



ICMR BULLETIN

Vol. 29, No. 8

August, 1999

RISK OF ALUMINIUM TOXICITY IN THE INDIAN CONTEXT

Aluminium is widely used in the production of medicines like analgesics, antacids and anti-diarrhoeals besides finding use as a food additive and water purification agent. Aluminium also has wide industrial uses. It is still a metal of choice in the making of various kinds of household cookware and storage utensils.¹ Today, the annual production of aluminium amounts to about 22,000 metric tonnes world wide.

Sources of Aluminium Exposure

Environment

The exposure to Aluminium can be through food, water and airborne dust particles. Aluminium salts such as aluminium sulphate are used to flocculate the organic matter in water. The higher concentration of aluminium in vegetables from certain regions is probably due to soil contamination or acid rains. Certain plants like tea are known aluminium accumulators. Normal adults ingest an average of 2-5 mg Al/day through food and significant amounts from drinking water. Recent reports across the globe indicate that most individuals consume 1-10 mg aluminium/day from natural sources.²

Cookware/Packaging

One of the potential sources of additional dietary aluminium is aluminium cookware like skillets, pressure

cookers, roasting pans, sauce pans, frozen dinner trays, foils and wrappers. The usage of aluminium in packaging of food stuffs is on the increase and is becoming a potential source of contamination. A number of studies support the leaching of aluminium from cookware and packaging materials.³ However, the type of aluminium utensils (new or old), pH, form and composition of the food, duration of contact with the food during cooking and presence of salt, sugar and ions such as fluoride, chloride and carbonate are likely to affect the extent of leaching of aluminium into the food.

Foods

Aluminium containing food additives are generally used as buffers, neutralizing agents, dough strengtheners, leavening agents, emulsifying agents for processed cheese, stabilizers, thickeners, etc.⁴ These additives include sodium aluminium phosphate, sodium aluminium sulphate and aluminium silicate. Besides these, aluminium hydroxide or aluminium oleate may migrate from paper or paper board which are used for food packing.⁵

Medicines

The use of aluminium in over-the-counter drugs such as antacids, analgesics and anti-diarrhoeals has increased substantially in recent times. Aluminium containing

antacids are widely used and the most common form of aluminium in these preparations is aluminium hydroxide.⁶ Another major use of aluminium in antacids is as a phosphate binding agent, particularly, administered to renal patients to lower the elevated serum phosphate levels. The antacids are estimated to provide between 800-5000 mg/day of aluminium to such patients.⁷

Limits

According to the World Health Organization, the Provisional Tolerable Weekly Intake (PTWI) of aluminium as a contaminant (including that as an additive) is 7 mg/kg body weight for adults. For children, the acceptable daily intake (ADI) of 2 mg is commonly used for risk assessment.⁸ The recommendations for the PTWI are, however, based mostly on short-term toxicity studies and are therefore, subject to change as and when toxicological data from chronic toxicity studies become available.

Absorption

Aluminium is mostly absorbed through the oral route, though a certain amount is also suspected to be absorbed through the pulmonary route. The mechanism of intestinal absorption of aluminium is fairly complex and not yet fully elucidated. This is because of different types of aluminium chemical speciation, depending on pH, ionic strength and presence of complexing agents and other ions like iron²⁺, zinc²⁺, calcium²⁺ or magnesium²⁺ in the intestine.⁹ In more acidic solutions (pH < 5.0), aluminium exists as the octahedral hexahydrate $[\text{Al}(\text{H}_2\text{O})_6]^{3+}$, largely represented as Al^{3+} . Successive deprotonations yield $\text{Al}(\text{OH})^{2+}$ and $\text{Al}(\text{OH})_2^{+}$, with increasing pH. In neutral solutions, aluminium precipitates as amorphous $\text{Al}(\text{OH})_3$ and slowly begins to redissolve and forms tetrahydral $\text{Al}(\text{OH})_4^-$. Ions such as fluoride, lactate, etc., form soluble complexes with aluminium and thus prevent precipitation of aluminium and increase absorption.^{10,11} There is evidence to show that aluminium interacts with the gastrointestinal calcium transport system and also with transferrin mediated iron uptake. There is consistent evidence that absorption of aluminium increases in the presence of citrate through formation of soluble aluminium citrate complex.¹² There are some data suggesting that aluminium absorption increases after fasting. The aluminium levels in the blood of healthy, occupationally unexposed humans are reported to be around 5 µg/l. The highest levels are found in tissues such as bone, liver and lung.

Toxicity

That aluminium is a potential toxin was known almost five decades ago. While the neurotoxic potential of aluminium is undisputed in various animal species, there is as yet no strong evidence to suggest that aluminium could be toxic to normal healthy humans. However, neurotoxicity of aluminium is well documented in individuals with renal insufficiency in whom aluminium excretion is compromised. The accumulation of aluminium in the body is reported to cause disorders related to bone, blood and brain.¹³ There is increasing evidence that Al^{3+} may affect many neurochemical processes in the central nervous system. These biochemical alterations are affected by influencing nuclear, cytoplasmic and cytoskeletal structures, blood components, membrane integrity, enzyme activities and neurotransmitter functions which may ultimately lead to altered memory/behavioural disorders.¹⁴⁻¹⁶

Diseases Caused by High Intake of Aluminium

Dialysis dementia (Aluminium dialysis encephalopathy)

This neurological syndrome was first described in patients who had long-term haemodialysis for chronic renal failure. This disorder is clinically characterized by changes in the electroencephalogram (EEG) followed by speech disorders, development of psychosis, progressive dementia, convulsions, loss of memory, movement disorders, myoclonic jerks and seizures followed by death within a year. A number of epidemiological studies from Europe recognised that in geographical areas where patients with dialysis dementia were detected, there was a high incidence of osteomalacia leading to fractures. It was also seen that the municipal water used in haemodialysis in renal patients contained high concentration of aluminium.¹⁷⁻¹⁹

Bone diseases

Bone is the major accumulator of aluminium in the body and consequently there are several bone diseases associated with increased plasma aluminium concentrations. The most common aluminium-induced bone diseases are renal osteodystrophy (low turnover osteomalacia), aplastic bone disease and bone disease associated with total parenteral nutrition.²⁰⁻²²

Microcytic anaemia

This condition has been known to occur in renal patients with increased plasma aluminium levels, however,

without iron deficiency. Reports show that reduced haemoglobin levels, preceded by microcytosis, result as a specific toxic manifestation of aluminium exposure²³.

Senile dementia of the Alzheimer's type (SDAT)

Dementia is the most common disorder of the elderly and nearly 46% of the population over the age of 85 years meet the diagnostic criteria for dementia. The most common form of dementia is reported to be that of the Alzheimer's disease (AD) type. It is a progressive neurodegenerative disorder with the clinical features of rapid loss of memory, inability to perform simple intellectual tasks, reduced flexibility, disorientation, speech problems, mental deterioration and emotional instability.^{24,25}

After the appearance of the first symptoms, the disease slowly progresses leading to death in 4-12 years. AD has been recognised as the main cause of neurodegeneration in the developed countries and accounts for nearly 75% of all dementias in the aged²⁶. Five per cent of the population aged above 65 years is estimated to be affected by Alzheimer's disease.

In India, no epidemiological survey has been carried out regarding dementia and dementing illness and therefore, data are scanty. However, AD is present in India although the age related prevalence rates are not available to permit comparisons with the West. It is reported that 30-38% of cases of dementia in India were in the group of senile and presenile dementia of the Alzheimer's type²⁷. Due to the changing demographic pattern, as longevity increases, the incidence of AD could well go up in the Indian population. Certain experimental and epidemiological evidences suggest that aluminium exposure is a risk factor in the etiopathogenesis of AD in humans. Though the evidence regarding the role of Al in the etiology of AD is equivocal, it must still be regarded as a possible risk factor in the pathogenesis of the disease. The focal accumulation of aluminium in brains of AD patients and its possible role in the senile plaques and neurofibrillary tangles cannot be ruled out. There are strong epidemiological evidences²⁸ which indicate a positive role of aluminium in AD. These include—

- (i) About eight studies conducted in five countries suggest a statistically significant association between the concentration of aluminium in drinking water and the number of AD cases.
- (ii) At least ten laboratories from four continents have reported elevated levels of aluminium in brain tissue from AD patients.

(iii) Other neurological disorders such as epilepsy, Parkinsonism, amyotrophic lateral sclerosis and diseases predisposing to multiinfarct dementia are not associated with increased concentrations of aluminium in drinking water.

(iv) Chelation of aluminium by desferrioxamine lowers the body and brain aluminium content and retards the progression of AD.

However, the precise pathogenic role of aluminium in AD is still controversial and highly debated as the studies in this area still fail to extrapolate the experimentally induced neurological changes in animals to the human situation.

Effect on respiratory tract

Historically, pulmonary fibrosis has been associated with various types of occupations within the aluminium industry. Occupational aluminium exposure is reported to cause pathological lung functions, abnormal chest X-rays, development of intestinal fibrosis²⁹, etc.

Effect of Nutrients and Dietary Factors

Recent evidences indicate that absorption of aluminium is much higher when certain organic acids such as citrate, lactate and ascorbate are present in the diets. It is reported that aluminium absorption increases several fold both in humans and other animals when it is ingested in small amounts (<5 mg) as compared to the absorption involving pharmaceutical doses (1-3g). Chronic nutrient deficiencies of certain divalent metals have been shown to induce an abnormal metabolism leading to the accumulation of non-essential elements. In addition, aluminium is reported to have a slow turnover in the body and therefore might accumulate in tissues over a long period of time^{30,31}.

Sub-populations at Risk

Aluminium toxicity has been reported to develop over weeks or months in patients with chronic renal failure when dialysis fluids or parenteral solutions contained aluminium, or when higher aluminium was ingested through aluminium containing oral phosphate binders. The increased aluminium content in brains of patients with renal failure seems to be major etiological factor in the development of dementia³².

The development of a specific form of osteomalacia and of microcytic, hypochromic anaemia is attributed to

aluminium. It has been demonstrated that aluminium absorption is modified by the presence of minerals such as iron, calcium and zinc in the medium. Iron deficiency is shown to be widely prevalent and the calcium intakes are sub-optimal in most of the Indian population, especially in children and pregnant and lactating women. Hence, these groups are at risk due to aluminium absorption. It is important to note that because of the wide use of aluminium cookware and storage vessels, the intake of aluminium by Indian population could be much higher than what has been reported for the West.

NIN Studies

Aluminium content of cooked foods

Extensive data are available from the western literature regarding the risk of aluminium toxicity, while it is scanty from India. As aluminium vessels are the most commonly used cookware in rural and semi-urban India, a study was undertaken to assess the contribution of aluminium cooking utensils to the total daily intake of aluminium. In addition, several commonly consumed food items were analysed for their aluminium content. The study revealed that the major contribution of aluminium from Indian foods are through consumption of vegetables, spices and pulses. Cereals, milk and milk products contribute negligible amounts. Green leafy vegetables and *sambar* (a popular legume and gravy-based preparation) contribute significantly to the total daily aluminium intake. Usage of aluminium utensils significantly contributes to the total daily aluminium intake and the type of food preparation determines the extent of leaching of aluminium from the vessels. More acidic food preparations containing green leafy vegetables, tomato containing *dhal* (split pulse)/*sambar*, etc., cause greater leaching of aluminium into food from the utensils. It appears that the daily intake of aluminium in certain populations where aluminium utensils are regularly used could be much higher when compared to those who use stainless steel cookware. New aluminium vessels contribute greater amounts of aluminium when green leafy as well as other vegetables and legume preparations are cooked in them (Table I).

Effect of Ca/Fe deficient diets on aluminium absorption

Aluminium has been implicated in diseases of the brain, bone and blood. Recent evidences suggest that certain nutrient deficiencies like iron and calcium deficiencies might enhance aluminium absorption and hence its toxicity³³.

Table I. Aluminium content of cooked food (µg/100 g)

Food commodities	No.	Type of vessel used for cooking		
		Stainless steel	Old aluminium	New aluminium
Vegetables	6	1.26 (0.66-2.71)	1.45 (0.97-2.75)	1.80 (1.3-2.81)
Leafy vegetables	4	7.36 (3.79-11.07)	10.73 (4.39-21.70)	13.37 (4.85-30.7)
Pulses (Redgram)	5	3.41 (0.94-6.65)	4.06 (0.97-7.23)	9.24 (1.93-22.2)
Roots & Tubers*				
Yam	2	1.57	4.80	4.80
Potato	2	1.08	1.46	1.68
Cereals (rice)*	2	0.32	0.50	0.85

* Average of two observations

Studies conducted on experimental rats showed that dietary factors such as citrate and nutritional deficiencies of essential minerals such as calcium and iron can significantly enhance aluminium absorption and tissue accumulation especially over a long period. The effects of long-term feeding of aluminium rich diets on age-associated degenerative changes, as reflected by alterations in specific parameters of neuronal function, were investigated. It was found that some of the direct effects of aluminium observed *in vitro* could be produced *in vivo* through dietary aluminium feeding in both iron deficient and calcium restricted rats. These include inhibition of brain hexokinase (glucose utilization), mitochondrial respiration (cerebral oxidative metabolism), choline acetyl transferase activity (cholinergic function) and depletion of intra-synaptosomal free calcium levels. Attempt was made to corroborate these biochemical changes with lesions in the cytoskeletal architecture, if any, to arrive at definite conclusions regarding neurodegenerative changes in experimental rats, attributable to aluminium. The results showed that the reduction in the brain protein kinase C (PKC) activity and also cytoskeletal abnormalities as revealed by increase in microtubule associated protein - tubulin associated unit (MAP -Tau) and neurofibrillary protein, (NF-200), and the tangle bearing neurons were found only in calcium restricted rats on moderately high aluminium diet (Table II). These observations suggest that aluminium-calcium interactions are perhaps more important in the development of characteristic neuropathology in chronic age associated aluminium toxicity state when compared to aluminium-iron interactions. Thus it appears that aluminium is able to

exert a greater toxicity in states of calcium restriction. It was also found that anaemic individuals have higher circulating aluminium levels perhaps due to higher intestinal absorption and binding to transferrin, which has more number of sites unsaturated in iron deficiency.

Table II. Effect of iron and calcium deficiency on parameters related to neuronal function in the brain of experimental rats.

Parameters	Fe deficiency + high Al	Ca restriction + high Al
Aluminium levels	↑	↑
Hexokinase	↓	↓
Oxidation of succinate	↓	↓
Succinate dehydrogenase	↑	↑
Oxidation of malate	—	↓
Malate dehydrogenase	—	—
Choline acetyl transferase	↓	↓
Membrane PKC	—	↓
Cytosolic PKC	—	↓
Synaptosomal membrane fluidity	↓	↓
Synaptosomal (Ca ²⁺) _i	↓	↓
Neurofibrillary tangles	—	↑
Tau: no. of cells	—	↑
NF-200		
intensity	—	↑
no. of cells	—	↑

The changes in Fe deficiency or Ca restriction were compared with respective normal Fe and Ca sufficient groups receiving some levels of aluminium. There were no significant changes in Na⁺, K⁺-ATPase, Mg²⁺-ATPase, acetylcholine esterase, Tau-intensity and gross histology.

Tau: Tubulin Associated Unit; PKC: Protein Kinase C; NF: Neurofibrillary protein

↑ : Significantly increased ; ↓ : Significantly decreased ; — : Change is statistically not significant.

Biomonitoring

Hazards to neurological development and brain function from exposure to aluminium have been identified through animal studies. However, aluminium has not been demonstrated to pose a health risk to healthy non-occupationally exposed humans. Aluminium has a very low absorption rate (1%) and also slow turnover in the body. Therefore, the risk of aluminium toxicity is probably due to prolonged chronic exposure. A single analysis of blood or urinary aluminium at one time point does not indicate aluminium toxicity. Hence, keeping in view the epidemiological evidence of high aluminium in drinking water with the incidence of SDAT along with experimental evidence from animal studies, reduction/control

in the intake of aluminium by patients with renal failure and aged persons is advisable. Meanwhile, regular monitoring of plasma aluminium levels in haemodialysed patients and those at risk for aluminium toxicity should be made mandatory. The use of aluminium cookware should be limited. While they are safe to use for most cereal preparations, their use for the preparation of acidic foods such as tomato/tamarind containing *dhal/sambar* and green leafy vegetables should be avoided, since leaching of aluminium from the vessel into food preparations occurs in greater proportions.

Conclusions

Aluminium is among the most plentiful elements in the earth's crust. Experimental evidence suggests that aluminium is a potent neurotoxin. Human exposure to aluminium has increased markedly and in the present scenario, man is more prone to absorb higher amounts of aluminium. Several disorders of the nervous system such as dialysis dementia, senile dementia of the Alzheimer's type, Parkinson's dementia besides osteodystrophy and dialysis associated arthropathy have been associated with increased ingestion of aluminium. Dietary factors like citrate and sub-optimal intake of nutrients like iron and calcium are shown to enhance the gut absorption of aluminium. Investigations also revealed that chronic exposure of rats to high aluminium on calcium-restricted diets resulted in neurodegenerative changes in ageing rats, as identified by formation of neurofibrillary tangles and abnormal accumulation of MAP-Tau and NF-200 proteins along with impairment in certain physiologically important biochemical functions in the brain. Being a metal of very slow turnover, there is perhaps no escape from the aluminium load in the body making it necessary to minimize chronic exposure to high levels of aluminium, especially through diet and water.

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ABSTRACTS

Some Research Projects Completed Recently

Cellular manifestations of p53 and bcl-2 genes in ovarian carcinoma

The study was carried out to determine the extent of apoptosis in various ovarian tumours and correlate it to the

expression of apoptosis regulatory genes p53 and bcl-2 as well as the total proliferative compartment of the tumour defined by the expression of the proliferating cell nuclear antigen (PCNA). Patients (138) with various histopathological

types, stages and grades of ovarian carcinoma were included in the study. Of these, 24 patients had benign cystadenomas and were grouped as controls. The malignant tumours were further sub-divided to include 51 patients with serous, 26 with mucinous, 18 with endometrioid, 6 with clear cell and 13 with undifferentiated carcinomas.

Expression of p53 and bcl-2 oncogenes were analysed by immunocytochemistry and Western blot assay. The levels of mutant p53 was estimated using a mutant specific p53 ELISA. Apoptosis was evaluated by analysing the presence of nucleosomes by ELISA and further confirmed by the TUNEL (Tdt-mediated dUTP biotin nick end labelling) assay.

The bcl-2 gene was found to be expressed predominantly in benign cystadenomas. It was also expressed by endometrioid carcinomas. However, it was mostly absent in serous tumours, clear cell carcinomas and undifferentiated carcinomas. None of the benign lesions expressed p53 while most of the undifferentiated (77%) and serous carcinomas (59%) expressed the protein. ELISA results for mutant p53 closely correlated with the immunocytochemistry data. The tumour proliferative compartment analysed by PCNA expression was also maximum in undifferentiated carcinomas and serous tumours. The presence of p53 protein and expression of PCNA were significantly correlated, supporting a major role of p53 in the regulation of cell proliferation in ovarian tissue. The lack of correlation between bcl-2 and PCNA suggested that bcl-2 is not a major regulator of cell proliferation. Higher levels of apoptosis were seen in mucinous carcinoma compared to the other tumour subtypes. Mucinous carcinoma also had lower levels of bcl-2 expression. There was an increased apoptosis and bcl-2 expression in benign cystadenomas.

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Serodiagnosis of invasive aspergillosis.

The study was carried out to identify and purify immunodominant antigens from circulating antigens of *Aspergillus fumigatus* present in invasive aspergillosis as also to evaluate the purified immunodominant antigens in antibody and antigen detection tests for the diagnosis of invasive aspergillosis in experimentally infected mice and in patients suffering from invasive aspergillosis. Crude antigens of the two strains used in the study (standard strain *Aspergillus fumigatus* ATCC 13077 and clinical isolate *A. fumigatus* MCC LS 77,0010) were prepared and rabbit hyperimmune sera raised against the respective crude antigens (CF-73, MYC-73 and C-10) were used for detection

of circulating antigens. Acute invasive aspergillosis was established in cyclophosphamide treated adult Swiss albino mice. After infection 100% mortality was observed in mice within four days of infection.

After the establishment of experimental animal model of acute invasive aspergillosis circulating antigens were detected by Western blotting. Prominent protein bands were found at 18 kDa position using anti CF-73 antibody. Prominent bands at 44 kDa regions were seen with anti C-10 antibody. Similarly anti-MYC-73 antibody produced prominent bands at 89 kDa region. These three immunodominant antigens (18, 44 and 89 kDa) were chosen for purification and further studies.

The 18 kDa antigen was purified using sepharose CL-6B gel filtration and Sephadex G-50 column chromatography. The 44 and 89 kDa proteins were purified by gel electrophoresis.

Various serological procedures were evaluated for the detection of antigen and antibody in experimental murine model of acute invasive aspergillosis as well as in patients of acute aspergillosis. The latex agglutination test and ELISA were used for antigen detection. Latex agglutination showed a sensitivity of 55% and specificity of 100% whereas ELISA showed 72% sensitivity and 96.6% specificity. Sensitivity of Pastorex latex agglutination was found to be 70%. The 18 kDa antigen detection ELISA in patients had a sensitivity of 77% in the immunosuppressed and 71.4% in the non-immunosuppressed patients.

Antibody detection was carried out by gel diffusion and ELISA. Overall, lower sensitivity and 100% specificity was observed in gel diffusion against all the three purified antigens. The highest sensitivity of 29% was found against 44 kDa antigen. The immunosuppressed patients had a sensitivity of 18.7-25% while the non-immunosuppressed patients 28.5-51.1%. The ELISA showed 80% sensitivity against 44 kDa antigen and 71% against 18 kDa and 89 kDa antigens. The specificity was 96.6% against all the 3 antigens. The highest sensitivity of 85.7% was observed against the 44 kDa antigen in the non-immunosuppressed patients and 75% against 89 kDa antigen in the immunosuppressed patients.

It is concluded that the ELISA for antigen detection against 18 kDa antigen is a better diagnostic test as compared to latex agglutination and amongst the antibody detection tests the ELISA using 44 kDa antigen is promising as compared to gel diffusion.

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ICMR NEWS

The XI meeting of the Directors of the ICMR Institutes/Centres located in different parts of India was held at New Delhi on August 4, 1999.

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

Meetings of the Expert Groups (EGs)/Scientific Advisory Group (SAG)/Task Force (TF)/Project Review Committee (PRC) held:

EG on Phase III Clinical Trial July 14, 1999
on "Risug" (Styrene maleic anhydride (at New Delhi)
dissolved in DMSO) as injectable
intravasal male contraceptive

EG on Phase II Clinical Trial on July 23, 1999
Praneem (at New Delhi)
and
August 10, 1999
(at Mumbai)

EG on Infertility and Assisted July 31-
Reproductive Technologies August 1, 1999
(at Mumbai)

SAG of the Division of August 5-6, 1999
Epidemiology and Communicable (at New Delhi)
Diseases

PRC on Mental Health, Neurology August 9, 1999
Orthopaedics, Environmental (at New Delhi)
Hygiene and Biomedical
Engineering

TF on Feasibility of Using August 10-11, 1999
Syndromic Approach for (at Calcutta)
Diagnosis and Treatment of
RTI/STD at PHC Level

Participation of ICMR Scientists in Scientific Events :

Dr. A.K. Gupta, Assistant Director, National Institute of Virology, Pune, participated in the XI International Congress of Virology at Sydney (August 9-13, 1999).

Book Fair

ICMR participated in the fifth Delhi Book fair, organised at Pragati Maidan, New Delhi (August 14-22, 1999)

ICMR AIDED SYMPOSIA/SEMINARS/WORKSHOPS/COURSES/CONFERENCES

Symposium/Seminar/Workshop/ Course/Conference	Date & Place	Contact Address
International Symposium on Atraumatic Restorative Treatment	August 12-14, 1999; (at Chennai)	Dr. S. Balagopal, Organising Secretary of the Symposium, SHIRAZ-47, 3rd East Street, Kamraj Nagar, Chennai-600041.
Biennial National Conference of the Association of Gerontology on Challenges of Ageing in the 21st Century	August 20-21, 1999; (at Hyderabad)	Sh. K.R. Gangadharan, Organising Secretary of the Conference, c/o Heritage Medical Centre, 7-1-59/4 & 8, Ameerpet, Hyderabad-500016.
Symposium on Cardiology for the Next Millenium	September 10-12, 1999; (at Chennai)	Dr. S. Thanikachalam, Director, Cardiac Care Centre, Porur, Chennai-600016.
Symposium on Research in Molecular Biology and Biotechnology in India: Challenges in the Next Millenium	September 13-14, 1999; (at Calcutta)	Dr. A.N. Bhaduri, Indian Institute of Chemical Biology, Jadavpur, Calcutta-700032.
International Seminar on Disability Caused by Mental Disorders	September 15-17, 1999; (at Chennai)	Dr. R. Thara, Organising Secretary of the Seminar, Schizophrenia Research Foundation, R/7A, North Main Road, West Anna Nagar Extn, Chennai-600101.
XXI Biennial Conference of Indian Association of Leprologists	September 17-19, 1999; (at Chandigarh)	Dr. Bhushan Kumar, Organising Secretary of the Conference, Department of Dermatology, Venereology and Leprology, Postgraduate Institute of Medical Education and Research, Chandigarh-160012.

Symposium/Seminar/Workshop/ Course/Conference	Date & Place	Contact Address
National Symposium and Update on Problem Areas in Diagnostic Oncopathology	October 8-10, 1999; (at Sevagram)	Dr. N. Gangane, Organising Secretary of the Symposium, Department of Pathology, Mahatma Gandhi Institute of Medical Sciences, Sevagram, Wardha-442102.
International Conference on Man, Environment and Nature	November 26-28, 1999; (at Calcutta)	Prof. Sunimal Chanda, Convenor of the Conference, Centre for Study of Man and Environment, Parivesh Kendra, CK-11, Sector-2, Salt Lake City, Calcutta-700091.
International Symposium on Chemotherapy: Problem and Perspectives in 21st Century	November 28-29, 1999; (at Lucknow)	Dr. R.C. Saxena, Head, Department of Pharmacology, K.G. Medical College, Lucknow-226003.
Indo-European Seminar-cum-Workshop on Advances in Human Cytogenetics	December 6-9, 1999; (at Lucknow)	Dr. S.S. Agarwal, Head, Department of Medical Genetics, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow-226014.

COUNCIL'S TRAINING PROGRAMMES FOR 1999-2000

Leprosy

At the Central JALMA Institute for Leprosy, Agra:

- Training Course for Medical Officers Working under the National Leprosy Eradication Programme (September, 1999).

Reproductive Biology

At the Institute for Research in Reproduction, Mumbai:

- Training Course in Molecular Techniques in Ovarian Function (September 27-October 2, 1999).
- Training Course on Cytological Detection of Reproductive Tract Infections (December 13-17, 1999).

Endocrinology

At the National Institute of Nutrition, Hyderabad:

- Annual Certificate Course on Endocrinological Techniques and their Application (August 1 - September 15, 1999).

Nutrition

At the National Institute of Nutrition, Hyderabad:

- M.Sc. in Applied Nutrition (June 1, 1999-February 28, 2000).
- Postgraduate Certificate Course in Nutrition (December 1, 1999-February 28, 2000).

Laboratory Animal Technology

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

- Training Course for Laboratory Animal Supervisors (September 1-November 30, 1999).

Medical Entomology:

At the Vector Control Research Centre, Pondicherry:

- Postgraduate Diploma Course in Medical Entomology (from July 1999).

Biomedical Statistics

At the National Institute of Epidemiology, Chennai:

- Training Course in Field Epidemiology (November, 1999).

Haematology

At the Institute of Immunohaematology, Mumbai:

- Training Course in Transfusion Medicine for Blood Bank Medical Officers (August 31-October 29, 1999).
- Training Course in Blood Group Serology and Blood Bank Methodology for Blood Bank Technicians (August 31-September 30, 1999).
- Training Course in Advanced Haematology and Immuno-haematology (October 11-29, 1999).

ICMR ON INTERNET

<http://www.icmr.nic.in>

A web site of ICMR has been developed inhouse and is hosted from a server located at the National Informatics Centre (NIC), New Delhi. The site contains detailed information about the activities of ICMR.

The welcome section gives general information like address and phone numbers of Chiefs of Divisions in the ICMR Hqs., Profile of the Director General, Highlights of activities, Achievements, History of the ICMR, Details of ICMR Awards and Prizes, Guidance for international collaboration, *etc.*

Information is available about Council's training programmes, meetings, ICMR aided Seminars/Symposia/Workshops and other announcements under 'News'.

General information on various funding schemes for Research & Development implemented by the ICMR is found under 'Grants'. Application forms for various schemes can be downloaded from the site. Information on extramural projects ever funded by ICMR can be searched from the dynamic web pages using search keys.

Issues of ICMR Bulletin, current and one year old are accessible under 'Publications'. The list of ICMR publications is also available.

An informative write-up on each of the ICMR Institutes/Centres is available under 'Institutes'. A searchable list of ICMR scientists is also available. It is planned to publish research results and results of epidemiological surveys, *etc.* of ICMR Institutes on the web.

Any comments/suggestions regarding the web site from readers of ICMR Bulletin are welcome. These may be sent to the ICMR (provision has been made on the homepage).

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Printed and Published by Shri J.N. Mathur for the Indian Council of Medical Research, New Delhi
at the ICMR Offset Press, New Delhi-110 029

R.N. 21813/71