cases.

3.4 DISCUSSION

Dr Leonardo Mata pointed out that salmonella was an indigenous flora in small numbers and special techniques were required for its culture. In the case of shigella, ten per cent of the women and children in Santa Maria Cauque were shedding the organisms but in women, diarrhea was of low frequency and mild. Consequently, the quantitative aspects of the methods were important.

Dr M Gueri sought information on:-

- (1) The time interval, the episode of diarrhea, and the anthropometric measurements and pointed out that weight/height was a better indicator than weight/age;
- (2) When bottle feeding was first introduced because he feels this is more important than the length of breast-feeding.
- (3) The birth weights of those who died, how many children were below a birth weight of 2.5 kg and how many were still being breast fed.

Ms Hull promised to supply him with the relevant data. In reply to the cause of death, Ms Hull stated that only 2 children had received post mortem examinations. It was her impression that the observed difference in children with rotavirus infection was due mainly to dehydration and not the length of the illness.

No valid explanation was given to the observation of the low incidence but high case fatality associated with shigella, except for the fact that the numbers involved were small. In the case of salmonella, it was felt that adults might escape serious effects but that the baby was a sensitive indicator.

With Salmonella, Dr M Levine drew attention to the fact that this pathogen has a high inoculum infection, usually spread by contaminated food vehicles. Since animals are a major reservoir of salmonella, Dr Levine pointed to the importance of cultures of animals living in the same environment as well as the stools of mothers. He too stressed the need for sensitive techniques to detect shigella in stools.

3.5 DIARRHEAL DISEASE RESEARCH AT THE UNIVERSITY OF THE WEST INDIES, JAMAICA - Prof P S E G Harland, UWI

1. Being responsible for training of physicians for the Caribbean, we have been trying to disseminate modern ideas about pathogenesis and treatment in Jamaica, Barbados, and Trinidad, in under-graduate and post-graduate teaching, especially in the new, community-orientated curriculum.

2. We are hoping to develop (funds permitting) an outreach programme to send lecturers to the LDCs to upgrade training and implementation in diarrheal disease and perinatal problems. So far, Prof. Harland has visited Belize and Dr. Swaby St Vincent, and seminars have been held in Jamaica.

In these areas, oral rehydration was demonstrated in seminars to local physicians and the Ministry was encouraged to disseminate oral fluid. This was successfully commenced in Jamaica where oral rehydration fluid (ORF) is now available.

3. In epidemiological research, Dr Alma Dyer has documented the present diarrheal situation in Jamaica and work is in progress to utilize the new structure of health services administration in management of cases of diarrhea.

4. Basic research in biochemical and pathophysiological aspects of malnutrition is being carried out by the Tropical Metabolism Research Unit by Drs Michael and Barbara Golden, especially in zinc metabolism. The importance of mineral metabolism is under scrutiny especially in relation to growth, utilization of nutrients, and the role of zinc in immune functions.

5. The clinical aspects of dehydration in terms of electrolyte balance and specific problems related to malnutrition are under investigation in the wards of the Department of Child Health. We hope to collaborate with Dr Levine's group in a study on composition of fluid.

DISCUSSION

With reference to community studies, Dr F Ramsey stated that in the approach to the solution of the problems of gastroenteritis the need was not so much for newer knowledge but rather for the improvement in the application of existing knowledge. History will show that we not unfrequently make recommendations which were first rooted many years earlier, but never implemented. Frequently changes in top level administrators and the need for Programme Directors to explain all aspects of the programme to each new incumbent requires tact and patience. There is a dire need for improvement of middle level managerial skills and motivation of the people. Good field programmes can be ruined by inadequate communications and poor interpersonal relationships. Dr Ramsey felt that updated legislation, priorities geared to economic considerations, and the necessary political will to improve the quality of life of the people were all important considerations in determining the outcome of community programmes.

THE CARIBBEAN FOOD AND NUTRITION INSTITUTE AND DIARRHEAL RESEARCH Dr M Gueri, CFNI

CFNI was established in 1967 as a result of an agreement between the Governments of the English-speaking Caribbean, the University of the West Indies, PAHO/WHO and FAO (the latter is no longer a

signatory). The Agreement provides for an Advisory committee on policy which acts in fact as a governing body which has been responsible to develop eight long term objectives. The eighth objective deals with research directed towards the other seven objectives; one of the activities is to develop means to implement the strategy and a plan of action to combat gastroenteritis and malnutrition in children under two years. This has been done so far by means of the Maurice Pate Travelling Seminars. Eight such seminars have been conducted and CFNI soon will start evaluation of its usefulness.

CFNI has also collected considerable amount of data in gastroenteritis during the process of nutrition surveys.

Finally, gastroenteritis is one of the indicators in the Food and Nutrition Surveillance Project which is being conducted in collaboration with the Government of St Kitts-Nevis-Anguilla. This project attempts to establish an early warning system to prevent malnutrition.

3.8

NATURAL HISTORY OF ROTAVIRUS INFECTIONS IN A GUATEMALAN RURAL COMMUNITY* - Dr J J Urrutia**, Dr L J Mata***, Dr R Schneider and M A Guzman*

A preliminary report on the natural history of rotavirus infection in 45 children followed prospectively from birth to age 3 years is presented. The children were followed in detail with regard to nutritional status, dietary intake, growth and the occurrence of infectious diseases. A total of 4395 faecal samples was collected from the children at weekly intervals between the years of 1964 and 1969. These faecal samples were processed for the identification of helminths and protozoa, Shigellae, Salmonellae, and enteropathogenic E.coli, enteroviruses and adenoviruses, for purposes of defining the pattern of intestinal infections by enteropathogens, and studying diarrheal disease. The stool preparations were kept frozen at -60°C , after entero and adenovirus identification. The results of the studies conducted between 1964 to 1969 have recently been published (The Children of Santa Maria Cauque, L J Mata, M I T Press, 1978). The ELISA technique is being applied to identify the rotavirus. At the time of this report, about 2500 faecal preparations are still pending analysis.

Rotavirus is found to be present in 10.5% of the faecal samples. A total of 280 infections (Rate - 7 per 100 child weeks) by this agent have been found to occur between birth and age 3 years. Twenty nine per cent of the infections were symptomatic. Infection tended to occur early in life; 50% of the children became infected during the first 5 weeks of life. Asymptomatic infection was found more frequently during the first trimester.

/Diarrhea

* Supported by the International Development Research Centre (IDRC) Canada

** Instituto de Nutricion de Centro America and Panama (INCAP) Guatemala

Diarrhea associated with rotavirus was more frequent between 3 and 21 months of age. So far no infection has been found to occur after 30 months of age. Vomiting and dehydration tend to be more frequent between 9 and 23 months of age. Infection is most common during the months of October to May, coinciding with the coldest period of the year.

The faecal samples will continue to be examined for a period of 2 months. A complete analysis aimed at determining the natural history of rotavirus infection will include: determination of faecal excretion and infection by this agent; its relationship with diarrheal disease and dehydration; the relationship between rotavirus and other intestinal pathogens; its seasonal distribution, and the contribution of rotavirus to nutritional damage.

DISCUSSION: Nil

3.9 THE INSTITUTE OF NUTRITION FOR CENTRAL AMERICA AND PANAMA AND DIARRHEAL DISEASE RESEARCH - Dr R Schneider, INCAP

In contrast with healthy populations from industrialized countries, individuals living in rural areas of Guatemala present alterations in their G.I. ecology characterized by an increased facultative and anaerobic upper G.I. flora associated with significant amounts of free bile acid in the luminal secretions and non-specific changes in the duodeno-jejunal mucosa. Variable degrees of digestive insufficiency and susceptibility to diarrhea and malabsorption were observed in subjects living in these environments depending on the degree of alteration suffered by their G.I. ecological system. As a result of this, a wide clinical spectrum of G.I. malfunction or insufficiency is observed in such populations. In one extreme, tropical sprue and other severe malabsorptive syndromes characterized by intense G.I. alterations represent the seriously diseased bowel, and, therefore, are bound to cause clinical manifestations. Below this relatively small group exists a far larger one formed by those cases suffering mild to moderate degrees of intestinal malfunction which represent the clinically silent or subclinical parts of the spectrum. Up until recently, the detection of such individuals was difficult due to the lack of suitable tests to evaluate their G.I. function and ecology.

Studies done by INCAP have documented that subclinical malabsorption represents a very important health problem in rural areas of Guatemala. The prevalence of D-xylose malabsorption in rural adult males has been 30 to 32%. Furthermore, 40 to 51% of rural adult males have a decreased capacity to absorb nitrogen, calories and fat from their regular diet losing through faeces 150 to 330 K cal/day/individual above the average faecal excretion observed in a reference group of Guatemalans with normal absorption. Diarrheal disorders, the most frequent clinical manifestations of this population's altered G.I. ecology, represents a leading cause of morbidity and mortality among the latter group also.

The preliminary evidence presented in this meeting suggests that the carbohydrate induced H₂ breath tests can be used as an epidemiological tool for the screening of subclinical mal-absorption in rural communities and also to evaluate further the relationship between those subjects G.I. ecology and the degree of digestive insufficiency they suffer. The results of initial attempts in modifying the G.I. ecology of a group of Guatemalan children by the oral administration of zinc sulphate were also presented.

3.10 DISCUSSION

Dr Leonardo Mata stressed the importance of improving what he termed "maternal technology". By this he meant the practice by the mother of basic hygiene, such as handwashing, etc.

3.11 DIARRHEAL DISEASE RESEARCH ACTIVITIES IN ARGENTINA - Dr B Barrera-Oro

J G Barrera-Oro, G H Lombardi, M I Berria, Virus Department, Instituto Nacional de Microbiologia, Av. Velez Sarsfield 563, Buenos Aires, Argentina.

D Stambouljan, A M Roseto, Ch Russ, Pediatric Service, Policlinico "Prof Alejandro Posadas", Ramos Mejia.

A Z De Verona, A Casaro, C A Verona, H Terzold, Eera-Inta, Balcarce.

In 1975, several groups of investigators followed with interest the reports on Peovirus-like agents (RLA) associated with acute gastroenteritis in various parts of the world and decided to start looking for them in Argentina. At the end of that year, they found particles of similar structure and size to RLA in stool suspensions of 3 children with acute sporadic gastroenteritis. This preliminary result was published in the Lancet, 17 December, 1975.

The RLA search was extended to 124 diarrheic children in 1976. A Control group of 33 children was included during autumn and winter months of that year. Additionally, RLA were looked for in calves and newborn mice with acute diarrhea.

The 124 sick children were 1 to 30-months old; 91% of them were less than 1-year old with a median of 5 months of age.

Half of the diarrheic children were eutrophic. Diarrhea was moderate in 87.2% of them and was associated with fever and/or vomiting in half of the cases. All patients recovered.

The control group was selected from children of similar age to that of the diarrheic ones, who were admitted to the hospital for non-infectious diseases.

3.12 DISCUSSION

Dr L Spence enquired whether the patient with a hernia was infected in hospital; Dr J Barrera-Oro replied that the clinical story was negative. He further stated that the present results were preliminary and that he would have to relate later questions to normal individuals who showed a conversion in their serology.

3.13 DIARRHEAL DISEASE RESEARCH ACTIVITIES IN COSTA RICAMODERN VIEWS ON DIARRHEAL DISEASE AND ITS RELATION TO NUTRITION

- Dr L Mata, A Simhon, E Mohs, H Villegas, and J J Urrutia

Diarrheal disease is a society-induced disease which has come about as a result of population density, faecal contamination of the environment and dependence on a few staple foods. Diarrhea morbidity has been underestimated. Based on studies in Santa Maria Cauque, an estimated 2 billion cases in children 0-4 years per year are expected in today's world. Deaths have been estimated in 5-20 millions per year for that age group.

Diarrhea is almost exclusively of infectious origin. The commonest single identifiable agent in Costa Rica is rotavirus (30% of cases; yearly average). During outbreaks, rotaviruses may be associated with 70% of cases. Overall, infectious agents are found in 60-80% of endemic and epidemic diarrheas. Incidence of diarrhea associated agents increases with age. Breast-feeding confers protection against infection, although some - generally mild - diarrhea is observed even during exclusive breast-feeding in poorly sanitized environments.

Diarrheal diseases are declining in most countries throughout the world. Such decline is highly correlated with the decrease in infant mortality observed throughout. Such change undoubtedly means, or will result in, improved child nutrition.

Diarrhea can be considered a cause of acute severe (energy-protein) malnutrition. Enteric infection reduces food consumption, impairs digestion and absorption, increases secretion and nutrient loss and causes metabolic alterations. Calories lost due to anorexia alone are 16% of total expected intake. Poor rural children appear to eat recommended levels and grow normally when they are healthy. Most reduced intakes and weight loss and faltering has been associated with diarrheal and other infectious processes.

Therefore, little scientific meaning can be ascribed to nutrition supplementation programmes if rates of enteric infection continue to be high. It appears that environmental control and personal hygiene and education are key factors to reduce infection, interrupt transmission and control disease. Such condition is sine que non to improved nutritional status, increased survival and eventual promotion of national development.

14 DISCUSSION

Dr Mata felt very strongly that diarrhea was more important than food availability in determining growth outcome. Dr Harland stressed the effect of maternal bonding on later development. Mata, citing Chandra, stated that babies who were small for gestational age were more prone to infection and consequent stunting. Damage to cellular immunity had been implicated in these babies whose infections were more prolonged and difficult to treat. In addition, small for dates babies do better in the United States than in Costa Rica because of better environments. One colleague wished that Mata had given more hard data to support the above assertions.

Dr Schneider pointed out that we have no real indicator to tell how the body is performing. At present we are measuring the end results such as diarrhea and malabsorption and he felt a need for a new battery of measurements to determine whether children in these studies can absorb food as well as children in the U.S. He stressed that we do not know how to measure the population at risk and how to provide the most efficient diet. Mata felt strongly that hygiene, love and environmental modification were more important than food supplements. Dr P Hamilton felt that this was an opportune moment to study the effect of the resurgence of malaria on growth in Honduran children.

Mata attributed the striking improvement since 1960 in the health parameters of Costa Rica to:-

- (1) The expenditure of 8 per cent of GNP on health. This is similar to the expenditure of Switzerland.
- (2) Coverage of 75 per cent of the country with a water supply.
- (3) Sustained immunisation campaign against 6 preventable diseases (via use of motorbikes).
- (4) Community promoters who build roads, bridges, etc.

There has been no direct intervention to nutrition and the holistic approach may be most dangerous. Mata stressed that he would include potable water supply, immunisation, roads, etc but remove food supplementation.

In reply to Dr Harland, Mata stated that he did not know the answer to the high IGM values found in small for date babies in one of their earlier studies. This study has not found universal acceptance, Mata stated.

4. ABSTRACTS FROM PRESENTATIONS - SESSION 2, October 17th4.1 ETIOLOGY OF ACUTE PEDIATRIC DIARRHEA IN MEXICO CITY - Dr. O. Munoz

During a 22 month period, 343 children with diarrhea and 88 age-matched controls attending clinic in Mexico, were prospectively evaluated for Enteric Pathogens. Enteropathogens associated with disease were Shigella (12%), Salmonella (10%), Rotavirus (18%), Toxigenic E.coli (8%) and others 10%, including 12 Proteus isolates that caused rounding of adrenal cells.

Enteropathogens were isolated from a greater (P 0.001) number of children with diarrhea (60%) than from asymptomatic controls (11%).

<u>ENTEROPATHOGEN**</u>	<u>ACUTE DIARRHEA</u>		<u>CONTROLS</u>	
	No.	%	No.	%
Rotavirus	63	18.4	4	4.5
Adenovirus	3	1	-	-
<u>Shigella</u>	42	12.2	1	1
<u>Salmonella</u>	33	10	1	1
<u>E.coli*</u> LT	11)	7.8	4	4.5
ST	6}		-	-
Proteus*	12	5.5	-	-
<u>E.coli Invasive*</u>	2	1	-	-
<u>E.histolytica</u>	7	2	-	-
<u>G.lamblia</u>	6	1.7	-	-
Unknown Etiology	138	40	Negative 78	89

* Done on initial 217 patients

** Multiple pathogens in 7% of patients

4.2 INFANTILE DIARRHEA RESEARCH ACTIVITIES IN VENEZUELA - Dr. J. Flores

Despite the large income that Venezuela obtains from oil, infantile diarrhea continues to be a major cause of infant mortality. In a population of 12 million inhabitants, 4500 - 5000 children die every year because of diarrhea.

With the knowledge of "new" pathogenic agents and the development of techniques to identify them, the possible etiologic agents accounting for the disease have been studied in a group of patients admitted to the Children's Hospital of Caracas. Their ages ranged from 1-23 months, and only those with 72 hours or shorter illness were accepted. They had not been sick at least

/...a month

a month prior to the present episode of diarrhea and had not received antibiotics for the same period of time.

Faecal pathogens were searched for by means of routine parasitological and bacteriological analysis. Additionally, Toxigenic E.coli was investigated by the following techniques: rabbit loops, immunoelectrophoresis, VERO and Y-1 adrenal cells incubations, ELISA, Radioimmunoassay and infant mouse tests. Rotavirus were identified by E.M. and ELISA.

The relative percentages of pathogens identified was as follows:

	<u>Patients</u>	<u>Controls</u>
Rotavirus	32.2%	5%
Toxigenic <u>E.coli</u> (LT)	41.8%	15%
"E.P." <u>E.coli</u>	16.1%	11%
<u>Shig.</u> and <u>Salm.</u>	5.3%	5%
None	27 %	70%
	n=523	141

Patients with rotavirus and Toxigenic E.coli presented syndromes of shorter duration than those seen with Shigella or "E.P." E.coli.

Rotavirus and Toxigenic E.coli had similar patterns of incidence throughout the year, being more frequent during the cold months and during the rainy season.

4.3 DISCUSSION OF DR. MUNOZ AND DR. FLORES PAPERS

Dr. Levine asked Dr. Munoz about the conditions under which the colonization factor assays (CFA)II were done. They were performed using bovine erythrocytes incubated with mannose at 4°C

Dr. Levine commented about the detection of heat stable toxin in the work presented by Dr. Flores.

By use of the infant Mouse Test, Dr. Flores initially found strains of E.coli that produce ST in 13% of the cases studied as compared with 3% of the control cases. However, after reading the paper of Levine et al on the subject, the filtrates of all the E.coli strain isolated by Dr. Flores will be retested after a 10 fold concentration.

Dr. Mata suggested the use of only one day old mice for the performance of this test and the oral administration of the filtrates to the mice.

Mr. Lambourne commented about the adequacy of the control cases in Dr. Flores' study. Controls were children of the same age range who during the same time of the year attended an outpatient

clinic in the same hospital for the administration of immunizations and routine check up.

The issue of clinical severity of rotaviral diarrhea was brought up. Ms. Hull did not seem to find rotavirus to produce specially grave cases of diarrhea. In her cases, 12 of the children died; most of them had Shigella besides belonging to the most susceptible group (younger, low birth weight). In Dr. Flores' study, rotavirus seemed to cause the mildest illness as judged by the duration of hospitalization; none of his patients with rotavirus died.

Dr. Spence reports that 21 fatal cases of rotaviral diarrhea have been observed in Toronto; however, those children probably arrived too late to the hospital and did not receive prompt therapy.

4.4 SEROLOGICAL STUDIES AND NEEDS - Dr. L. Spence

The bovine rotavirus was used to prepare reagents for use in the counterimmunoelectrophoresis (CIEOP) test for detection of human rotavirus in stool. These reagents were supplied through PAHO to laboratories in the Caribbean, and South America. A review of the literature indicates that several sensitive and specific tests are available for the detection of rotavirus. At the present time, the most fashionable test is the ELISA test.

Cases of gastroenteritis admitted to the pediatric wards of a general hospital in Toronto were monitored for rotavirus infection from October 1976 to May 1978. 196 (34.6%) of 537 patients were positive for rotavirus. The highest infection rates were found in the winter months with a peak of 56.5% (35 positives in 62 specimens tested) in January 1976.

A haemagglutinin was prepared from a strain of the bovine rotavirus. This antigen was used to test paired sera from twelve cases of human rotavirus infection. Five of these cases showed rising antibody titres to the bovine virus. Twelve human sera were tested by complement fixation and haemagglutination inhibition tests with the bovine virus. Ten sera reacted in the former test and six in the latter test. The results indicated that the haemagglutination-inhibition test detected specific antibody and that the bovine virus was related to one of the human serotypes of rotavirus.

Five bovine rotaviruses were compared by haemagglutination-inhibition. Antigenic differences were noted among the viruses.

Further needs in serological studies include the production of standardised reagents for distribution to laboratories performing tests for rotavirus and the provision of a test panel of stools containing various concentrations of rotavirus for distribution to laboratories.

4.5 DISCUSSION OF DR. SPENCE'S PAPER

Dr. Barrera-Oro asked how to get antigen to perform HA1 Tests.

At the moment Dr. Spence has not been able to collect large volumes of stool from children excreting rotaviruses and has not tried to prepare haemagglutinins from human rotaviruses. However a recent report by a Japanese group reported the use of agglutinins from large sample of human rotavirus stools.

A comment was made by Dr. Levine about the mild nature of the illness associated with rotavirus infection in Baltimore. Other groups in that city have had similar experience. Dr. Harland commented that the well nourished status of the children may have prevented diarrhea.

Dr. Levine stated that a good number of children with rotavirus are admitted to several hospitals in Washington, D.C., as well as to many other "well-sanitated" cities. Going further, Dr. Levine commented on the fact that several decades ago, the epidemiology of diarrhea in the U.S. was similar to what is being seen today in underdeveloped countries. There was a clear summer peak of diarrhea above an underlying endemic incidence. After sanitation of the cities, the summer peak disappeared but a winter rotavirus peak was unmasked. The same process might occur in the future in the underdeveloped countries.

Dr. Schneider proposed the high standard of hygienic conditions in Canadian hospitals to explain Dr. Spence's observation of absence of rotavirus in newborn stools despite the fact of the high frequency observed in other studies.

Dr. Mata brought in the concept of dose of rotaviruses needed to produce disease. The higher incidence and even the intensity of the clinical picture may be related to the amount of rotavirus particles contaminating the environment.

Dr. Spence mentioned the recent paper by Leece et al that appeared in "Science" in which this point is clearly demonstrated by rearing piglets in clean versus dirty conditions.

Dr. Hamilton wondered about the existance of evidence to support the transmission of rotaviruses through the water. Dr. Spence answered that there is no published evidence to support such contention.

4.6 ORAL REHYDRATION STUDIES AND NEEDS - Dr. M. Levine

A study of rehydration with an oral glucose-electrolyte solution was undertaken in 62 Costa Rican children with 5-10% dehydration due to acute watery diarrhea, to determine whether success rates of oral therapy differed in children with rotavirus or bacterial diarrheas.

/The oral...

The oral therapy formula used contained (g./L of water): NaCl, 3.5; KCl, 1.5; NaHCO₃, 2.5; Glucose, 2.0. Fluid deficits were clinically estimated from weights measured on admission by multiplying the weight times the estimated percent dehydration based on clinical signs. Since oral fluids may not be entirely absorbed during diarrhea, during the first 6 hours infants received an amount of oral solution plus free water equal to twice the estimated fluid deficit. After every two baby bottles (200 ml each) of oral solution, one bottle (200 ml) of plain water was given. Skin turgor was used as a bedside guide to rehydration, and the 2:1 therapeutic regimen was repeated until skin turgor became normal, then the oral solution was stopped and feedings were resumed.

Balance data and serial monitoring of weights, haematocrits and plasma sp.gr. showed that the simple oral therapy regimen corrected electrolyte abnormalities and dehydration promptly in 94%. Results in infants with rotavirus or bacterial diarrheas did not differ significantly except for a clinically insignificant increase in glucose excretion in the stool of rotavirus cases. Infants with or without malnutrition and those with a variety of serum electrolyte abnormalities on admission responded equally well.

Since children with dehydration of the same range admitted to hospital prior to this study had all routinely received intravenous therapy, the elimination of all need for intravenous fluid in 94% of the study patients indicates the value of oral therapy for reducing costs and patient trauma in the treatment of infant diarrheas.

A comparison was also made between glucose and sucrose-containing formulas. Glucose was minimally but consistently superior in all instances. Where a choice is available, glucose is preferred to sucrose in preparation of oral therapy formulas. If glucose is unavailable, sucrose will suffice.

4.7 DISCUSSION OF DR. LEVINE'S PAPER

Dr. Schneider asked why if the amount of Na⁺ in the WHO formula is higher than needed a new correct recipe is not used for western world children.

Dr. Levine remarked that the major advantage of the WHO formula, particularly in Africa and Asia where there is cholera, is that it may be used in children or adults for cholera or non-cholera diarrhea.

Dr. Levine thinks it may be desirable but logistically difficult to introduce a new and different lower Na⁺ formula only for children of the West. Even more with the continuous chance of cholera spreading in the U.S. and Latin America.

Dr. Urrutia commented on the problem of introducing oral rehydration therapy as proposed by Dr. Levine. A particular problem is related with the introduction of baby bottles in villages where breast feeding is the rule. Dr. Urrutia has been using the spoon by spoon method to introduce oral rehydration in villages.

Dr. Schneider worried about the population acceptance of this type of therapy in places where people's beliefs and traditions oppose the use of water as treatment. He proposed the research of such type of opposition by conducting previous socio-cultural studies in the areas where this treatment is going to be applied. He also suggested that implementation of the treatment should be done in subrural areas before rural areas.

Dr. Ramsey brought in the problem of the need of more staff to give medication. Although the procedure is simple and is given by the mothers, it is difficult for all mothers to do it in the Caribbean society.

Dr. Levine has thought about that and an alternative will be teaching people interested in community activities who do not have other occupations and do not need a special background preparation such as adolescent girls or grandmothers.

4.8 WHO ACTIVITIES AND INTEREST - Dr. D. Barua

Dr. D. Barua explained the evolution and the objectives of the WHO programme of Diarrheal Diseases Control. He pointed out that while this is a programme of technical co-operation with member states in implementing their national programmes for diarrheal diseases control and training, there is a very important component of research in this programme. He requested the participants to take into consideration the areas of research needs identified in the Report of the Advisory Group on Development of a Programme on Diarrheal Diseases Control (Geneva 2-5 May 1978) and in the draft report of the Scientific Working Group on Immunity and Vaccine Development (Geneva 14-16 August 1978) for the purpose of defining their regional priorities in both operational and basic goal-orientated research. The proposed mechanism of review of scientific proposals and for possible support by WHO/PAHO was also described.

4.9 I.D.R.C. ACTIVITIES AND INTEREST - Dr. J. Garcia

Dr. Garcia spoke about the history and organization of the International Development Research Centre. The Centre was founded in 1970 by the Canadian Parliament which provides the necessary funds for keeping it functioning.

The main purpose of the Institution is to support research activities in underdeveloped countries in the areas of Agriculture, Social Sciences, Information Sciences, and Population and Health.

Although the budget is provided by the Canadian Government, the policies and decisions depend directly on the resolutions of the Board of Governors. A high percentage of its members belong to underdeveloped countries. Research proposals are sent to the corresponding Divisions which in turn send their recommendations to the Board of Governors that makes the final decision about funding the submitted projects.

/The main...

The main offices are located in Ottawa but there are also regional offices in Bogota, Singapore, Dakar, Nairobi and Cairo.

In the Health Science Division, the main sub-areas being supported are:

Primary Health Care;
Fertility regulation methods;
Tropical Diseases; and
Environmental Sanitation.

In this last sub-area projects are financed for studies of water supply, sewage control and gastroenteritis. Currently CAREC and INCAP projects are being supported.

The Centre is now open to receive new proposals, not only from Centres but also from local Universities and other research institutions.

4.10 DISCUSSION OF DR. GARCIA'S PAPER

Dr. Hamilton asked about the closeness between I.D.R.C. and C.I.D.A. Dr. Garcia answered that they are two completely independent agencies; though they have good relations with each other, CIDA depends upon government decisions, IDRC does not.

Dr. Harland worried about the limited amount of funds available to permit travelling of North American and European scientists to the Caribbean to give lectures or participate in conferences, and wondered about possible help from IDRC. Dr. Garcia stated that this activity could be supported only as a part of specific research projects requiring them, such as the present meeting.

OUTLINE OF PLANNED ACTIVITIESARGENTINA - INSTITUTO NACIONAL DE MICROBIOLOGIA - Dr J Barrera-Oro

In Argentina we are interested in extending epidemiological studies on Rotaviruses in urban and rural areas, in studying for a year at least, rotaviruses in several families, regardless of whether they have diarrheic diseases or not. We are also interested in establishing a national centre on rotavirus to help other countries in: EM detection, CF, Elisa, etc. A co-operative programme was presented by three groups of Argentine investigators and CEPANZO to PAHO in this respect, and we are looking forward to their opinion, suggestions, corrections, etc of our programme and their support.

.2 INSTITUTO DE INVESTIGACIONES EN SALUD (INISA) UNIVERSITY OF COSTA RICA - Dr L Mata

1. Continuous surveillance of rotavirus and other agents in hospitalized cases.
2. Study of autopsy material.
3. Community study of diarrhea, enteric infection, and milk antibody.
4. Prophylactic programme of colostrum in normal neonates.
5. Milk programme for high risk neonates.
6. Search for new agents by ultracentrifugation and immunoelectron microscopy.
7. Appropriate technology for breast-feeding and oral rehydration.

.3 GUATEMALA - FUTURE ACTIVITIES OF INCAP NUTRITION-INFECTION PROGRAMME
Dr J Urrutia

1. Typing of the rotavirus that has been found to be prevalent in the area of Santa Maria Cauque, Guatemala.
2. Identification of the sources of infection of rotavirus and the mechanisms of spread.
3. To investigate further the problem of infections early in life by rotavirus and investigate the significance of asymptomatic infection.
4. To investigate if rotavirus is included in the diarrheal disease of other age groups besides preschool children.
5. To determine the role of rotavirus, toxigenic strains of E.coli and other bacteria in the etiology of diarrheal diseases in different settings of Guatemala: highland and lowland areas.

6. To determine if the H_2 tests can be used to define the prevalence of enteric pathogens.
7. To implement oral rehydration action programmes in a large section of Guatemala, utilizing auxiliary health personnel as well as health promoters. These programmes should be utilized to demonstrate the usefulness of the oral rehydration in diarrheal diseases and to extend them later at a national scale.
8. To implement a surveillance program of enteropathogens to be able to predict epidemics, especially cholera.

5.4 MEXICO - INFECTIOUS DISEASES DEPARTMENT, HOSPITAL DE PEDIATRIA - INSTITUTO MEXICANO SEGURO SOCIAL - Dr O Munoz

1. Continue etiological/epidemiological studies.
2. Continue working on toxigenic E.coli (LT) and colonization factor I-II, others?
3. Serological survey of antibodies to LT and colonization factor to know the importance of the problem of of toxigenic E.coli in Mexico.
4. Studies on transmission mechanisms of toxigenic E.coli in open controlled population.
5. Continue studies on factors influencing cellular differentiation in cycle of E.histolytica (TRNA patterns in cyst and trophozoytes).
6. Utilization of C.I.E.O.P. and E L I S A test for typhoid fever diagnosis.
7. Cellular immunity alterations or mechanisms for protection for typhoid fever.
8. Cellular immunity and phagocytosis related to zinc alterations on protracted diarrhea in malnourished children.

5.5 VENEZUELA - Dr J Flores

1. Extend the etiology study to other cities in Venezuela, particularly to hospitals with higher mortality rates.
2. Attempts to purify heat labile toxin(s) from human strains of toxigenic E.coli are under way for three purposes:
 - (a) To study their internal mechanism of action.
 - (b) To improve available assay tests based on immunological reactivity.
 - (c) To experimentally study its immunizing capacities.
3. The response to V.cholerae and E.coli toxins by the intestine of malnourished rats is being studied.

4. The mechanism by which elevation of cyclic nucleotides produce changes in intestinal transport is being studied experimentally. The identification of specific membrane components that are phosphorylated in the presence of cyclic AMP and cyclic GMP and their possible functions is the goal of this project.

5.6 CAREC - TRINIDAD AND TOBAGO - FUTURE PLANS FOR GASTROENTERITIS RESEARCH - Ms B Hull

1. On completion of the current case/control study on gastroenteritis in infants in June, 1979, we plan to study the impact of diarrheal disease in the community by conducting a longitudinal study of selected infants and their families from birth to three years. Investigations will include the incidence of diarrheal illness, the pathogens involved and the effect of mild or severe episodes of diarrhea on the development of the child.
2. Rotavirus infections have been reported in neonates in nurseries and appear to be more prevalent in certain nurseries. We plan to seek rotaviruses in infants in the nursery of a public hospital, a private clinic and, if possible, in home-delivered infants and to relate the presence and duration of excretion to breast-feeding.
3. We have detected bovine rotavirus in calves from a number of small farms and would like to set up a study of possible transmission to the families living on these farms.

5.7 CFNI - WORK PLANS FOR 1979 IN RELATION TO GASTROENTERITIS - Dr M Gueri

1. Continue co-operating with Caribbean Governments in implementing the Strategy and Plan of Action to combat Gastroenteritis and Malnutrition (SPACGEM).
2. Evaluate Maurice Pate Seminars for improving implementation of SPACGEM.
3. Conduct 1-2 day national seminars for Public Health Nurses and Hospital Nurses to standardize methods of diagnoses, prevention, and treatment of malnutrition and gastroenteritis as well as data collection for surveillance.
4. Assess the importance of gastroenteritis surveillance within a food and nutrition surveillance programme.
5. Assess the value of oral rehydration in the improvement of nutritional status.
6. Continue promotion of breast feeding as means of preventing gastroenteritis and malnutrition in infancy.

5.8 FUTURE ACTIVITIES OF INCAP'S HUMAN NUTRITION AND GI FUNCTION
 - Dr R Schneider

Many of the projects mentioned in the Infection-Nutrition programme will be collaborative enterprises between that programme and the G.I. function programme. Our main interests for next year are:-

- (1) To develop further non-invasive methodology with the aim of detecting groups of population at risk of GI disease.
- (2) To implement a sanitary education programme in rural communities with the objective of decreasing the degree of faecal contamination within the rural home.
- (3) To modify the GI ecology of rural Guatemalan subjects in order to decrease the incidence of GI insufficiency and/or diarrhea.

5.9 CENTRE FOR VACCINE DEVELOPMENT PROJECTS FOR 1979 - UNIVERSITY OF MARYLAND - Dr M Levine

I. EPIDEMIOLOGY SECTION:

- (i) Epidemiologic, seroepidemiologic, and bacteriologic studies of endemic typhoid fever in Chile with Dr Jose Manuel Borgono.
- (ii) Intervention study at the population level to determine the ability of oral therapy use in the home to decrease the incidence of potentially fatal, severe diarrheal dehydration in infants.
- (iii) Search for a field area for large-scale field trial of an oral attenuated Salmonella typhi vaccine.

II. CLINICAL IMMUNOLOGY SECTION:

- (i) Pathogenicity and immunogenicity tests of Escherichia Coli purified pill vaccines in man.
- (ii) Studies of the mechanisms of immunity to enterotoxigenic E.coli, particularly local intestinal secretory antibody.
- (iii) Studies of mechanisms of immunity to Vibrio cholerae El Tor.
- (iv) Studies of local immunity to 27 nm gastroenteritis agents (with Dr H Greenburg of NIH).

III. PHYSIOLOGY SECTION:

- (i) Comparison of efficiency of a low Na⁺ (60 meq/L) glucose/salt solution and WHO solution in oral rehydration of infants with diarrheal dehydration. To be carried out in collaboration with Dr P S E G Harland and others in Jamaica.

/(ii)...

- (ii) Comparison of modified high K+ formula with WHO oral therapy formula.
- (iii) Evaluation of the effect of metaclopramide and chlorpromazine on reducing purge rate in infant diarrhea.
- (iv) Investigation of levels of gut hormones in diarrhea (with Dr S Bloom of Hammersmith Hospital).
- (v) Studies of malabsorption of vitamins secondary to diarrhea.

IV. LABORATORY SECTION:

- (i) Characterisation of new enterotoxin discovered in enteropathogenic E.coli (Levine et al, Lancet 1, 1978).
- (ii) Measurement of local intestinal antibody, to E.coli pili, and heat-labile enterotoxins.
- (iii) Studies of pathogenesis of Yersinia enterocolitica infections.

REPORT FROM WORKING GROUPS6.1 IDENTIFIED NEEDS - ETIOLOGY/EPIDEMIOLOGY

1. Studies are needed to investigate the effect of intervention affecting the environment of communities, particularly in respect of water supply, sewerage and refuse disposal.
2. Studies on the long-term effect of gastroenteritis on child nutrition and development are needed.
3. Effective methods of Health Education need to be established by pilot studies and follow-up; the most suitable methods may differ in different populations.
4. Sources and modes of transmission of the more recently described agents remain to be determined. Studies are needed on the serotypes of human and animal rotaviruses, on adult rotavirus infections and on the significance of asymptomatic infection in neonates as well as the possibility of animal reservoirs of infection.
5. Studies that might lead to the development of rotavirus vaccine should include the serotyping of human viruses, studies on cross-protection by immunisation with rotaviruses from other species and efforts to cultivate human rotaviruses.
6. Studies are needed on local immunity, particularly in respect to rotavirus, bacterial toxins. The transfer of transplacental antibody and transfer of antibody or other factors in milk must also be examined.
7. Information is needed on the susceptibility of rotaviruses to physical and chemical agents and to antiviral drugs.
8. The pathophysiology of gastroenteritis due to rotavirus and campylobacter infection needs further investigation.
9. Search for new aetiologies should continue: in this, immune EM employing convalescent sera should be included, and the examination of faecal samples for other enterotoxin-producing bacteria in addition to E.coli and the significance of Astro-, Calici-, Parvo- and Corona- viruses as agents of gastroenteritis need to be investigated.
10. Recognising the limitations of studies based on single faecal samples, more detailed studies of small numbers of cases are needed to establish more accurately the proportion of cases for which no known pathogen can be found.
11. Prospective community-based studies are needed to determine factors which indicate high risk of gastroenteritis.

- 12. Investigations are needed on improved methods of surveillance.
- 13. Studies are needed on maternal nutrition in relation to quality and quantity of breast milk.
- 14. Investigations of jejunal as opposed to faecal flora should be extended.

6.2 IDENTIFIED NEEDS - CLINICAL

- 1. Further studies are still needed on the physiological alterations induced by the various etiological agents as well as special efforts to characterize diarrhoeas of non-infectious origin.
- 2. Studies are needed to identify new drugs (antisecretory agents, etc.) that may be of value both in therapy of diarrhoeal disease with the associated dehydration and in prophylaxis. Efforts should also be expended on the evaluation of traditional or folk remedies in this regard.
- 3. Appropriate diets for use during and after diarrhoeal episodes need to be identified taking into consideration the availability of foods and local practices.
- 4. Research is needed to improve or modify the composition of oral fluid considering cost, efficacy and ease of administration.
- 5. Studies need to be carried out on sequelae of diarrhoeal episodes including reduced disaccharidase levels, malabsorption of Vitamin A, hypochloridria as well as immune response in terms of local and systemic antibodies and cell mediated immune responses. Persistence of certain abnormalities may be monitored using H₂ breath tests.

6.3 IDENTIFIED PRIORITIES - RESEARCH

- 1. Studies arising from the availability in the region of an abundance of clinical material should receive priority consideration.
- 2. Priority needs for laboratory-based research are centrally-distributed high quality immunological reagents for enterotoxin and rotavirus investigations and standard methods of laboratory investigations against which new procedures should be measured.
- 3. Priority investigations (using standard techniques) would be:-
 - (a) Comparative studies on the seasonal aetiology in different areas and populations.
 - (b) Investigation of the effects of changes in sanitary conditions.
 - (c) Community-based studies on the effects of diarrhoeal disease on child health nutrition.

4. The priority need in basic applied research is for studies directed towards the development of vaccines and new therapeutic agents.
5. The fundamental epidemiological need is the development of effective method(s) of surveillance.
6. Clinical priorities should be oriented towards improved therapeutic regimens in management of dehydration and simplified convalescent dietary schedules.

7. RECOMMENDATIONS OF THE WORKSHOP

The group felt that recommendations pertain to two general areas:-

Implementation of measures based on current knowledge aimed at reducing mortality and morbidity due to gastroenteritis in the region, and co-ordination of research efforts in priority areas of activity, with the purpose of obtaining additional information required for further control and prevention.

The general areas to look into are:- the environment, host resistance, and therapy.

7.1 APPLICATION OF CURRENT KNOWLEDGE TO DECREASE DIARRHOEAL DISEASE

(a) ENVIRONMENT

Although the knowledge on rotavirus transmission is very limited, the role of several factors of environmental sanitation and personal hygiene in the spread of diarrhoeal disease caused by most organisms is well recognised. Emphasis should then continue on extending coverage with safe water supply, adequate systems of faecal disposal and improved education and personal hygiene. The role of maternal technology in interrupting transmission in the home and improving child nutrition should be emphasised. This requires education and training, mechanisms to deliver knowledge to mothers and to enhance existing technologies in the home environment. Specific aspects are techniques for handling drinking water and food preparation, method of handling faeces, the practice of breast-feeding of infants and young children, particularly during convalescence, and techniques for oral rehydration.

(b) HOST RESISTANCE

While no vaccines are available to prevent the diarrhoeas observed in the region, breast-feeding is recognised as the most important protective mechanism in lieu of the specific antibodies against the agents of gastrointestinal disease. Breast-feeding should be encouraged from birth and in an exclusive manner for 4 to 6 months, extended with food supplements for up to 9 to 12 months. Colostrum must be given to children. Good nutrition is promoted by prompt oral rehydration and adequate feeding practices particularly during convalescence from infectious diseases.

2 USES OF ORAL THERAPY

Oral rehydration has been conclusively shown to be optimal as a life-saving mechanism, and the best method available to re-establish a state of well-being, and to avoid or correct weight loss and stunting of children following diarrhoea.

- 7.2.1 Oral rehydration should be made available in home, accompanied by the appropriate technology for prompt administration of oral rehydration. Emphasis should be on coverage of remote rural areas and marginal and poor belts of cities.
- 7.2.2 The group recommends that special pilot project oral rehydration units be established in the pediatric wards of hospitals in each of the islands. The purpose of these units will be to introduce pediatricians, nurses and others to the efficacy and practicality of oral therapy.
- 7.2.3 Concomittantly with the oral therapy demonstration unit, study protocols should be carried out quantitating the savings in money, days of hospitalization, and specialized personnel time that will accrue from use of oral therapy. Other study protocols could compare nosocomial infection rates between oral therapy patients and those who received intravenous therapy. It is suggested that the epidemiologic and statistical resources of the CAREC be utilised in design and performance of these studies.
- 7.2.4 The group suggests that it would be appropriate for one of the more sophisticated facilities in the Caribbean (such as the Pediatric Department of the University of the West Indies in Jamaica) to study that minority of infants that fail to respond to oral therapy. They should be studied to determine small bowel colonization with bacteria, malabsorption of monosaccharides, and intestinal morphology.

7.3 CO-ORDINATION OF RESEARCH EFFORTS

The group felt that co-ordination of research on diarrhoeal diseases in Latin America, with special reference to tropical areas, is urgently needed.

(a) CO-ORDINATION

The co-ordinating body should be the Pan American Health Organization (PAHO) in Washington, D.C. Centers where special tasks could be carried out include CFNI (Jamaica), INCAP (Guatemala), CAREC (Trinidad), INISA (Costa Rica) and special laboratories in Mexico, Venezuela, and Argentina, in view of existence of facilities and methods for comprehensive studies on diarrhoeal diseases.

(b) OBJECTIVES

The co-ordinating body should prepare a census of on-going and planned and approved investigations on the problem.

/The ...

The co-ordinating body should stimulate research on issues pertaining to environmental control of diarrhoea, enhancement of host resistance and therapy, with an emphasis on health services research and other types of applied research.

The co-ordinating body should try to increase funds by aggressive negotiation with international agencies (UNDP, WHO), financial entrepreneurs (World Bank), and national agencies (SIDA, IDCR, AID).

The co-ordinating body should promote standardisation of procedure and reagents to be used in investigations in the area. Special emphasis must be given to epidemiological methods in the case of comparative field studies when several nations are participating.

(c) MECHANISMS

Technical Advisory Committee on Diarrhoeal Disease to assist the PAHO co-ordinating effort.

Newsletter on diarrhoeal disease, including advances on research projects and summaries of situation of diarrhoea in the region.

Periodic meetings to exchange, criticise, and summarize information on the various research projects and health interventions.

Co-ordination of multinational research programmes, particularly those of epidemiologic nature involving field work in rural areas.