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HIGHLIGHTS OF RESEARCH ON DIARRHOEAL DISEASES UNDER THE INDIAN COUNCIL OF MEDICAL RESEARCH

The problem of cholera has been with us for centuries. As a matter of fact, the Indian sub-continent came to be known as the "home of cholera". A great deal of work has been done in India and abroad on various aspects of the problem of cholera including its control, but even today there exist many gaps in our knowledge and understanding. The Indian Council of Medical Research established the Cholera Research Centre in February, 1962 to conduct in-depth studies on cholera and to suggest remedial measures. The Centre initiated a number of studies in collaboration with WHO, Geneva including two cholera vaccine field trials, cholera carrier, serological and chemoprophylaxis studies and a number of hospital-based clinical trials. The Centre was recognized as the WHO International Reference Centre for Vibrio Phage Typing in 1968, and designated as the WHO Collaborating Centre for Reference and Research on Vibrios in 1978, for providing referral services to the member countries. In view of its expanded scope and activities covering a large number of microorganisms in relation to enteric diseases, the Centre was renamed as the National Institute of Cholera and Enteric Diseases (NICED) in 1979. It was designated as the WHO Collaborating Centre for Research and Training in Diarrhoeal Diseases in 1980. In the recent past, the efforts of the National Institute of Cholera and Enteric Diseases have been supplemented by the scientists working at the ICMR Centre for Advanced Research in Enteric Diseases, at the Christian Medical College (CMC) Hospital, Vellore and at the ICMR Advanced Centre for Enteric Diseases Research and Training at the All India Insitute of Medical Sciences, New Delhi.

Studies on Cholera

The global cholera scenario experienced an unprecedented event during 1992-93, when a new toxigenic non-O1 strain[1-6], designated as *Vibrio cholerae* O139 Bengal[7], appeared in the Indian subcontinent and later was reported from many other countries of the region as well as from developed countries like the UK and USA. Scientists of the NICED have the credit of bringing this to the notice of global scientific community for the first time. The NICED with its expertise in various disciplines immediately embarked upon research related to *V.cholerae* O139 in the areas of microbiology, clinical medicine and epidemiology. These studies revealed that from the beginning of November 1992, there was an unusual increase in the relative rate of isolation of *V.cholerae* non-O1 as compared to *V.cholerae* O1 from patients of cholera-like illness admitted to the Infectious Diseases Hospital, Calcutta[1]. By December 1992, *V.cholerae* non-O1 became the predominant organism (>95%) isolated from patients with cholera-like diarrhoea examined in this hospital[1,3]. The unusual trait of these isolates is their ability to produce large amounts of cholera toxin (CT)[1]. Simultaneously, similar strains were identified from different parts of the country[3]. This was the first report of a major epidemic of cholera caused by CT producing *V.cholerae* non-O1. Clinical studies clearly showed that the

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disease produced by *V.cholerae* non-O1 (O139) was clinically indistinguishable from the disease caused by *V.cholerae* O1 and that the management is essentially the same[4,8]. It was earlier demonstrated by a well controlled clinical trial that norfloxacin, a fluoroquinolone, is an effective alternative to tetracycline for the treatment of O1 cholera[9] and after the appearance of O139 cholera, these workers also demonstrated that multiple dose of the same drug is perhaps superior to doxycycline[10]. In 1975, scientists from the NICED, Calcutta, had showed that single dose of doxycycline (300 mg) is as effective as multiple doses of tetracycline for the treatment of cholera[11]. WHO also advocates doxycycline for adult cholera. A highly specific monoclonal antiserum for detection of O139 strains was developed at NICED which has been supplied to WHO (SEARO), New Delhi for distribution to various national and international laboratories.

Studies carried out at NICED showed that cholera carriers actually act as reservoirs for ElTor cholera vibrios in the community during the interepidemic period even when cholera cases are absent[12,13]. It was further observed that carriers are responsible for the transmission of *V.cholerae* infection to other family members by contaminating unprotected stored water and cooked food with their infected fingers[14]. Transmission studies with *V.cholerae* O139 also showed that at the community level there exists a large (14.6%) number of asymptomatic infected persons which indicates an epidemiological similarity to that of ElTor cholera[15].

In order to find interventions for blocking the transmission of infection at the community level, studies conducted at NICED showed a lower incidence of cholera carriers amongst contacts in cholera affected houses provided with narrow-necked pitchers (*sorai*)[14] and this led to the concept of preventing contamination of stored water by storing water in narrow necked storage containers which has been widely accepted. Studies also demonstrated the effectiveness of simple measures like hand washing with soap and water[16], coupled with health education, in reducing the incidence of diarrhoeal diseases particularly dysentery cases in Calcutta slums. The WHO has recommended these strategies for prevention of diarrhoea.

Development of oral rehydration therapy (ORT) is considered a significant discovery in medicine of this century. However, such oral rehydration therapy was not much practised particularly for children. A study[17] conducted at NICED in 1974 showed that if repeated small amounts of oral rehydration solution (ORS) were administered orally at frequent intervals, nearly 91 per cent of diarrhoeal children below 5 years of age with moderate degree of dehydration could be successfully rehydrated by ORS alone. This led to the widespread acceptance of ORT, particularly for children. Further studies[18] demonstrated that neonates and young infants could also be safely and effectively rehydrated with WHO recommended formula of ORS, provided breast feeding is continued along with the ORS feeding. It was further demonstrated[19] that ORS of WHO formula was safe and effective in the treatment of dehydration owing to acute diarrhoea in malnourished (marasmic) children. Based on these studies as well the 3-tier implementation strategy developed by NICED in a community-based study where mothers were found to play a pivotal role in preventing dehydration with early institution of "home-available fluid" therapy, the Government of India in a comprehensive manner launched the National Diarrhoeal Diseases Control Programme on a high priority basis with a target of reduction of diarrhoea-related mortality by 50 per cent by 1990.

In view of some limitations of the conventional phage typing scheme for ElTor vibrios, a much needed new phage typing scheme for *Vibrio cholerae* biotype ElTor strains has been developed at the NICED[20]. A total of 1000 *V.cholerae* O1 biotype ElTor strains were phage typed with a set of 10 phages. Over 99 per cent of strains were found to be typable with this scheme and the strains could be clustered into 27 types. This new phage typing scheme is expected to be useful as an epidemiological marker for tracing the source of infection[20].

In a case-control study to understand the risk factors for development of life-threatening dehydration, in children upto the age of 2 years suffering from acute watery diarrhoea, it was shown[21], by univariate analysis, that the presence of vibrios in the stool, withdrawal of breast feeding during diarrhoea, not giving fluids, including oral rehydration solution (ORS) during diarrhoea, frequent purging (>8/day), vomiting (>2/day) and malnutrition were identified as risk factors. However, by multivariate analysis, after controlling the confounders, withdrawal of breast feeding during diarrhoea, and not giving ORS during diarrhoea were identified as significant risk factors. It is felt that these findings will be useful for both the Global and National Diarrhoeal Diseases Control Programmes for formulating strategies for preventing death due to diarrhoeal dehydration.

A pathophysiological study of cholera undertaken by the Department of Gastrointestinal Sciences, CMC Hospital, Vellore, revealed characteristic microvasculature lesions in rectal and small intestinal mucosa of patients with

cholera[22,23]. The vascular lesion is apparently caused by lipid A, the toxic moiety of the lipopolysaccharide (LPS) antigen. Biophysical studies, including two-dimensional NMR spectroscopic analysis of the interaction of LPS with polymyxin B suggested that pentamidine might be a potential antagonist of therapeutic value[24]. The role of short-chain fatty acids in the absorption of water and sodium in the large intestine was investigated. Since malabsorbed carbohydrates *in vitro* are fermented by the faecal flora of cholera patients, it appears that cereal-based oral rehydration solutions provide a source of short chain fatty acids in the large intestine[25,26]

The molecular mechanism of pathogenesis of cholera, with emphasis on the bacterial components that mediate adhesion of the microorganisms to the host intestinal epithelium, is an important area researched at the NICED. Since lectins, a class of proteins capable of binding specifically to cell surface sugars, are recognized as important candidates for mediating host-cell interaction, purification and molecular characterization of *V. cholerae* lectins was undertaken. A cell-free haemagglutinin (HA) was isolated and purified to homogeneity and characterized as a disc-like oligomer of noncovalently associated polypeptides of M_r 62,000 Da[27]. The HA recognizes specifically terminal ß1-galactosyl residues of complex glycoproteins and glycolipids. However, due to intrinsic low affinity for individual galactosyl residues, the HA showed strong avidity only when the sugar residues are presented in a clustered configuration to enable multiple interactions with the protein[28]. A cell-associated non-fimbrial HA has been isolated by detergent extraction of intact cells and purified by affinity chromatography on columns of chitin, a polymer of N-acetyl glucosamine. The cell-associated HA has been characterized biochemically, morphologically and antigenically[29].

Studies on *Shigella*

Epidemics of bacillary dysentery due to multiple drug resistant *Shigella dysenteriae* type 1 (Shiga bacillus) have been reported from Central America, Mexico, Bangladesh, Sri Lanka and Central Africa since 1969. When the disease spread to West Bengal in 1984 affecting over 3,50,000 people with 3,500 deaths, the NICED Scientists identified the causative agent as *S.dysenteriae* type 1, which was multi-drug resistant[30]. The local clinicians were not sure about the drug of choice to treat shigellosis and we recommended the use of nalidixic acid which was found to be highly effective[31,32]. More recently, norfloxacin, a fluoroquinolone[33,34], which is a nalidixic acid derivative, was found to be superior to nalidixic acid in the treatment of Shigellosis caused by nalidixic acid resistant *Shigella*. A single dose of ciprofloxacin[35] (1 g) was found to be quite effective for Shigellosis. A team from the NICED investigated a similar epidemic of bacillary dysentery in the Andaman & Nicobar Islands[36] and identified the causative agent to be multi-drug resistant *S.dysenteriae* type 1 and also reported a number of extraintestinal complications which included among others, leukemoid reaction in about 31 per cent of patients[37].

Rapid emergence of multiple drug-resistant strains of *S.dysenteriae* has led to a concerted global effort to develop effective immunoprophylactic measures against the disease. The humoral immune response of patients convalescing from shigellosis, against bacterial components like lipopolysaccharide (LPS)[38] and outer membrane proteins[39,40] has been analyzed by ELISA and immunoblotting. The role of gut mucosal T and B lymphocytes as well as non-T and non-B cells in cellular immune response to shigellosis was examined in guineapig model[41]. The subpopulations of lymphocytes were identified by immunofluorescence using specific monoclonal antibody markers. The efficacy of a 57 kDa antigenic polypeptide of the outer membrane of *S.dysenteriae* 1 in eliciting delayed type hypersensitivity (DTH) in mice was evaluated[42]. Porin of *S.dysenteriae* type 1 was purified to homogeneity and characterized as a noncovalently associated trimer of polypeptides with M_r 38 kDa[43]. The pore-forming activity of the protein was demonstrated in proteoliposomes reconstituted from the protein and phospholipids. Porin was found, by ELISA and immunoelectron microscopy, to be labeled by antibody, indicating its surface exposure[43]. In another study, the proliferation of murine splenocytes by *Shigella* LPS was found to be inhibited by the monosaccharide, L-rhamnose, indicating specific recognition of the oligosaccharide moiety, presumably by a cell surface receptor[44]. This is contrary to the accepted mechanism of endotoxin-induced proliferation of B cells. Genetic studies on *S.dysenteriae* 1 showed that plasmids and specially a 70 kb large plasmid contributed to the growth characteristics as well as cell wall morphology of the organisms[45].

Studies on Rotavirus

Rotavirus (double stranded segmented RNA virus) is an important etiological agent of acute diarrhoea in children below 2 years of age. Rotavirus infection accounts for more than 22 per cent of hospitalized children with diarrhoea in Calcutta[46,47]. However, in Manipur, as high as 90 per cent of hospitalized babies excrete rotaviruses in the winter months[46,48]. A detailed epidemiological study conducted by the NICED in Manipur over a period of five years revealed

a very unusual rotavirus strain associated with an epidemic and having a characteristic of long electropherotype but subgroup I in nature suggesting zoonotic transmission of rotaviruses[48]. These strains have greater medical significance than similar strains occasionally isolated earlier, as such strains had never been implicated in an epidemic before this study. Further, molecular biological characterization by cloning and sequencing of the same strain revealed that genetically this strain was related to the human VP 7G serotype 2 strain[49] but antigenically reacted to bovine VP 7G serotypes 6 and 10 but not with any known major human VP 7G serotypes 1 to 4. This study suggested that the strain might have developed by *in vivo* reassortment between human and bovine rotaviruses.

In a study carried out at the All India Institute of Medical Sciences, New Delhi, the infecting rotavirus strain 116E was cultivated and the gene 4 and gene 9 characterized. The strain showed highest homology (92.2%) with a bovine serotype 10 strain. Neonatal infection induced a significant rise in IgA titres in saliva and showed a protective efficacy of 53 per cent in the first 2 years of life[50-52].

Studies on Parasitic Diarrhoea

Some parasites, *viz. Entamoeba histolytica*, *Giardia lamblia* and Cryptosporidium are important causes of diarrhoea. Studies from the NICED identified Cryptosporidium in 5.6 per cent of faecal samples from children with acute diarrhoea admitted to local hospitals in Calcutta[53,54]. Basic studies revealed the complex nature of *E.histolytica* and *Giardia* antigens[55,56], and monoclonal antibodies to 29 kDa antigen was helpful in differentiating pathogenic strains from non-pathogenic strains of *E.histolytica*[57]. A 118 kDa antigen was found to be highly specific for Indian *Giardia* isolates.

Studies on *V. parahaemolyticus*

Vibrio parahaemolyticus is an important causative agent of diarrhoea, especially that associated with consumption of marine foods. Kanagawa-positive, clinical isolates of *V.parahaemolyticus* were found to adhere to rabbit intestinal epithelial cells with a significantly higher affinity than Kanagawa-negative environmental isolates[58]. Adherence was not correlated with cell surface hydrophobicity and there was no evidence for a role of haemolysin in the process[58]. Despite a similar composition of outer membrane proteins (OMPs) of Kanagawa-positive and Kanagawa-negative strains of *V.parahaemolyticus* as indicated in SDS-PAGE, OMPs of Kanagawa-positive, clinical isolates were significantly less immunogenic in mice. In comparison to environmental isolates, the OMPs of clinical isolates were buried to a greater extent[59]. However, antisera to OMPs of Kanagawa-positive strains could block adherence of bacteria to rabbit intestinal epithelial cells[60].

Studies on Typhoid Fever

The widespread and indiscriminate use, often in subtherapeutic doses of antityphoid drugs (*eg*, chloramphenicol for the treatment of any fever or diarrhoea) in many parts of the developing world probably led to the emergence of multidrug resistant *Salmonella typhi* from different parts of the country including Calcutta. Scientists from NICED identified the multidrug resistant *S.typhi* strains from typhoid fever patients admitted to the local hospitals[61-63]. In a randomized clinical trial, it was shown that multidrug resistant typhoid fever responded to furazolidone in about 86.2 per cent of cases. Furazolidone is a cheap drug particularly for the people of the developing countries[64].

Studies on *Escherichia coli*

Different varieties of *Escherichia coli* are important causes of acute diarrhoea, particularly in children in the developing countries. Heat-stable enterotoxin (STa) of *E.coli* triggers intestinal secretion by stimulating the guanylate cyclase of the enterocytes. Recent studies from the NICED revealed that the pathophysiological effect of STa is initiated by binding with a receptor and stimulation of particulate guanylate cyclase results from a cascade mechanism associated with inositol triphosphate Ca++ protein kinase C signalling system[65-68].

Investigation of Epidemics

Teams consisting of epidemiologist, microbiologist and clinicians from the NICED, Calcutta, have investigated a large number of epidemics of acute diarrhoeal diseases in the whole of the country from time to time and identified the cause and suggested appropriate remedial measures both as short and long term, thereby extending help to the respective state governments in tackling epidemics of diarrhoeal diseases.

Very recently, three Institutes, *viz.*, the Institute of Microbial Technology Chandigarh, the National Institute of Cholera and Enteric Diseases, Calcutta and the Indian Institute of Chemical Biology, Calcutta, have developed a recombinant cholera vaccine which has been successfully tested in animal model and awaiting human volunteer trial.

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The write-up has been contributed by Dr. S.K. Bhattacharya, Dr. S.P. De, and Dr. Kalyan Banerjee, National Institute of Cholera and Enteric Diseases, Calcutta.

ABSTRACTS

Some Research Projects Completed Recently

Clinical application of tumour growth fraction associated markers in the radiotherapy of cancer of the uterine cervix

The study was undertaken on 312 cervical cancer patients (stage IIB or III) to define the role of tumour growth fraction and its relationship to the clinical course of the disease, as also to know whether cell kinetics had an association with response of the tumour to radiotherapy. Tissue biopsies and smears of exfoliated cells were taken from all patients before treatment. All pre-treatment biopsies were analysed for labelling index using bromo deoxy uridine (BrdUrd) labelling of DNA and Ki 67 antigen expression. In addition, immunocytochemical localization was carried out for argyrophillic nucleolar organiser region (AgNOR), expression of epidermal growth factor (EGF) and its receptor (EGF-R), transforming growth factors alpha and beta (TGFα and TGFβ), HPV transforming protein E6, tumour suppressor protein p53 and the anti-apoptotic product bcl-2. Of the 312 patients, 152 (106 disease free - Group 1, and 46 with residual/recurrent disease - Group 2, after treatment) were evaluated through their course of radiotherapy and upto a follow up of 12 months and correlation was made between pre-treatment status of tumour growth fraction associated markers and clinical outcome after radiotherapy. To study the transition of parameters analyzed during radiotherapy, cervical smears were obtained before the therapy, and after 1000, 2000, 3000 and 4000 cGY.

Pre-treatment analysis of AgNORs significantly correlated to disease status after treatment. Lower AgNOR counts were significantly associated with Group 2 patients suggesting that increased proliferative activity may be a positive prognostic indicator. Observations made during various phases of radiotherapy revealed consistent higher AgNOR counts in Group 1 patients. However, the other proliferative associated markers did not show such an association. EGF and EGF-R showed significant pre-treatment correlations with the final disease outcome. Both these markers were expressed more by patients belonging to Group 2, whereas the TGFα was expressed more by patients belonging to Group 1. Group 1 patients mostly showed mild to moderate expression for TGFβ while most Group 2 patients were negative for this growth factor. This conspicuous difference

was also evident during the various phases of radiotherapy. Pre-treatment expression of bcl-2 was different in the two groups of patients. Most patients in Group 1 showed mild expression while in Group 2, the majority showed a moderate to intense expression. Similarly, during the various phases of radiotherapy, Group 2 patients showed consistently higher levels of bcl-2.

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Certain basic immune functions in intracranial tumour patients

In order to elucidate the role of neuralmodulation of immune response in patients of intracranial tumours, immune parameters were studied before and 30 days after treatment in these patients. Normal individuals matched for age, sex and socio-economic status served as controls. Patients with benign tumours were treated by surgery whereas those with malignant tumours were treated by surgery, radiotherapy and chemotherapy.

It was found that patients with benign and malignant tumours had higher total leukocyte count before treatment which decreased significantly after treatment. Lymphocyte percentage showed a reduction but absolute monocyte count and monocyte percentage showed an increase in both benign and malignant tumour patients. There was an elevation in neutrophil functions as evidenced by increased phagocytic index, avidity index, NBT (Nitroblue tetrazolium) reduction and SIC (serum soluble immune complex) index in brain tumour patients. As compared to controls total T cell and T4 counts were reduced in both benign and malignant tumour patients before and after treatment whereas there was an increase in T8 counts. Serum IgA and IgG levels showed a decrease and IgM level an increase. Preoperatively altered immune parameters like lymphocyte percentage, monocyte percentage, absolute T lympocyte count, T8 count and IgA levels returned to base-line levels after treatment in benign tumour patients.

The study confirmed the altered innate, cell mediated and humoral immunity in brain tumour patients before and after treatmenet. Most of the immune changes observed were related to cell mediated immunity and were immunosuppressive. Though the pituitary region tumours are benign, patients with these tumours showed either marked increase or decrease in the levels of immune parameters studied than observed in those with tumours in other areas. The immunomodulatory effects of malignant tumours were more marked than those of benign tumours.

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85TH ANNIVERSARY CELEBRATIONS OF ICMR

Diarrhoeal diseases was the theme selected for the dissemination of scientific information to various groups of individuals in the month of July 1996.

The National Institute of Cholera & Enteric Diseases, Calcutta has brought out a number of publications on diarrhoeal diseases which include a booklet on "Management and Prevention of Diarrhoea : Role of Mothers" (English and Hindi); posters on (i) ORS- A Simple Effective Weapon to fight Diarrhoea (English and Hindi), (ii) Diarrhoeal Diseases - A Major Global Health Problem and Management of Diarrhoea Cases (English and Hindi), (iii) Awareness about Diarrhoea; and a folder on "Prevention of Diarrhoea", and a video film on "Diarrhoeal Diseases".

Various topics were highlighted by other institutes/ centres during June 1996. The Regional Medical Research Centre, Bhubaneswar, organized a health awareness campaign at the Headquarters of the Orissa State Branch of the Indian Red Cross Society (IRCS), Bhubaneswar on June 6, 1996. The topic of this programme was non-communicable diseases. Shri I.C.Das, General Secretary of IRCS, Bhubaneswar, inaugurated this funcion. Dr. K. Satyanarayana, Director, RMRC, Bhubaneswar, outlined the role of ICMR and its institutes/centres in tackling various health problems in the country.

The Vector Control Research Centre (VCRC) Field Station, Cherthala, Kerala, organized a field demonstration on the use of medicinal plants at the Ayurveda Medicinal Plants Herbarium at Thaliaparambu, Poochakal on June 26, 1996 by an Ayurveda physician Dr. Sugadhan Vaidhyar for the IX and X Standard students. Dr. K.H. Krishnamoorthy, retd. Professor of Botany, JIPMER, Pondicherry, delivered a guest lecture on "Medicinal Plants & Ayurveda" at the VCRC on July 1, 1996.

The Regional Medical Research Centre, Port Blair, organized various activities over the last few months to celebrate the 85th anniversary. The Centre organized various programmes (lectures/seminars) to create awareness about leptospirosis among the people and medical professionals of these Islands. Health camps were organized among the *Shompens*, a Mongoloid tribe of the islands of Great Nicobar, to create health awareness. Health education material on nutrition, diarrhoeal diseases and intestinal infections, vector-borne diseases, leptospirosis, tuberculosis , AIDS, *etc.* was displayed in the exhibition organized during the tourism festival "Islands on the march" in the month of February this year.

ICMR NEWS

Participation of ICMR Scientists in Scientific Events:

Dr. V.P. Sharma, Director, Malaria Research Centre (MRC) , Delhi, participated in the III Neem Awareness Workshop at Mbita, Kenya (June 22-28, 1996).

Dr. G.V. Satyavati, Director-General, ICMR, participated in the XIX session of the Joint Co-ordinating Board of the Special Programme for Research and Training in Tropical Diseases at Geneva (June 24-27, 1996).

Dr. K. Vijayaraghavan, Dy. Director, National Institute of Nutrition (NIN) , Hyderabad, participated in the Workshop on Consultative Meeting on the Regional Networking Activities of the Regional Training Programme on Food and Nutrition Planning (RTP-FNP) at Chiang Mai, Thailand (June 30-July 5,1996).

Dr. Padam Singh, Director, Institute for Research in Medical Statistics, New Delhi, participated in the III Iranian Statistics Conference at Tehran, Iran (July 1-3, 1996).

Dr. Bela Shah, Dy. Director General, ICMR, participated in the International conference on "Population Ageing" and a workshop on "Research Priorities on Health Ageing" at Brasilia, Brazil (July 1-4, 1996).

Dr. T. Adak, Assistant Director, MRC, Delhi, visited Martsinovsky Institute of Medical Parasitology and Tropical Medicine, Moscow, Russia in connection with the Modelling of Transmission Dynamics of Short and Long term incubating *P. vivax* Malaria in India (July 6-16,1996).

Dr. D.A. Gadkari, Dy. Director and Officer-in-Charge, Drs. S. M. Mehendale and R.S. Paranjape, Assistant Directors and Dr. S.P. Tripathy, Senior Research Officer, National AIDS Research Institute , Pune, participated in IX International conference on AIDS at Vancouver, Canada (July 7-12,1996).

Dr. I. Khatkhetay, Research Officer, Institute for Research in Reproduction, Mumbai, participated in the International Congress on Clinical Chemistry at London (July 7-12,1996).

Dr. G.V. Satyavati, DG, ICMR, participated in the X meeting of the Joint Working Group of the Indo-US Vaccine Action Programme at Washington, D.C. (July 8-15, 1996).

Dr. P. Bhaskaram, Dy. Director, NIN, Hyderabad, participated in the Indo-UK workshop on Host Parasite Relationship at Maryland (July 9,1996).

Dr. Kamala Krishnaswamy, Dy. Director (Sr. Grade), NIN, Hyderabad, participated in the expert panel meeting on Diet and Cancer Project at London (July 10-12,1996).

ICMR AIDED SYMPOSIA/SEMINARS/WORKSHOPS/COURSES/CONFERENCES

Symposium/Seminar/Workshop/ Course/Conference	Date & Place	Contact Address
International Congress on Ageing	August 19-21, 1996; (at Thiruvananthapuram)	Dr. P.K.B. Nair, Coordinator of the Congress, Centre for Gerontological Studies, Thiruvananthapuram.
Workshop on Design and Evaluation of Targeted Drug Delivery System	September, 1996; (at Manipal)	Dr. N. Udupa, Convenor of Workshop, College of Pharmaceutical Sciences, Manipal.

COUNCIL'S TRAINING PROGRAMMES FOR 1996-97

Leprosy

At the Central Jalma Institute for Leprosy, Agra:

- Multidrug Therapy Orientation Course in Leprosy for Medical Officers (September 9–20, 1996).

Virology

At the National Institute of Virology, Pune:

- Diploma in Medical Virology (June 1996–May 1997).

Reproductive Biology

At the Institute for Research in Reproduction, Mumbai:

- Training Course on Current Trends in Management of Infertility and Reproductive Disorders (September 2–13, 1996)

Endocrinology

At the National Institute of Nutrition, Hyderabad:

- Annual Training Course on Endocrinological Techniques and their Applications (August 1–September 15, 1996).

Nutrition

At the National Institute of Nutrition, Hyderabad:

- M.Sc. in Applied Nutrition (June 1, 1996–February 28, 1997).
- Annual Training Course in Nutrition (December 1, 1996–February 28, 1997).

Occupational Health

At the National Institute of Occupational Health, Ahmedabad:

- Orientation Course on Occupational Health for Industrial Medical Officers (September 17–29, 1996).

Medical Entomology

At the Vector Control Research Centre, Pondicherry:

- M.Sc. in Medical Entomology (from August 1996; for 2 years).

Laboratory Animal Technology

At the National Centre for Laboratory Animal Science, National Institute of Nutrition, Hyderabad:

- Training Course for Laboratory Animal Technicians (June 15–July 31, 1996).

  Training Course for Laboratory Animal Supervisors (September 2–November 29, 1996.

Haematology

At the Institute of Immunohaematology, Mumbai:

- Training Course in Transfusion Medicine for Blood Bank Medical Officers (August 5–October 4, 1996).
- Training Course in Blood Group Serology and Blood Bank Methodology for Technicians (August 5–September 4, 1996).
- Training Course in Advanced Haematology and Immunohaematology (September 17–October 4, 1996).

ICMR PUBLICATIONS

	Price (Rs.)
Nutritive Value of Indian Foods (1985), by C. Gopalan, B.V. Ramasastri and S.C. Balasubramaniam, Revised and Updated (1989), by B.S. Narasinga Rao, K.C. Pant and Y.G. Deosthale (Reprinted 1995)	23.00
Growth & Physical Development of Indian Infants and Children (1972, Reprinted 1989)	10.00

Studies on Weaning & Supplementary Foods (1974, Reprinted 1996)	15.00
Studies on Pre-School Children (1974, Reprinted 1984)	6.00
A Manual of Nutrition (Second Edition 1974, Reprinted 1995)	6.00
Low Cost Nutritious Supplements (Second Edition 1975, Reprinted 1994)	4.00
Menus for Low Cost Balanced Diets and School Lunch Programmes Suitable for North India (Second Edition 1977, Reprinted 1994)	4.50
Some Common Indian Recipes and their Nutritive Value (Fourth Edition 1977, Reprinted 1995) by Swaran Pasricha & L.M. Rebello	10.00
Nutrition for Mother & Child (Third Edition 1978, Reprinted 1994) by P.S. Venkatachalam & L.M. Rebello	9.00
Japanese Encephalitis in India (Revised Edition 1980)	5.00
Some Therapeutic Diets (Fourth Edition 1988, Reprinted 1995) by Swaran Pasricha	4.50
Nutrient Requirements & Recommended Dietary Allowances for Indians (1990, Reprinted 1995)	16.00
Count What You Eat (1989, Reprinted 1994) by Swaran Pasricha	9.00
Diet & Diabetes (Second Edition 1993) by T.C. Raghuram, Swaran Pasricha & R.D. Sharma	18.00
Dietary Tips for the Elderly (1992) by Swaran Pasricha & B.V.S. Thimmayamma	3.50
Diet and Heart Disease (1994, Reprinted 1996) by Ghafoorunissa and Kamala Krishnaswamy	26.00
*Depressive Disease (1986) by A. Venkoba Rao	58.00
**Medicinal Plants of India Vol.2 (1987)	136.00

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ERRATA

ICMR Bulletin, Vol.26, No.3&4, March-April, 1996 **"Highlights of Tribal Health Research under Indian Council of Medical Research"**

On page 25, column 2, para 3, last sentence — ß-thalassaemia mutation should be read as Hb Hofu [ß 126 (H_4) Val→Glu]-ß^0-thalassaemia [Codons 8/9 (+G)]

In para 4, lines 2,5 and 7 — a thalassaemia and a Thal type II should be read as α and ß-thalassaemia, α Thal type II and α thalassaemia, respectively.

ICMR Bulletin, Vol.26, No.6, June 1996 **"Control of Iodine Deficiency through Safe Use of Iodized Salt"**

On page 42, column 1, para 2, line 6 "is dependent on the soil content of iodine." should be read as "is dependent on the iodine content of soil."

EMERITUS MEDICAL SCIENTISTS

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