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## IMMUNITY IN LEPROSY : II. CELL MEDIATED IMMUNITY

A large body of evidence suggests that in lepromatous leprosy (LL) there is a selective unresponsiveness (anergy) of T cell response to *Mycobacterium leprae* antigens and therefore, the host is unable to mount an adequate cell mediated immunity (CMI) which could protect the host from the infection. In this form of the disease macrophages, primarily in the nerves, skin and mucous membranes get heavily infiltrated with the bacilli.

### CELLULAR INTERACTIONS IN CMI

The phagocytic cells (macrophages, Langerhans cells, dendritic cells), known to engulf and process the invading pathogens and their soluble products and also designated as antigen presenting cells (APCs) are capable of presentation of the processed antigens to the T cells through their receptors[150]. It has been well documented that at the initial stages of CMI response, T cells cluster around the surface of the APCs before transforming into blast cells. Thereafter, APCs release interleukin (IL-I) which induces the production of interleukin-2 (IL-2) by T cells alongwith expression of IL-2 receptors for multiplication by replication of these antigen specific lymphocytes for clonal expansion[151]. While such a clonal expansion goes on, the cellular interaction further liberates a variety of other interleukins (IL-I, IL-3, IL-4 to 8) and lymphokines [granulocyte monocyte colony stimulating factors, interferon-$\gamma$ (IFN-$\gamma$), tumour necrosis factor-$\alpha$ (TNF-$\alpha$)] which influence the morphological and functional behaviour of various CMI inducing cells. In general, all these cells consisting of activated mononuclear phagocytes, cytotoxic T cells, natural killer (NK) cells and lymphokine activated killer (LAK) cells create an environment of cell mediated immune effector population. Effector molecules like IFN-$\gamma$ and TNF-$\alpha$ are known to activate macrophages to make them more armed with enhanced production of toxic reactive oxygen intermediates (ROI), superoxide anions[152] and also by generation of reactive nitrogen intermediates (RNI)[153] for more effective killing of both intracellular and extracellular microbial agents. Further, IL-2 and IL-6 influence T-, NK- and LAK-cells to become cytolytic by increasing the perforin (pore forming protein) contents and leukolexin[154] in them. These interleukins are also known to modify the functions of other cells like endothelial cells, keratinocytes and Langerhans cells. All these factors collectively influence the cellular functions *in situ* and also further recruit appropriate cells from the circulation and ultimately lead to an immune granuloma formation for destruction of the invaders.

### CMI IN LEPROSY

#### Generalised Defect

Over more than two decades ago, researchers often reported on a generalised defect for CMI responses in LL. A majority of LL patients from different geographic origins and belonging to different ethnic groups have

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been shown to exhibit lowered intradermal skin reactions to a variety of reagents[134,155-165], allergic skin sensitization to a hapten[155,158,161-164,166] and homograft rejection[167]. In addition to this,a lowered response to antigen[168-172] or mitogen[155,169-181] induced lymphocyte transformation, number of T lymphocytes in the peripheral blood[180-185] and production of lymphokine[157,163] have been noted. However, from a few of the above studies it was also noted that within a group, showing generalised depression in CMI, many of the individuals actually did not exhibit any depression in CMI[163,166]. Further, in many studies[157,158,178,184] no depression of CMI was observed in the entire LL population although the patients remained unresponsive to *M. leprae* antigen.

It was further revealed that those who showed improvement in generalised CMI improved considerably after antileprosy treatment[162,177] but still showed unresponsiveness to lepromin reaction[185,186]. In a recent study of skin reactions against new tuberculin and lepromin in untreated LL patients, all have been shown to induce a very strong tuberculin reaction equivalent to those of controls while being negative to lepromin reaction[187]. This indicates that the state of unresponsiveness in LL patients is so specific to *M. leprae* that they are able to respond even to other mycobacterial antigens. The mechanism responsible for the generalised depression in CMI, if any, in LL is largely unknown. Muthukkaruppan *et al*[188,189] using OKT11 monoclonal antibody, a marker for CD2+ cells or SRBC receptor, noted a significant lowering in the number of T cells in the circulation as observed by earlier workers[180-185]. However, using a pan T cell marker (OKT3) they failed to find a reduction in the T cell number in the peripheral blood of LL patients. This observation alongwith a recent observation of the lack of alteration in the CD4/CD8 ratio in the peripheral blood of LL patients[190] strengthened the view that generalised CMI in LL remains almost unimpaired. However, the reported association of other diseases alongwith leprosy is very difficult to interpret. High incidence of tuberculosis[191], basal cell carcinoma[192] and lymphoma[193] in leprosy patients is very rare and may be related to some local environmental factors. Generally, it has been noted that whenever there is a generalised depression in CMI, an opportunistic infection take an upper hand which consequently invades the host, as is being observed in HIV-1 and HIV-2 infected individuals[194-196].

**Specific Defect**

Immunological basis for understanding the disease led to the establishment of a polar concept[6] in leprosy. Further, the finer classification of the disease spectrum has also taken into account the CMI response of the host to *M. leprae* antigen and has been reviewed elsewhere[8]. The depression for CMI in leprosy has always been determined using either whole or soluble antigen of *M. leprae in vivo* or *in vitro*.

*In vivo use of M. leprae*

*M. leprae* suspension designated as lepromin[197] or soluble *M. leprae* antigen[198,199] have been used to determine the CMI status of patients being classified under the Ridley-Jopling scale[5,6].

The lepromin reaction is an immunological skin test for leprosy first reported by Mitsuda[200]. This preparation termed Mitsuda antigen, now a whole bacillary suspension (40 million/ml) in normal saline, when injected intradermally evokes a weak 24-48 hour skin reaction and a strong 3-6 week skin reaction in sensitized individuals. Later Dharmendra[201] reported on a lepromin preparation of defatted bacillary suspension which has been subsequently standardised[202]. This antigen evokes both 24-48 hour and 3-4 week skin reaction equally well. After the successful purification of *M. leprae* from the infected armadillo tissue[203] it was possible to sonicate a large number of bacilli and the cell-free extract of *M. leprae* could be standardised by its protein content (10μg/ml)[198]. This soluble antigen evokes only 24-48 hour skin reaction.

Although a lepromin test has no diagnostic potential[197], it has a considerable prognostic value[6] and provides confirmatory evidence for classification of the disease. In most TT/BT patients the test is strongly positive while in BL/LL cases it is negative. The negative reaction in BL/LL leprosy patients tends to become positive after the reversal reaction. On the contrary, the positive reaction in tuberculoid leprosy tends to become negative before the occurrence of downgrading reaction.

It has been accepted that 24-48 hour skin reaction is an expression of pre-existing delayed type of hypersensitivity (DTH) to protein antigen of *M. leprae*. Although two kinds of soluble proteins were isolated from leprosy nodules by Abe[204], these proteins did not induce Mitsuda reaction. It has been proved beyond doubt that for generation of the 3-4 week skin reaction, the presence of whole intact bacilli in the skin antigen is essential[205]

*Use of M. leprae antigen in vitro*

As early as in 1973, Godal and Negassi[206] while studying the lymphoproliferative response to *M. leprae* antigen in different categories of people noted that individuals who were not in contact with the disease generally remained unresponsive whereas 80 per cent people who were exposed to leprosy for more than one year responded to the antigen. This observation pointed to the sensitization effect of normal individuals who were subclinically infected due to contact with patients. Myrvang *et al*[207] studied the lymphoblastic response of patients in the Ridley-Jopling scale[5,6] and noted a gradual fall in the lymphoproliferative response in TT through LL. Further, various *in vivo* and *in vitro* studies carried out earlier confirmed that lepromatous patients exhibit a long lasting anergy to *M. leprae* antigens, which has been extensively reviewed elsewhere[208,209].

Doubt has been expressed as to whether the lymphoproliferative response to specific antigen is an *in vivo* correlate of CMI or a measure of hypersensitivity and not a measure of resistance at all[210,211]. Experimental proof[212] is available in mice where challenge with different doses of *M. lepraemurium* in a susceptible strain resulted in infection (at a certain dose) alongwith a strong skin DTH reaction against the same pathogen. Moreover, human lymphocyte responses to antigen has been found to be variable on several occasions due to the presence of suppressive factors in the plasma of mothers with leprosy[213] and DDS in DDS treated patients[214]. Subsequently, it was also indicated that variability in the lymphoproliferation and leucocyte migration inhibition could be due to the heterogeneous nature of the antigens used in these assays[210,215,216].

It has been recently noted that a significant number of reactional BT patients (type 1 reaction) showed lowered *M. leprae* antigen induced lymphoproliferative response, suppressor cell generation and lymphokine production[217]. On the other hand, the lymphocyte responses showed much improvement in type I reaction of BB and BL patients[216]. Similarly, LL patients with ENL (type II reaction) generally showed heightened T cell reactivity to *M. leprae* antigen[185,218].

THE STATUS OF T CELL SUBSETS AND IN SITU PROFILE OF ACCESSORY CELLS AND CYTOKINES

**In Peripheral Blood**

Bach *et al*[186] and Wallach *et al*[219] noted, while studying the pattern of distribution of T cell subsets, a reduction in percentages of helper/inducer OKT4+ or CD4+) and suppressor/cytotoxic (OKT8+ or CD8+) cells in bacilliferous leprosy patients. On the other hand, the bacillary negative LL patients showed CD4+ and CD8+ cell numbers equivalent to those of controls. An increase in CD4+/CD8+ ratio was also noted in ENL patients which returned to normal after subsidence of reaction. In 1982, Mshana *et al*[190] while observing no change in the percentage of pan T (OKT3+ or CD3+) cells in TT, untreated LL and ENL patients and controls reported a reduced percentage of OKT4+ cells and increased percentage of OKT8+ cells resulting in a reduced OKT4+ OKT8+ ratio only in untreated LL patients. Further, they also established that during ENL reactions, the helper/suppressor ratio gets heightened due to the increase of helper and corresponding decrease in suppressor cell percentage. However, at the same time, Van Voorhis *et al*[220] reported an unaltered helper/suppressor cell population in all the disease types.

These studies gave an account of the percent population of the T cell subsets rather than their absolute values in the blood. While enumerating the absolute values of these subsets in a mixture of treated and untreated lepromatous patients, Bullock *et al*[221] noted a reduction in the total number of T cells and their helper and suppressor subsets. However, like the previous workers they also failed to record any change in the helper/suppressor ratio. Rea[222] using the same yardsticks observed a significant cytopenia of pan T, helper and suppressor cells in leprosy patients compared to normal individuals. However, when the results were expressed as percentage of total lymphocytes the differences in the groups were abolished. Even when the values of these parameters of ENL patients were compared with their control values no signifcant differences were observed.

Hence, from the afore-mentioned studies it becomes clear that the observed reduction in CD4+ cells with an increase in CD8+cells simply indicates a state of immunosuppression. On the other hand, enumeration of absolute numbers of these cells demonstrated a pan T-cell cytopenia but failed to find any abnormalities in CD4+/CD8+ ratios. Considering that lepromatous patients are not prone to get other infections which are known to inflict immunosuppressed individuals[196,223-227], it is more rational to assume that in lepromatous leprosy there is no real alteration in the CD4+ CD8+ ratios in the peripheral blood.

**In lesions**

*In situ* distribution of the T cell subsets with respect to their proportions and pattern of distribution in the tissues, the granuloma has been widely studied[220,228-231]. Van Voorhis *et al*[220] noted large number of T cells in leprosy lesions and the helper/suppressor ratio was found to be 5.6:1 in tuberculoid granuloma whereas in the lepromatous granuloma they noted this ratio to be as 1:1.8. In addition, they observed clusters of OKT4+ cells distributed in the form of rings in tuberculoid granuloma. OKT6+ cells, on the other hand, were scattered in both tuberculoid and lepromatous granuloma. In contrast to this, Narayanan *et al*[232] and Modlin *et al*[231] could not account for such a large number of T cells in the granuloma and the helper/suppressor ratio ranged mostly from 1.2 to 5.0 in tuberculoid and 0.2 to 1 in lepromatous lesions[232]. Moreover, Narayanan *et al*[232] unlike Van Voorhis *et al*[220] found that in tuberculoid granulomas (concentric variety) OKT8+ cells were scattered in a "ring like" fashion amongst lymphocytes. Conversely, OKT4+ cells showed a scattered distribution either singly or in clusters within the lymphocyte cuff as well as in association with epithelioid cell aggregates. Similarly, Modlin *et al*[230] found lymphocytes expressing CD8+ cells predominantly in the mantle, while CD4+ cells were seen in large numbers within the epithelioid cell aggregates. This type of histological distribution of T cell subsets has also been noted in tuberculoid granuloma of sarcoidosis[230], tuberculosis[230] and DTH skin reactions[233-236]. In addition, all these studies unequivocally showed all lymphocytes and macrophages of leprosy granulomas to be Ia positive.

Recently Narayanan and colleagues[237-239] isolated the granuloma infiltrated cells *in vitro* and studied their characteristics and functions[240]. The OKT4+ OKT8+ ratios were found to be similar to those in *in situ* situations. Functionally, the immune cells obtained from tuberculoid granulomas exhibited a high incorporation of $^{3}H$ thymidine and $^{14}C$ leucine. In contrast, cells from the lepromatous granulomas showed poor division without any impairment in their protein synthesis. A similar study[241] was carried out to compare the characteristics of infiltrates in skin and nerve granulomas of tuberculoid and lepromatous types. With the use of phenotypic markers, CD4+ and CD8+ cells of nerves showed similar distribution and proportions as observed with those of skin granulomas. Moreover, in tuberculoid granulomas a higher proportion of lymphocytes of both skin and nerves were activated T cells as compared to those in lepromatous granulomas. In both the types, granulomas were populated with mature macrophages which expressed HLA-DR (Ia) antigens. With regard to the helper/suppressor ratio in lesions of both type I and type II reactional cases it was noted that the ratio was more than 2 in the lesions[232]. Further, in type I reaction in BT leprosy, there was fall in the mean value of helper/suppressor when compared to that of untreated leprosy.

While working with T cell receptor (TCR) in the granulomas across the leprosy spectrum, reversal reaction and lepromin reaction, Modlin *et al*[242] noted 25-35 per cent of CD3+ cells in the granulomas of lepromin reaction and reversal reactions while in other types of leprosy these cells were ~5 per cent in the lesions. When sections of lesions were immunostained for TCR$\gamma\delta$ positivity, a 5 to 8-fold increase in the concentration of these cells was noted in granulomatous lesions, as compared to normal skin, lymphoid tissues and peripheral blood. Further, these TCR$\gamma\delta$+ T cells isolated from skin were shown to be specifically responsive to mycobacterial antigens. Finally, the finding of the supernatant of these activated cells to contain colony stimulating factor indicated that the $\gamma\delta$ bearing T cells may play a role in immune response by formation of a granuloma. Further, while expanding the T cells with *M. tuberculosis* ($H^{37}Ra$) stimulus it was noted that expansion of $\gamma\delta$+ T cells was greater (32±4%) in TT patients than in LL patients (9±2%)[243].

Accessory cells (Langerhans cells, keratinocytes) other than macrophages are known to play a pivotal role in the presentation of antigens to T cells and also have been shown to be associated with allergic contact sensitivity and hypersensitivity reactions[244-247]. Using phenotypic markers for T6 and Ia like antigens, Langerhans cells have been identified in leprosy lesions. While adequate numbers of these cells were noted in polar tuberculoid leprosy, the cells were virtually absent in polar lepromatous leprosy. However, Ia like antigens were also found to be associated with macrophages in these lesions[248]. Recent observations[249,250] have documented that during type I and type II reactions there is also a significant increase in Langerhans cells. Ia was seen in all keratinocytes in type I reaction whereas in ENL patients a patchy distribution of Ia positive keratinocytes was observed. All these events are indicative of a temporary T cell reactivity in the lesions

during manifestation of reactional phase. Further. Cooper *et al*[251] using mRNA probes for IFN-γ in *in situ* hybridisation in reversal reactional biopsy specimens have elegantly shown that there was a 10-fold rise in IFN-γ containing cells as compared to lepromatous patients who are not in reaction. When a probe for human serine esterase gene (huHF), a marker for cytotoxic T cells, was used, it was noted that expression of huHF serine esterase was four times more in the reversal reaction and tuberculoid lesions than those present in lepromatous lesions. Their study further confirmed a selective increase of CD4+ and CD8+ cells indicating a rise in DTH response which helps in killing bacilli and results in tissue damage. On the other hand, reduction in the expression of IFN-γ and serine esterase in an atmosphere of CD4+ rise and transient fall in CD8+ cells suggested a partial or transient boost in the CMI which may be sufficient for antibody production without any effect on bacillary clearance.

Very recently[252], the functional parameters for cytokine production for the locally proliferated immune cells have been worked out extensively in TT and LL groups. It was noted that while mRNAs encoding for IL-2 and IFN-γ were most evident in the TT granulomas, in LL granulomas mRNAs for IL-4, IL-5 and IL-10 were observed predominantly. Although definite cytokine profiles have been found to be associated with resistant and susceptible types of leprosy, no definite conclusion could be made towards the role of these lymphokines in the etiopathology of such lesions in leprosy.

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*To be contd.*

# ABSTRACTS

## Some Research Projects Completed Recently

**Assay of antibiotics in the body fluids of patients undergoing antibiotic therapy.**

The study was undertaken to determine the bioavailability of antibiotics in relevant body fluids in order to correlate *in vitro* susceptibility of the organisms and *in vivo* concentration of antibiotics with clinical response. Efforts were made to monitor the presence of high concentration of the antibiotics which may have toxic effects and to formulate modified dosage schedule in such patients as also to prevent certain antibiotics from reaching toxic levels especially in patients with impaired renal function.

In a group of 114 hospitalized patients of chronic lung diseases studied for serum levels of cephalexin, 26 (22.81%) showed normal levels (13-18 μg/ml), 48 (42.11%) less than normal levels and 40 (35.08%) above normal levels of cephalexin. Seventy (61.40%) patients showed good clinical response, 11 (9.65%) moderate and 33 (28.95%) poor clinical response after cephalexin therapy. Of the 40 patients showing above normal levels of cephalexin, 11 (27.5%) showed very high levels (more than 35 μg/ml). Schedule of therapy was modified in these patients to avert toxic effect.

Forty isolates of *Klebsiella pneumoniae* and 40 of beta haemolytic streptococci were isolated from 80 patients of chronic lung disease whereas the cultures were negative in 32 patients. All isolates of *K. pneumoniae* were sensitive to gentamicin, kanamycin and penicillin whereas 4 showed resistance to cephalexin. On the other hand all isolates of beta haemolytic streptococci were sensitive to cephalexin, ampicillin, gentamicin, and kanamycin but 11 were resistant to chloramphenicol.

Patients of typhoid on chloramphenicol (10) amoxycillin (10) and a combination (10) showed good clinical response in those on combination therapy. They had above normal serum levels of drugs. Patients with normal serum levels of drugs showed moderate clinical response. The study showed that the combination of drugs have a synergistic effect and patients showed better clinical response than the individual drug regimens.

In hospitalized patients with varying degrees of renal failure (30) and normal renal function (4), serum concentrations of gentamicin were below toxic levels (<10 μg/ml) in 28 (82.5%) whereas it reached toxic levels (≥10 μg/ml) in 6 (17.5%). The results suggest that regular antibiotic assays are essential to monitor the presence of high concentration of antibiotics which may have toxic effects in patients with impaired renal function.

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**Pathogenic fungal isolations from respiratory tract of patients with chronic lung diseases and malignancies.**

A total of 669 patients with chronic lung diseases and malignancies with suspected fungal lung infections were investigated. Efforts were also made to demonstrate the development of hypersensitivity and correlate the development of mycotic disease with pre-existing/pre-disposing disease or environment. The patients studied had haematological malignancies (51), bronchogenic carcinoma (9), pulmonary tuberculosis (110), pneumonia (85), lung abscess with pneumothorax (32), chronic bronchitis with bronchiectasis (26), bronchial asthma (32), allergic bronchopulmonary aspergillosis (98), aspergilloma (6) and other conditions such as chronic obstructive airways disease, seconadaries in the lung, pulmonary eosinophillia *etc.* (220).

Of the 51 patients with haematological malignancies, 19 showed significant growth of *Candida albicans*, one for *C. tropicalis* and 3 for *Aspergillus flavus*. Serology confirmed presence of *Candida* in 13 and *Aspergillus* in all 3 patients. In the case of bronchogenic carcinoma, 2 patients showed significant growth of *C. tropicalis* and one *C. albicans*. Serology was positive in two patients.

Of the 110 patients of pulmonary tuberculosis, 53 showed significant growth of *C. albicans*, 5 of *C. tropicalis*, 1 each for *C. krusei*, *C. guilliermondii*, *A. flavus* and *A. fumigatus*. Serology performed in 26 patients showed higher titres of *Candida* agglutinin in 12 patients, 11 of whom showed significant *C. albicans* isolation. Precipitin against *Aspergillus* was observed in 5 patients, with significant detection of *A. fumigatus* by smear and culture in one patient only.

Significant growth of *C. albicans* (11 patients), *C. tropicalis* (7), *C. parapsilosis* (1) and *A. flavus* (1) was found amongst 85 patients of pneumonia. Serology done in 25 patients confirmed *Candida* in 14 and *A. flavus* in one patient.

Of the 58 patients with lung abscess and chronic bronchitis, growth of *C. albicans* was observed in 22, *C. tropicalis*, *C. glabrata* and *Trichosporon cutaneum* in one each and *A. flavus* in 2 patients. Serology performed in 14 patients confirmed *Candida* in 4 and *Aspergillus* in 2 patients.

Amongst 220 patients with miscellaneous disorders significant growth of *Candida* was seen in 102, *A. flavus* and *A. fumigatus* in 2 each and *Cryptococcus neoformis* in one. Serology done in 60 patients confirmed *Candida* in 22 patients and *A. fumigatus* and *Cryptococcus neoformis* in one each.

Of the 32 patients of bronchial asthma, sputum sample of 7 patients showed significant growth of *C.*

*albicans* only, whereas of the 98 patients of allergic bronchopulmonary aspergillosis significant growth of *C. albicans* was observed in 15 patients from sputum and in 3 from throat swab. Culture of sputum grew *A. fumigatus* in 9, *A. flavus* in 5, *A. niger* in one and all these fungi in 2 patients. Amongst 6 patients of Aspergilloma, confluent growth of *A. fumigatus* was seen in 3 and *Aspergillus* sp. (unidentified) in 3 patients.

Serology, skin test as also total and specific IgE against *Aspergillus* were studied in 19 patients of bronchial asthma, 23 patients of allergic bronchopulmonary aspergillosis (ABPA) and 6 patients of aspergilloma. All the 19 bronchial asthma patients were negative on culture and immunodiffusion (ID) test. Type I hypersensitivity was observed in 7 patients who also had raised total serum IgE. Six of the 7 patients showed specific IgE by both RIA and ELISA. Of the 23 patients of ABPA, type I hypersensitivity was observed in 18 and type III in 3. Raised total IgE was observed in 17 of 18 patients, whereas specific IgE was observed by RIA in 6, ELISA in 9 and AB-ELISA in 7 of 12 patients. In case of patients of aspergilloma, type I hypersensitivity and raised total IgE was observed in 3 patients.

Significant fungal isolation was found in 38 per cent patients with testing of single sample as compared to 61.5 per cent with 2-4 samples and 77.3 per cent with 5 or more samples. Thus 5 or more samples on consecutive days helped in detecting more respiratory fungal infections.

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## ICMR NEWS

The following meetings of various Scientific Advisory Groups (SAGs)/Task Forces (TFs)/Expert Groups (EGs)/Project Review Committees (PRCs) and Review Panels of the Council were held:

| | |
|---|---|
| TF on Epidemiology and Management of Glaucoma | January 19, 1994 (at New Delhi) |
| PRC on ICRC Leprosy Vaccine Trials | January 19, 1994 (at New Delhi) |
| EG on Assisted Reproductive Technologies | January 24, 1994 (at Bombay) |
| Meeting of the Toxicology Review Panel of the Division of Human Resource Development Research | January 28, 1994 (at New Delhi) |
| Inter-departmental meeting of TF on Product Development for Indigenization of Copper T 200B Materials | January 28, 1994 (at New Delhi) |
| SAG of the Division of Epidemiology and Communicable Diseases | February 3, 1994 (at New Delhi) |
| SAG of the Division of Basic Medical Sciences | February 8, 1994 (at New Delhi) |
| PRC on Human Genetics, Immunology, Allergy and Physiology | February 9, 1994 (at New Delhi) |

**Participation of ICMR Scientists in Scientific Events:**

Dr. Arti Roy, Asstt. Director, Malaria Research Centre, Delhi, participated in the meeting on Clinical Disease and Pathogenesis of Malaria jointly organized by the Rockfeller Foundation and Special Programme for Research and Training in Tropical Disease of the WHO at Colombo (January 16-19, 1994).

Dr. D.K. Shukla, Asstt. Director-General, ICMR, New Delhi, participated in the Regional Scientific meeting of the International Epidemiological Association at Chiangmai, Thailand (January 23-28, 1994).

Dr. R. Prabhakar, Director, Tuberculosis Research Centre, Madras, participated in the 12th Annual Scientific meeting of the International Epidemiology Network at Chiangmai (January 23-29, 1994).

Dr. Veena Shatrugna, Asstt. Director, National Institute of Nutrition, Hyderabad, participated in the International Women's Health Conference (Cairo '94) at Rio de Janeiro (January 24-28, 1994).

**Honours/Awards:**

Dr. Sekhar Chakraborti, Deputy Director, National Institute of Cholera and Enteric Diseases, Calcutta, who is the recipient of Prof. S.R. Maitra Memorial Oration Award of the Physiological Society of India (1993) delivered the Oration on the "Quest for Prevention of AIDS: Drug and Vaccine Approaches" during the fifth Annual Conference of the Physiological Society of India held at Izatnagar on November 26, 1993.

**Conference/Workshop:**

An International Conference on Dengue Haemorhagic Fever and also a National Brain Storming Session on Dengue was organised by the National Institute of Virology, Pune on February 7-8, 1994.

## ICMR AIDED SYMPOSIA/SEMINARS/WORKSHOPS/COURSES/CONFERENCES

| Symposium/Seminar/Workshop/ Course/Conference | Date & Place | Contact Address |
|---|---|---|
| National Symposium on Reproductive Health Care. | February 4-6, 1994; (at Jaipur) | Dr. N.K. Lohiya, Organising Secretary of the Symposium, Department of Zoology, University of Rajasthan, Jaipur. |
| VI Biennial Conference of the Indian Society of Oncology. | February 4-7, 1994; (at Calcutta) | Dr. Jayasree Roy Chowdhury, Organising Secretary of the Conference, Chittaranjan National Cancer Institute, Calcutta. |
| National Thalassemia Conference. | February 5-6, 1994; (at New Delhi) | Dr. V.P. Chaudhary, Additional Professor, Department of Haematology, All India Institute of Medical Sciences, New Delhi. |
| Brain Storming Session on Dengue and International Seminar on Dengue, Haemorrhagic Fever and Shock Syndrome. | February 7-8, 1994; (at Pune) | Dr. Kalyan Banerjee, Director, National Institute of Virology, Pune. |
| Workshop on Palliative Care in Oncology. | February 8-9, 1994; (at New Delhi) | Dr. G.K. Rath, Organising Secretary of the Workshop, Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi. |
| National Symposium on Recent Advances in the Management of Viral Diseases. | February 8-10, 1944; (at Hisar) | Dr. R.N Srivastava, Organising Secretary of the Symposium, Department of Veterinary Microbiology, CCS Haryana Agricultural University, Hisar. |
| International Symposium on Genes and Human Development. | February 8-10, 1994; (at Hyderabad) | Dr. R. Rudrama Devi, Organising Secretary of the Symposium, Genetic Toxicology Division, Department of Zoology, Osmania University, Hyderabad. |
| I National Conference of Alzheimer's and related Disorders Society of India (ARDSI) on Trends in the Management of Dementia. | February 9, 1994; (at Madras) | Sri Ravi Samuel, Organising Secretary of the Conference, Department of Psychiatry, Govt. General Hospital, Madras. |
| National Convention on Recent Advances on Environmental Management for Vector-borne Diseases Control. | February 10-12, 1994; (at Dehradun) | Dr. R.K. Jauhari, Organising Secretary of the Convention, Department of Zoology, D.A.V. (Postgraduate) College, Dehradun. |
| National Symposium on Pigment Metabolism in relation to Disorders of Skin and Hair. | February 12-13, 1994; (at Calcutta) | Prof. D.P. Chakraborty, Convenor of the Symposium, Indian Science Congress Association, 14, Dr. Biresh Guha Street, Calcutta. |
| I National Symposium on Trauma, Anaesthesia and Critical Care. | February 18-19, 1994; (at Delhi) | Dr. R. Chawla, Organising Secretary of the Symposium, Department of Anaesthesia and Critical Care, University College of Medical Sciences, Delhi. |

| Symposium/Seminar/Workshop/ Course/Conference | Date & Place | Contact Address |
|---|---|---|
| VI All India Meeting for Women in Science. | February 18-20, 1994; (at New Bombay) | Dr. J.J. Nadkarni, Convenor of the meeting, Indian Women Scientists Association, Plot No. 20,Sector 10A, Vashi, New Bombay. |
| National Symposium of Chronobiology and IX Biennial Meeting of Indian Society for Chronobiology. | February 21-23, 1994; (at Lucknow) | Dr. Vinod Kumar, Convenor of the Symposium, Department of Zoology, University of Lucknow, Lucknow. |
| XI National Congress of Parasitology. | February 22-24, 1994; (at Udaipur) | Dr. P.N. Sharma, Organising Secretary of the Congress, Department of Zoology, College of Science, Mohan Lal Sukhadia University, Udaipur. |
| National Symposium on Alzheimer's Dementia. | February 25, 1994; (at New Delhi) | Dr. S.K. Khandelwal, Additional Professor, Department of Psychiatry, All India Institute of Medical Sciences, New Delhi. |
| I Conference of Vidarbha Chapter of the Anatomical Society of India and Symposium-cum-Workshop on Cytogenetics. | February 28, 1994; (at Sevagram) | The Head, Department of Anatomy, Mahatma Gandhi Institute of Medical Sciences, Sevagram, Wardha. |
| International Conference on Safe Motherhood in South Asia : Challenges Ahead. | March 3-5, 1994; (at Chandigarh) | Dr. R.S. Goyal, Conference Director, SID International Conference on Safe Motherhood, SCO-809-810, Chandigarh. |
| Indo-German Training Course and Workshop on Application of Flow-Cytometry in Cellular and Molecular Biology. | March 14-16, 1994; (at Delhi) | Dr. V.P. Bhardwaj, Course Coordinator, Institute of Nuclear Medicine and Allied Sciences, Delhi. |
| National Symposium on Cellular and Molecular Biophysics. | March 15-17, 1994; (at Chandigarh) | Dr. M.P. Bansal, Organising Secretary, Biophysics Symposium, Department of Biophysics, Punjab University, Chandigarh. |

## COUNCIL'S TRAINING PROGRAMMES FOR 1994-95

### Leprosy

*At the Central Jalma Institute for Leprosy, Agra:*

... Orientation Course in Leprosy for Medical Officers (January 31-February 11, 1994).

### Virology

*At the National Institute of Virology, Pune:*

... Diploma in Medical Virology (June 1994-May1995).

### Reproductive Biology

*At the Institute for Research in Reproduction, Bombay:*

... Workshop on Gynaecologic Cytology and Immunocytochemistry (September 26-October 1, 1994).

### Endocrinology

*At the National Institute of Nutrition, Hyderabad:*

... Annual Training Course on Endocrinological Techniques and their Applications (August/ September 1994).

### Nutrition

*At the National Institute of Nutrition, Hyderabad:*

... M.Sc in Applied Nutrition (June 1,1994-February 28, 1995).

... Annual Training Course in Nutrition (December 1, 1994-February 28, 1995).

**Occupational Health**

*At the National Institute of Occupational Health, Ahmedabad:*

... Orientation Course on Occupational Health for Industrial Medical Officers (September 19-24, 1994).

... Training Course on Air Pollution Monitoring and Risk Assessment (October 19-25, 1994).

... Training Course in Pesticide Residue Analysis (December 5-9, 1994).

**Medical Entomology**

*At the Vector Control Research Centre, Pondicherry:*

... M.Sc in Medical Entomology (from August 1994: for 2 years).

... Short-term Course on Malaria, Filariasis and Urban Vector Control for in-service candidates (June 1994).

**Laboratory Animal Technology**

*At the Laboratory Animal Information Service Centre, National Institute of Nutrition, Hyderabad:*

... Training Course for Laboratory Animal Technicians (June 15-July 31, 1994).

... Training Course for Laboratory Animal Supervisors (September 12- December10, 1994).

**Clinical Pharmacology**

*At the Seth G.S. Medical College, Bombay:*

... Training Course in Clinical Pharmacology (March 1-25, 1994).

## SOME AVAILABLE ICMR PUBLICATIONS

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| 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 | 18.00 |
| Growth & Physical Development of Indian Infants and Children (1972), Reprinted 1989 | 10.00 |
| Studies on Weaning & Supplementary Foods (1974), Reprinted 1984 | 6.00 |
| Studies on Pre-School Children (1974), Reprinted 1984 | 6.00 |
| A Manual of Nutrition, Second Edition (1974), Reprinted 1990 | 4.50 |
| Low Cost Nutritious Supplements, Second Edition (1975), Reprinted 1990 | 3.00 |
| Menus for Low Cost Balanced Diets and School Lunch Programmes Suitable for South India Third Edition (1977), Reprinted 1991 | 4.50 |
| Menus for Low Cost Balanced Diets and School Lunch Programmes Suitable for North India Third Edition (1977), Reprinted 1984 | 2.00 |
| Some Common Indian Recipes and their Nutritive Value, Fourth Edition (1977), Reprinted 1991, by Swaran Pasricha and L.M. Rebello | 10.00 |
| Nutrition for Mother and Child, Third Edition (1978), Reprinted 1991, by P.S. Venkatachalam and L.M. Rebello | 9.00 |
| Japanese Encephalitis in India, Revised Edition (1980) | 5.00 |
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| Nutrient Requirements and Recommended Dietary Allowances for Indians (1990) | 13.00 |
| Lathyrism: A Preventable Paralysis, Revised Edition (1983) | 3.50 |
| A Manual of Laboratory Techniques (1983), Edited by N. Raghuramulu, K. Madhavan Nair and S. Kalyanasundaram | 30.00 |

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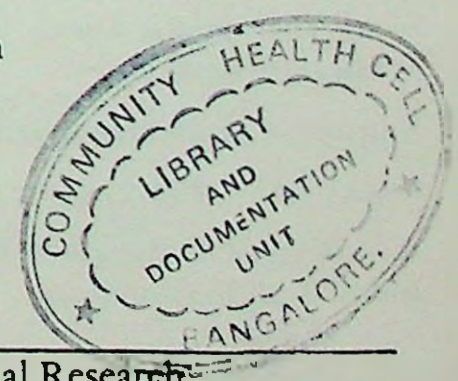



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