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NUTRITION: A CRITICAL DETERMINANT OF RESPONSE TO VACCINES IN CHILDREN

Information available from epidemiological and clinical studies supports the association of inadequate diet and infection and forms the basis for the modern concept of the vicious cycle of malnutrition and infection[1-2] (Fig.1).

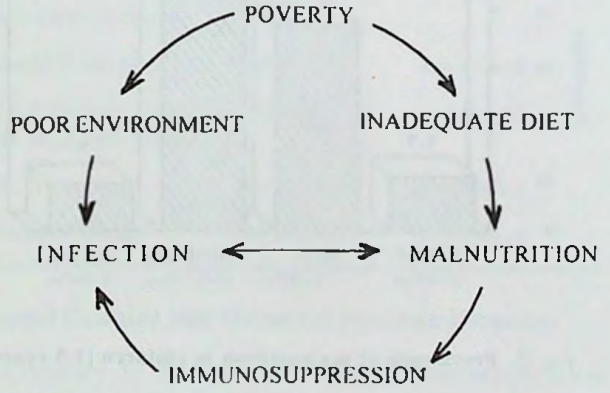


Fig. 1. Malnutrition-infection. The vicious cycle.

Poverty through food deprivation is the root cause of malnutrition while infectious diseases act as aggravating factors. This interaction assumes greater significance in developing countries where both malnutrition and infection are widely prevalent and often co-exist. Infections precipitate malnutrition particularly in an already marginally nourished child. While nutritional supplements bridge the dietary deficits, prevention and control of infections ensure optimal utilisation of the nutrients. Thus, prevention of infections should take an important place in national programmes aimed at controlling malnutrition in children.

Immunization is the most powerful and cost-effective tool for preventing infections and promoting child survival and health in developing countries. However, the efficacy of various vaccines depends upon the ability of the host to mount an adequate and appropriate immune response to the concerned vaccine. Nutrition is an important modulator of immune response. Severe protein energy malnutrition (PEM) among preschool children is a nutritional problem of public health concern which induces immunosuppression and increases the susceptibility of the child to infections. It also contributes to the severity of illness in a malnourished child.

The host's immune mechanisms may generally be classified as innate and acquired immune responses. While innate mechanisms are non-specific and do not carry memory of the infecting organisms, acquired immune mechanisms are endowed with the characters of specificity and memory to the concerned antigen. These two fundamental characters of acquired immune mechanism form the basis for vaccination.

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Acquired Immune Responses of Children with Severe PEM

Humoral Mechanisms

Children suffering from severe forms of clinical PEM, such as kwashiorkor/marasmus, have poor response to typhoid vaccine and certain other bacterial and viral antigens[3]. Nevertheless, these children are found to raise adequate antibody responses to protein antigens like diphtheria and tetanus and certain viral antigens like measles[4]. Total immunoglobulin levels of IgG, IgM and IgA classes have been documented to be normal or elevated in such children[5]. Their B lymphocyte counts also remain unaltered. This indicates that humoral mechanisms in children with severe PEM are partly impaired and the magnitude of the response probably depends upon the nature of the antigen administered, the route of administration, dose and cellular interactions required for raising optimal immune response.

Cell Mediated Immune Mechanisms

Thymolymphatic atrophy has been well documented in autopsy studies conducted on children dying during the acute phase of kwashiorkor[6]. The peripheral blood T cell count, along with the helper cell subset (CD^{+}_{4}) and their *in vitro* response to various mitogens and antigens were found to be impaired, which explain their increased susceptibility to viral, fungal and intracellular bacterial infections like tuberculosis[7,8].

Macrophage Function

Children with severe PEM also exhibit a number of functional deficits of macrophages. Macrophages which play a significant role as accessory cells in cell mediated immune reactions, carry out the functions of antigen processing and presentation to T cells in addition to providing maturation signals (through interleukins) to the T cell. This apart, macrophages are powerful phagocytic and bactericidal cells. On *in vitro* activation, peripheral blood monocytes, obtained from children with kwashiorkor were significantly less mobile and less bactericidal compared to those in normal children. Their ability to produce nitrite, an important intracellular bactericidal agent, was low[9-13].

Based on extrapolation of these results on immunosuppression in severe PEM, doubts have been expressed whether immunization programmes would be successful in communities where malnutrition is widely prevalent. Persistence of infections like measles and poliomyelitis in underprivileged communities has been attributed to the prevailing malnutrition. Concern has also been expressed regarding the efficacy and safety of using live attenuated vaccines in malnourished children for fear of precipitating vaccine induced illness. Use of live measles vaccine has been viewed with concern in communities which are endemic for both malnutrition and tuberculosis because of the potential danger of activation of latent tuberculosis in immunocompromised children.

Severe PEM is considered a public health problem in India. It constitutes only the tip of the iceberg of the problem of malnutrition among preschool children. A recent report on the profile of PEM in the country, by the National Nutrition Monitoring Bureau (NNMB), indicated that the extent of severe PEM (<60% weight for age) in the community is not more than 10% of the preschool child population, while more than 80% of the children look apparently normal but suffer from mild to moderate grades of malnutrition presenting with growth retardation (Fig. 2)[14]. These children constitute the major beneficiaries of any national health programme, including the immunization programme, and their response to various vaccines determines the success of the latter.

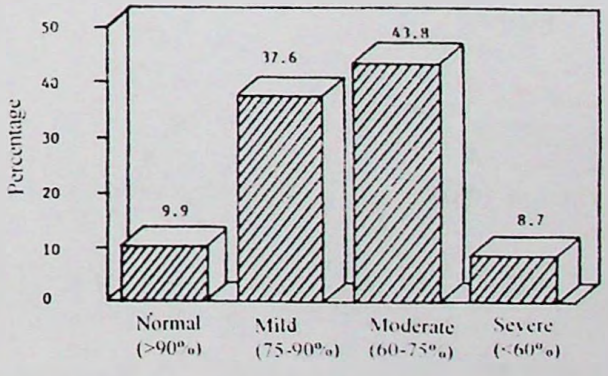


Fig. 2. Prevalence of malnutrition in children (1-5 years).

Source: NNMB Report of Repeat Surveys (1988-90).

Mild-moderate Malnutrition and Immune Response

Clinical and experimental studies have been conducted at the National Institute of Nutrition (NIN), Hyderabad, using immunological methods to determine the degree of nutritional status that modulates immune responses in children in general, and the response to various vaccines used in the National Immunization Programme in particular. Children aged 1-5 years were investigated and their nutritional status assessed using Gomez classification and NCHS Standards. Humoral and cell mediated

immune responses to various vaccines were investigated. Immune responses of children with severe and mild-moderate grades of malnutrition compared to normal children are summarised in the Table.

Table. Effect of various grades of malnutrition on immune response.

	Effect observed	
	Severe malnutrition	Mild- moderate malnutrition
INNATE IMMUME MECHANISMS		
Phagocyte Response		
Neutrophil Macrophage	impaired	No change
Chemotaxis	impaired	
Nitrite production	impaired	
Interleukin-I production	impaired	
Humoral Response		
Complement & Lysozyme	Reduced	Not altered
CELL MEDIATED IMMUNE RESPONSES		
T cell number	decreased	not altered
T cell function	decreased	not altered
HUMORAL IMMUNE MECHANISMS		
Total immunoglobulin levels	not altered	not altered
Response to vaccines		
D and T antigens	not altered	not altered
TAB vaccine (H and O antigens)	impaired	not altered
BCG vaccine	not altered	not altered
Measles vaccine	not altered	not altered

General Cellular and Humoral Immune Response

Contrary to the observation of immunosuppression in severe PEM, children with mild and moderate malnutrition showed both T cell number and proliferative responses adequate on stimulation with mitogens/antigens and were comparable to those of normal children. IgG, IgM and IgA levels were also in the normal ranges.

Immune Response to Specific Antigens

Diphtheria and tetanus vaccine

Two doses of diphtheria and tetanus toxoid were administered at an interval of one month and specific antibody titres were determined prior to the administration of the first dose and one month after the second dose. The antibody titres to both these antigens were found to be in the protective range and the mean titres were comparable among all groups of children irrespective of their nutritional status.

TAB vaccine

Antibodies to 'H' and 'O' antigens of *Salmonella typhi* were measured in response to two doses of TAB vaccine administered one month apart. Children with severe PEM had low mean titres of antibodies to both these antigens, while mild and moderately malnourished children had higher antibody titres which were comparable with that of normal children.

BCG vaccine

Though BCG vaccine has been in use for a long time, its efficacy has been under constant debate, particularly in children of developing countries. However, in view of its protective efficacy against extrapulmonary forms of tuberculosis in children, routine BCG vaccination is recommended.

Response to BCG vaccine is generally measured by (Mantoux) skin reaction to PPD following administration of the vaccine. Very often the Mantoux reaction is negative in children with severe PEM and is attributed to the observed immunosuppression. Contrary to this, children with mild and moderate grades of malnutrition have positive Mantoux conversion as in normal children[15]. Positive response to a skin test depends on two components *viz.*, the inflammatory response and immune reaction to the injected antigen.

Studies were conducted to assess the status of these two components under the influence of PEM. Inflammatory response to a superficial injury was studied in children with kwashiorkor, using the skin window technique. Mobilisation of neutrophil leukocytes and monocytes to the site of injury was studied periodically over 72 h. In normal children, initially the neutrophils move to the site of inflammation in large numbers and are replaced by monocytes by 24 h which persist even at the end of 72 h[9]. The mononuclear infiltration is responsible for the induration observed. However, in children with kwashiorkor, mononuclear mobilization was impaired, and this

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dysfunction of macrophages could be contributing to the negative skin test reactions in these children (Fig. 3).

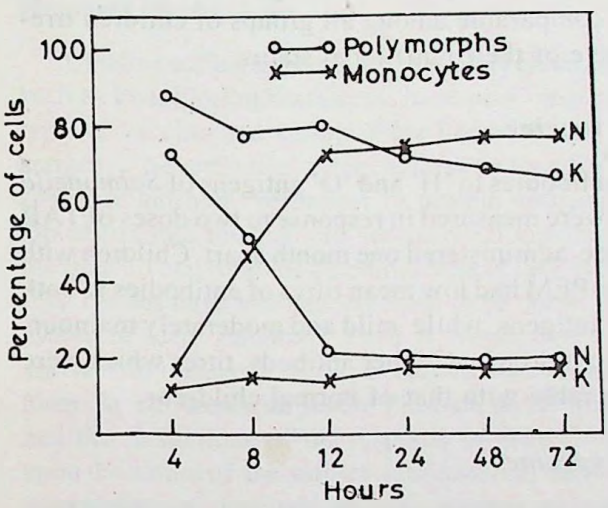


Fig. 3. Cutaneous inflammatory response in kwashiorkor
N: Normal; K: kwashiorkor

Further studies were also conducted to explore the effect of malnutrition on immune response to PPD. Lymphocytes, collected from severely malnourished children 12 weeks after they had received BCG vaccine, were stimulated *in vitro* with PPD and the production of leukocyte migration inhibition factor (MIF) was measured. It was observed that despite severe malnutrition, these children were able to produce a positive migration inhibition response. This study demonstrated that the sensitization of the lymphocytes to tubercular antigens is successful even in children with severe malnutrition[15]. However, due to lack of macrophage mobilisation, the Mantoux test was negative. Children with milder grades of malnutrition developed both inflammatory and immune responses positively. These results indicate that BCG vaccination even in a malnourished community could achieve the expected degree of protection against tuberculosis. This observation was further strengthened by recent clinical studies by Bhaskaram *et al*[16] in children suffering from tuberculosis.

BCG vaccinated children had a more localised infection confined to either the cervical or the mediastinal lymphnodes. While most of the unvaccinated malnourished children suffered from more severe/progressive forms of tuberculosis, BCG vaccination produced similar effects of localising the disease even in children with malnutrition. This observation further strengthened the laboratory studies. BCG was found to prevent progressive forms of tuberculosis in malnourished children as effectively as in wellnourished children[16].

Measles vaccine

It is well established that measles is a major contributor to malnutrition in Indian children. Measles infection is known to cause severe and persistent immunosuppression leading to recurring morbidity in the post measles period[17]. Activation of latent tubercular lesions and worsening of the existing forms of tuberculosis are common phenomena observed after measles. Doubts have therefore been expressed and concern has been voiced regarding administration of measles vaccine to malnourished children living in communities where tuberculosis is prevalent. Specific immune responses were determined in children after administering measles vaccine and were correlated with the nutritional status. Haemagglutination inhibition (HI) antibodies to measles and *in vitro* T cell proliferative response to measles antigen were measured. The results showed that both the antibody production and T cell responses were adequate in all the children irrespective of their nutritional status[3]. This also suggests that unlike infection with natural measles virus, vaccine induced infection did not have immunosuppressive properties. Further, malnourished children did not exhibit any side-effects following vaccination and there was no evidence of any activation of latent tubercular lesions over a 3 month period of follow up. These observations indicate the effectiveness of measles vaccination and its safety even in communities simultaneously carrying the load of malnutrition and tuberculosis.

Measles vaccination and morbidity

Apart from these beneficial effects, measles vaccination was found to significantly reduce morbidity in children probably due to non specific stimulation of immune mechanisms by activating macrophages[4]. It has been reported that measles vaccine not only reduces morbidity and mortality related to measles but also prevents the risk of severe malnutrition in children who are already undernourished[18].

Measles vaccine was introduced in India through the Universal Immunization Programme (UIP) during 1985-86. In a recent retrospective case analysis (Bhaskaram P. *et al*, Unpublished observation), it was observed that the hospital admissions of children with measles and its complications were significantly (69%) reduced from the prevaccination to the postvaccination period. However, this reduction was far from the mid decade goal of

90% reduction of measles from the prevaccination prevalence. Mortality, however, registered a decline of 90% from the prevaccination to the postvaccination period. The observations also demonstrated that the incidence of measles significantly increased in older children (above 5 years) compared to the prevaccination period where almost 100% of the children were affected by measles before 5 years of age. Though the UIP focuses on infants, the prevalence of measles in infancy has not shown any significant decrease over the years. These observations demonstrate the changing pattern of measles in the community following the introduction of the immunization programme. Persistence of measles in infants despite vaccination at 9 months suggests inadequate coverage while periodic large outbreaks in the community indicate the accumulation of susceptible children who trigger the outbreaks. However, to achieve the goal of elimination of measles by at least 2010, there is need to intensify the measles vaccination programme and modify it so as to cover all susceptible children upto 5 years of age. This strategy is very essential not only to promote child survival but also to reduce malnutrition.

Poliomyelitis

Persistence of poliomyelitis in India has often been attributed to associated malnutrition. In a recent outbreak in Andhra Pradesh, it was observed that the prevalence of the infection was not related to the nutritional status[19]. Out of 400 patients of acute paralytic poliomyelitis investigated, 49.5% were wellnourished and 50.5% malnourished. In addition, it was observed that oral polio vaccine (OPV) conferred low herd immunity[20]. Lower antibody titres and also inadequate local immune response were noticed in natural infection as well as with OPV[21]. These impaired responses were not related to the nutritional status of the children. Thus, sub-optimal vaccine efficacy and interference by the enteroviruses in the gut, both being unavoidable problems in tropical countries, could be the factors responsible for the development of low levels of immunity leading to persistence of poliomyelitis in the country. Malnutrition does not seem to play any role in the persistence of poliomyelitis. Though the load of poliomyelitis has been significantly reduced following the implementation of the Pulse Polio Programme, a strong disease system has to be established to prevent resurgence of the disease.

Role of Nutrient Supplements in Vaccine Responses

Certain nutrients like ß carotene, vitamins A and D_3 are known to act as immune adjuvants. Among these, ß carotene and vitamin A have been found to reduce morbidity and mortality due to certain clinical conditions characterised by immunosuppression.

Immune Adjuvant Effects of Vitamin A

The immunological adjuvant effects of administration of vitamin A/β carotene are well documented . In a study carried out in preschool children, administration of 100,000 and 200,000 units of vitamin A was found to significantly enhance the production of bactericidal molecules like hydrogen peroxide (H_2O_2) by phagocytes. Non specific activation of immune cells resulted in increase in antibody production on antigenic challenge[22]. The large dose of 100,000 IU also led to increase in interleukin 1 production by *in vitro* activated macrophages[22].

Interactions between Vitamin A and the Viral Vaccines

Vitamin A deficiency is widely prevalent among children in developing countries. Apart from xerophthalmia in 5-10% of preschool children, there appears to be a much larger problem of subclinical vitamin A deficiency as evidenced by lowered serum retinol levels without obvious clinical manifestations in nearly 30-40% of the children including infants. Several studies have reported that even mild/subclinical forms of vitamin A deficiency could increase child morbidity by increasing susceptibility to mucosal infections and also increase mortality[23,24]. Vitamin A supplements were found to reverse these effects significantly [25]. In view of these beneficial effects of vitamin A, WHO has recommended the routine administration of 100,000 IU of vitamin A to infants above 6 months of age in developing countries to improve vitamin A status and also child survival. To achieve the maximum cost-effectiveness, this supplementation programme is linked with the Universal Immunization Programme[26].

Vitamin A supplements and seroconversion to measles vaccine

Recent studies from Indonesia, however, raised concerns about the possible immunosuppression that could be caused by large dose vitamin A administration along with measles vaccine in young infants who still possess transplacentally acquired maternal antibodies[27]. Thus the combined schedule of large dose vitamin A administration along with live viral vaccine administration to young infants has become a subject of intense debate[28].

In India, administration of 100,000 IU of vitamin A to infants of 9 months age at the time of measles vaccination has been introduced into the Expanded Programme on Immunization.

In a recent study conducted by Bhaskaram and Rao[29], seroconversion rates and vitamin A status of infants who received vitamin A dose at the time of measles vaccine were compared with those of the infants who received only the vaccine. Under existing field conditions, seroconversion to measles vaccine is generally low. However, in children who received vitamin A, a significantly higher percentage seroconverted to measles (84%) compared to those who received only the vaccine (63%). Vitamin A status of all the infants improved over the one month period of the study, the improvement being significantly higher in children who received vitamin A[29].

Vitamin A administration to mothers in puerperium and response to neonatal dose of OPV

In recent times, in countries with endemic vitamin A deficiency, the usefulness of administering a large dose of vitamin A with each dose of DPT and OPV to infants below the age of 6 months is suggested as a strategy to improve their vitamin A status. However, such an exercise frequently resulted in the intracranial tension being raised in a number of infants. Though the neurological significance of a transient rise in intracranial tension at this age is not known, it is not an acceptable phenomenon. Administration of about 200,000 IU of vitamin A to mothers soon after delivery has been suggested as an alternative strategy to improve the vitamin A status of the breastfed infants[30].

The WHO has recommended the routine administration of a dose of OPV to new borns within the first 3 days of life to supplement the routine 3 dose schedule in order to achieve better seroconversion rates[31].

About 100 women along with their infants were studied to examine the effect of administering a large dose of vitamin A to the mother soon after delivery and the sero-response to OPV administered to the breastfed newborns. Administration of a large dose of vitamin A to lactating mothers increased vitamin A levels in breast milk for a short period, thus increasing the vitamin A intakes of the infants. There was, however, no effect on the sero-response to OPV. Seroconversion rates to all the 3 types of polio viruses in the vaccine were comparable between infants belonging to mothers who received vitamin A and those who did not[32]. Thus, these studies document the safety of administration of live viral vaccines along with a large dose of vitamin A. This observation is of practical relevance in developing countries where the interactions between infection and malnutrition pose a serious threat to child health and survival.

Thus, malnutrition does not appear to be a contraindication to immunization programmes. Judicial supplementation of nutrients having immunoadjuvant properties could improve the results with certain vaccines.

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This write-up has been adopted from the article entitled "Nutrition - immunization interactions and relevance to child health" by Dr. P. Bhaskaram, published in the *Nutrition News 17(4):* 1996.

ABSTRACTS

Some Research Projects Completed Recently

Role of 'S' transactivator in hepatocarcinogenesis: *In vitro* expression and purification of transactivating proteins.

The study was carried out to elucidate the effect of 'S' (463-851) transactivator on various promotor enhancer systems; raise monoclonal/polyclonal antibodies against this transactivator protein prepared either by recombinant DNA method or by using synthetic peptides; and demonstrate and localize the transactivator protein in hepatocarcinoma cells.

The association of hepatitis B virus (HVB) in hepatocellular carcinoma (HCC) is well established. Insertional mutagenesis, transactivation by truncated X or pre S2/S regions and activation of growth regulated genes or oncogenes have been suggested as possible mechanisms for carcinogenesis. The transactivating properties of a frequently detected fragment, which form part of the 'S' reading frame, extending from 426 nt. to 855 nt., has been reported.

The clones were sequenced and subcloned into pRSET vectors in all the three reading frames and expressed using IPTG induction. A Western blot analysis was done using polyclonal anti HBsAg and the presence of 19.24 kDa functional protein in the correct reading frame was obtained. The expressed protein was checked for by commercial ELISA. However, the antigen could not be detected by ELISA in any of the three reading

frames. The 'S' protein was purified by SDA-PAGE and was used to raise polyclonal antibodies in rabbits. These polyclonal antibodies were then used to screen the presence of 'S' protein in hepatocellular carcinoma tissues. The 'S' region being a very small part of the surface region of the virus (426-824 ntds), could not be detected by immunofluorescence. The region, extending from 426-824 ntds was proved to be a generalized transactivator of the viral promoters and enhancers. Using chloramphenicol acyl transferase as a reporter gene, in transfection assays it was found to be capable of activating HIV promoter, HTLVI promoter, RSV promoter and enhancer, c-Fos and c-Jun promoter to a high degree.

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Interaction of melatonin and circadian rhythmicity in Antarctic conditions.

The study was carried out to evaluate the coupling pattern of melatonin and other circadian rhythmicity in the human subjects in Antarctic conditions and on rats under simulated Antarctic exposure of diversifying light and dark cycle. The experimental study was carried out on 42 male Wistar strain rats (200-300 g) divided into 3 groups *viz* normal (control without surgical intervention);sham operated; and superior cervical ganglionectomized. The human study was conducted on eight volunteers from the 12th Indian scientific expedition to Antarctica (Antarctic winter – extended dark conditions) and six volunteers from the 13th expedition (Antarctic summer – extended light conditions). The human volunteers, divided into two groups were given either beta adrenergic blocker (atenolol) or placebo.

The results of both the animal and human studies showed that under the influence of constant dark and light, sympathetic innervation to the pineal primarily has tonic inhibitory influence on the suprachiasmatic nucleus, the biological clock, which alters the amplitude and mean level of various rhythms to keep the synchrony and coupling of various physiological and hormonal rhythms. The rat study also provided convincing data for the presence of extra-sympathetic inputs (probably neuropeptide-Yergic and cholinergic) to the pineal which are stimulated only if melatonin level is severely depressed as in cases of absence of sympathetic innervation or on exposure to continuous light.

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Publications:

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ICMR NEWS

The following meetings of various technical groups/ committees of the Council were held:

Meetings of the Scientific Advisory Committees of the following ICMR Institutes/Centres:

National Institute of Cholera and Enteric Diseases, Calcutta	October 25-26, 1998
Central JALMA Institute for Leprosy Agra	November 13-14, 1998
National AIDS Research Institute, Pune	November 16-17, 1998
Enterovirus Research Centre, Mumbai	November 16-17, 1998
Rajendra Memorial Research Institute for Medical Sciences, Patna	November 16-17, 1998

Meeting of the Project Review Committee (PRC) held at New Delhi:

PRC for Cardiovascular Diseases, Urology, Gastroenterology, Nephrology, Geriatrics and Ophthalmology	October 30, 1998

Participation of ICMR Scientists in Scientific Events:

Dr. D.A. Gadkari, Director, National Institute of Virology, Pune, participated in a joint meeting of the United Nations Programme on HIV/AIDS (UNAIDS), WHO Global Programme on Vaccines and Immunization and the Japanese National Institute of Infectious Diseases, to discuss AIDS Vaccine in Asia : Needs and Opportunities at Tokyo (October 28-30, 1998).

Dr. Z.M. Patel, Dy. Director and Officer-in-Charge, ICMR Genetic Research Centre, Mumbai, participated in the VIII International Conference on Ultrasound at London (November 1-5, 1998).

Dr. N.K. Ganguly, Director-General, ICMR, delivered the keynote address at the International Symposium on Biotechnological Approaches to Parasitic and Bacterial Diseases at the Indian Institute of Chemical Biology, Calcutta (November 6, 1998).

Dr. K.D. Ramaiah, Sr. Research Officer, Vector Control Research Centre, Pondicherry, participated in a workshop on Economic Research Agenda for the Global Programme to Eliminate Filariasis at Atlanta (November 12-13, 1998).

Dr. Kamala Krishnaswamy, Director, National institute of Nutrition (NIN), Hyderabad, participated in a consultative meeting on Severe Anaemia in Pregnancy in India and Bangladesh at Dhaka (November 15-17, 1998).

Dr. B. Sivakumar, Dy. Director (Sr.Grade), NIN, Hyderabad, participated in a workshop on Micronutrient Fortification at Dhaka (November 18, 1998).

Workshop:

The ICMR-WHO Workshop on New Challenges in Intellectual Property Rights in Medical Research was organised in New Delhi during November 17-18, 1998. It was attended by Directors of ICMR Institutes, Chiefs of Technical Divisions of ICMR Hqrs, senior professionals from sister agencies and WHO representatives.

Annual Day Celebrations:

As part of the ICMR's Annual Day celebrations, the Council organised orations on (i) Molecular Biology: The Continuing Challenge by Prof. Asis K. Datta, Vice Chancellor, Jawaharlal Nehru University, New Delhi, and (ii) Perspectives in Medical Research in India by Prof. P.N. Tandon, Emeritus Professor, All India Institute of Medical Sciences, New Delhi on November 19, 1998.

ICMR AIDED SYMPOSIA/SEMINARS/WORKSHOPS/COURSES/CONFERENCES

Symposium/Seminar/Workshop/ Course/Conference	Date & Place	Contact Address
International Symposium on Major Histocompatibility Complex.	October 29 - November 1, 1998; (at New Delhi)	Dr. N.K. Mehra, Prof. and Head, Department of Histocompatibility and Immunogenetics, All India Institute of Medical Sciences, New Delhi-110029.
Precongress Workshop on Andrology and Male Infertility and National Congress on Andrology and Reproductive Medicine.	October 29 - November 2, 1998; (at Calcutta)	Dr. A.K. Bhattacharya, Organising Secretary of the Congress, Department of Biochemistry, University College of Science, Calcutta-700019.
Continuing Medical Education-cum-Workshop on Brachytherapy for Head and Neck Cancers and Breast Cancer	October 30 - November 1, 1998; (at Imphal)	Dr. Th. Tomcha Singh, Organising Secretary of the Workshop, Department of Radiotherapy, Regional Institute of Medical Sciences, Imphal-795004.
International Congress and Workshop on Recent Advances in Medical Toxicology and Legal Medicine	November 2-7, 1998; (at New Delhi)	Dr. O.P. Murthy, Organising Secretary of the Conference, Department of Forensic Medicine and Toxicology, All India Institute of Medical Sciences, New Delhi-110029.
International Conference on Medical Physics and XIX Annual Conference of Association of Medical Physicists of India	November 6-9, 1998; (at New Delhi)	Dr. M.M. Rehini, Organising Secretary of the Conference, Medical Physics Unit, Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi-110029.
Indo-Japanese Symposium on Frontiers of Electron Microscopy in the 21st Century and XXII Annual Meeting of Electron Microscopy Society of India	November 9-11, 1998; (at Hyderabad)	Dr. P.D. Gupta, Convenor of XXII EMSI Meeting, Centre for Cellular and Molecular Biology, Hyderabad-500007.
International Workshop on Adverse Drug Reaction Monitoring	November 9-12, 1998; (at Aligarh)	Prof. K.C. Singhal, Organising Secretary of the Workshop, Department of Pharmacology, J.N. Medical College, Aligarh-202002.

Symposium/Seminar/Workshop/ Course/Conference	Date & Place	Contact Address
International Workshop on Medical Mycology	November 16-21, 1998; (at Chandigarh)	Dr. A. Chakrabarti, Organising Secretary of the Workshop, Department of Microbiology, Post-graduate Institute of Medical Education and Research, Chandigarh-160012.
Seminar on Integration of Advances in Biostatistics into Medical Research	November 19-21, 1998; (at Vellore)	Dr. J. Richard, Prof. and Head, Department of Biostatistics, Christian Medical College, Vellore-632002.
International Conference on Organization and Management of Blood Transfusion Service, Plans and Policies	November 22-24, 1998; (at Mumbai)	Dr. Z.S. Bharucha, Prof. and Head, Department of Transfusion Medicine, Tata Memorial Hospital, Mumbai-400012.
Workshop on Ending Malnutrition by 2020: An Agenda for Change in the Millennium	November 23-26, 1998; (at Chennai)	Dr. S. Rajagopalan, Distinguished Fellow, M.S. Swaminathan Research Foundation, Chennai-600113.
Symposia on (i) Public Health Nutrition Problems; (ii) Frontiers in Nutrition Science; and (iii) Growth and Development of Children of South- East Asia	November 26-28, 1998; (at Hyderabad)	Dr. T.C. Raghu Ram, Joint Secretary, Nutrition Society of India, National Institute of Nutrition, Hyderabad-500007.
XI Annual Conference of Indian Society for Atherosclerosis Research and International Symposium/CME on Prevention of Coronary Artery Disease : Concerns and Perspectives	November 27-29, 1998; (at New Delhi)	Dr. S. Dwivedi, Organising Secretary of the Conference, Prevention Cardiology Clinic, University College of Medical Sciences, Delhi-110095.
XXXV Guha Research Conference 1998	December 1-5, 1998; (at Port Blair)	Dr. Lalji Singh, Convener, GRC 1998, Centre for Cellular and Molecular Biology, Hyderabad-500007.
All India Workshop/Training Course on Application of Direct Methods in Crystallography for Solving Small/ Medium sized Molecules	December 1-21, 1998; (at Chennai)	Dr. D. Velmurugan, Convener of the Workshop, Department of Crystallography and Biophysics, University of Madras, Chennai-600025.
International Conference on Quality of Psychiatric Care	December 2-4, 1998; (at Calcutta)	Dr. A.N. Chowdhury, Prof. and Head, Department of Psychiatry, Institute of Postgraduate Medical Education and Research, Calcutta-700025.
Seminar on Responsiveness in Pulmonary Tuberculosis – Clinical Relevance	December 12, 1998; (at Chandigarh)	Dr. S.K. Jindal, Head, Department of Pulmonary Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh-160012.
XXVIII Annual Conference of the Endocrine Society of India	December 14-16, 1998; (at Varanasi)	Dr. S.K. Singh, Organizing Secretary of the Conference, Department of Endocrinology, Institute of Medical Sciences, Banaras Hindu University, Varanasi-221005.
XXXI Annual Conference of the Indian Pharmacological Society	December 17-20, 1998; (at Lucknow)	Dr. V.N. Puri, Organisng Secretary of the Conference, Division of Pharmacology, Central Drug Research Institute, Lucknow-226001.
V International Symposium on Biochemical Roles of Eukaryotic Cell Surface Macromolecules	January 4-8, 1999; (at Bangalore)	Dr. A. Surolia, Convener of the Symposium, Molecular Biophysics Unit, Indian Institute of Science, Bangalore-560012.
National Symposium on Biological Control of Insects in Agriculture, Forestry, Medicine and Veterinary Science	January 21-22, 1999; (at Coimbatore)	Dr. K. Murugan, Organising Secretary of the Symposium, Division of Entomology, Department of Zoology, Bharathiar University, Coimbatore-641046.
VII Annual Meeting of Molecular Immunology Forum - 1999	February 13-15, 1999; (at Hyderabad)	Dr. Ashok Khar, Convener of the Meeting, Centre for Cellular and Molecular Biology, Hyderabad-500007.

COUNCIL'S TRAINING PROGRAMMES

Leprosy

At the Central JALMA Institute for Leprosy, Agra:

- Multidrug Therapy Orientation Course in Leprosy for Medical Officers (October 26-November 6; and December 7-18, 1998).

Reproductive Biology

At the Institute for Research in Reproduction, Mumbai:

- Workshop on Andrology for Clinicians (November 16-30, 1998)

Nutrition

At the National Institute of Nutrition, Hyderabad:

- Postgraduate Certificate Course in Nutrition (December 1, 1998-February 28, 1999).

Occupational Health

At the National Institute of Occupational Health, Ahmedabad:

- Training Course on Environmental Hygiene Practice (November 16-20, 1998).

Biomedical Statistics

At the Institute for Research in Medical Statistics, Chennai:

- Basic Course in Statistics for Medical Officers (November 30-December 6, 1998).

ICMR PUBLICATIONS

	Price(Rs.)
Nutritive Value of Indian Foods (1985) by C. Gopalan, B.V. Rama Sastri and S.C. Balasubramanian, Revised and Updated (1989) by B.S. Narasinga Rao, Y.G. Deosthale and K.C. Pant (Reprinted 1996)	23.00
Growth and Physical Development of Indian Infants and Children (1972, Reprinted 1989)	10.00
Studies on Weaning and Supplementary Foods (1974, Reprinted 1996)	15.00
A Manual of Nutrition (Second Edition 1974, Reprinted 1995)	6.00
Low Cost Nutritious Supplements (Second Edition 1975, Reprinted 1996)	5.00
Menus for Low-Cost Balanced Diets and School-Lunch Programmes Suitable for North India (Second Edition 1977, Reprinted 1994)	4.50
Menus for Low-Cost Balanced Diets and School-Lunch Programmes Suitable for South India (Fourth Edition 1996)	6.00
Some Common Indian Recipes and their Nutritive Value (Fourth Edition 1977, Reprinted 1995) by Swaran Pasricha and L.M. Rebello	10.00
Nutrition for Mother and Child (Fourth Edition 1994, Reprinted 1996) by P.S. Venkatachalam and L.M. Rebello	11.00
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Diet and Diabetes (Second Edition 1993, Reprinted 1997) by T.C. Raghuram,Swaran Pasricha and R.D. Sharma	18.00
Dietary Tips for the Elderly (1992, Reprinted 1997) by Swaran Pasricha and B.V.S. Thimmayamma	5.00
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Dietary Guidelines for Indians – A Manual (1998)	23.00
पोषण नियमावली (द्वितीय संस्करण 1974, पुनर्मुद्रण 1990)	6.00
अपने आहार को जानें (1997)	9.00

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