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Activities and Achievements of INMAS

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ABSTRACT

The paper brings out in detail the activities and achievements of INMAS in its formative years and in the post-Mazumdar period. In addition to carrying out investigations on endemic goitre, Brig. Mazumdar pioneered the methodology of the management of thyrotoxicosis by low-split doses of ^{131}I. In post-Mazumdar period, INMAS saw an all-round growth with the establishment of an advanced non-invasive Organ Imaging Centre and setting up of a TLD-based Personnel Monitoring Centre (for radiation workers in Defence), etc. Studies were undertaken in thyroid epidemiology, radiobiology with emphasis on understanding the basic mechanisms of regulation and control of DNA repair processes, and the development of chemical radioprotectors with particular reference to the role of 2-deoxyglucose as an adjunct to radiotherapy.

1. INTRODUCTION

INMAS (Institute of Nuclear Medicine and Allied Sciences) witnessed a healthy all-round growth under Brig. Mazumdar's guidance not only in nuclear medicine as such but also in a variety of allied sciences like health physics, radiopharmaceuticals, radiobiology, radiation entomology, experimental medicine, analytical biochemistry, respiratory physiology, and nuclear instrumentation. The present paper brings out in detail the activities and achievements of INMAS during its formative years and the subsequent post-Mazumdar period.

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2. THRUST AREAS OF INMAS IN ITS FORMATIVE YEARS

2.1 Thyroid Research

Right from the days of the Radiation Cell, thyroid research had been the first love of Mazumdar, and it has remained even today the most important thrust area of INMAS. The prevalence of endemic goitre along the entire Himalayan range, running approximately west to east over 2500 km, the sub-Himalayan belt, as well as in isolated pockets in almost every state of our country is well known. The number of persons suffering from thyroid disorders exceeds 10 million. Even the troops from non-endemic areas posted in the endemic regions for a few years as well as members of their families staying with them exhibited a higher than normal incidence of goitre, the problem acquired special significance to Col. Mazumdar as an officer of the Armed Forces Medical Services. His thyroid clinic (catering to both civilians and armed forces personnel) overflowed with patients every day, and the legacy continues even now. Statistics for recent years show 8500 new cases and 35,000 patient visits (both old and new cases) per year. Over 1,00,000 persons have been investigated so far. The full battery of radioisotopic, conventional biochemical and pathological tests has been employed for obtaining a better understanding of the aetiopathology of thyroid disorders. The influence of familial and socioeconomic factors, age, sex, possible presence of goitrogens in soil/water, etc., have all been studied and valuable conclusions drawn. As early as 1962, Col. Mazumdar recommended that an adequate supply of iodine should be assured for the troops stationed in the endemic areas as a prophylactic measure.

2.2 Therapy

Col. Mazumdar found that ^{131}I combined with antithyroid drugs brought about long-lasting remission in hyperthyroidism and also helped in reducing goitre size. He further noticed that patients with benign goitre with or without nodules showed a tendency for transition towards hyperthyroid state. These cases were managed with fractionated ^{131}I therapy. Patients with single nodule or adenomatous hyperplasia did not develop into clinical malignancy, thus a nodule in an endemic area does not carry the same implication for malignancy as in a non-endemic area. Treatment with thyroxine for long periods was the first choice for such cases as well as for multinodular goitre. Cold nodules were advised surgery.

Col. Mazumdar pioneered the methodology of thyrotoxicosis therapy by fractionated doses of radioiodine with periodic clinical monitoring and was able to bring down the incidence of late onset of hypothyroidism among the treated patients to about 3 per cent (as against 40 per cent or so reported from single dose therapy). Although the technique did not receive much attention at that time, more and more centres are gradually switching to it. A paper by Ravi Shankar, *et al* in this issue deals with the subject in greater detail[1].

Col. Mazumdar also used radioiodine therapy effectively for congestive heart failure, angina pectoris and cor pulmonale. He attempted to give temporary relief to Parkinsonism patients by radioactive iodine but the methodology has not found much

favour in the medical community. He continued to be enthusiastic about its efficacy in spite of non-acceptance of the methodology by other nuclear medicine specialists in the country.

Palliative therapy for malignant effusions of the pleural and peritoneal cavities by ^{198}Au was carried out in a few cases in the early days around 1963, but, as in the rest of the world, was soon given up. ^{32}P therapy for polycythaemia vera and certain types of leukemia is being practised but not on a large scale. Since INMAS does not have in-patient hospital facilities till now, radioiodine therapy for thyroid cancer is not being carried out.

2.3 Other Nuclear Medicine Investigations

In 1962 Major R.N. Banerjee started radioisotopic investigations on haematological, hepatobiliary and renal disorders. His special interest was in the aetiopathology of diabetes and its investigation by radioisotopic techniques. At the same time Dr. Kanti Rai devoted his attention to the study of electrolytes, body fluids, blood volumes in normal and disease states. The studies on iron deficiency anemia as well as on body fluids were particularly relevant in our country's health context.

The Radioisotope Unit at Safdarjang Hospital acquired a rectilinear scanner in mid-1961 (this was probably the first scanner to be installed in the country) and organ scanning started around 1962 on a routine basis. Soon after ^{99m}Tc-labelled radiopharmaceuticals became available from Bhabha Atomic Research Centre (BARC) around 1970, brain scanning and isotopic studies of craniocerebral studies gained momentum.

2.4 Radiopharmaceuticals

INMAS has built up a strong school of radiopharmaceutical scientists under the leadership of Shri Bikram Singh. The emphasis has been on indigenous modifications to several widely used ^{113m}In and ^{99m}Tc-labelled pharmaceuticals, development of newer radiopharmaceuticals, tagging pharmaceuticals with ^{99m}Tc at the Hot Laboratory of the clinical department itself, and evolving simplified quality control procedures. Periodic visits by Dr. Gopal Subramanian starting from around 1975 provided inspiration to the scientists to keep themselves abreast with the state of the art. There was also close interaction with Dr. V.K. Iya, Dr. R.S. Mani and other scientists from BARC.

2.5 Radioimmunoassays

Somehow INMAS entered the RIA field rather late, only around 1975. Since then, however, the scientists have caught up.

2.6 Health Physics, Radiation Hygiene and Instrumentation

Right from the inception of the Radiation Cell in 1956, Col. Mazumdar had been laying special emphasis on radiation hygiene and safety. Under his guidance a compact

but highly effective Health Physics Division was set up, the staff of which included Shri A. Nagaratnam, Dr. M.M. Gupta, Dr. K.K. Kapoor, Dr. A.R. Reddy, Shri N.K. Verma and Dr. M.P. Jain. (For a few years in the early period, the number of physicists in INMAS exceeded the number of physicians!) When the INMAS building was being planned, special thought was given to the design of the Hot Laboratory to handle curie quantities of unsealed radioisotopes.

Starting from an amount of 30 mCi handled in 1959 (almost entirely ^{131}I), the usage of radiopharmaceuticals touched the 1 Ci mark in 1962, and the present level exceeds 100 Ci per year (mostly ^{99m}Tc). INMAS and the Radiation Medicine Centre of BARC at Bombay are the two largest users of unsealed radioisotopes in the country. The number of radiation workers started with 11 in 1959, reached 100 in the next five years, and now stands at about 125. Through out the history of INMAS, no worker has exceeded the ICRP dose limit, in spite of the tremendous increase in activity handled. The highest individual annual dose has been around 700 mrem and the average annual exposure 30 mrem. Particular care has been taken whenever a new procedure is initiated to ensure control and minimisation of exposure.

Scientists of the Health Physics Division have carried out outstanding research work in practically all aspects of health physics. In fact the Division has contributed the largest percentage (around 30 per cent) of the publications from INMAS. Special areas of interest have been theoretical internal dosimetry, microdosimetry, low energy photon dosimetry, dosimetry of newer radiopharmaceuticals, pediatric and fetal dosimetry, thermoluminiscence dosimetry (TLD) applications in diagnostic radiology, radiotherapy, nuclear medicine and radiation protection, and critical review of ICRP recommendations. The Division was involved in two IAEA projects, one on the use of ^{252}Cf for educational, training and research purposes, and another, a collaborative project for south-east Asia on the maintenance of nuclear medicine instruments in tropical countries. The scientists of the Division have continuous and close academic interactions with the Health and Safety Group of BARC. Another paper by Reddy, *et al* in this issue gives an account of the work in internal dosimetry carried out at INMAS[2].

Commendable work has been done in whole body counting for radiation protection and clinical applications. Several types of whole body counting systems have been designed and fabricated. A new counting geometry (Buddha posture) has been evolved to suit Indian conditions. Modifications to existing criteria have been developed for evaluation of whole body counter performance.

2.7 Technical Workshop

Col. Mazumdar had the foresight to visualise that a technical workshop would be an asset to all the activities of the Institute. (It is not often that a medical institution has a good workshop!) The INMAS Workshop built up excellent competence in the design and fabrication of a variety of remote handling devices, shielding equipment, focusing collimators for radioisotope scanning, several types of phantoms, moving beds for whole body counters, etc., as well as a variety of training aids. Shri N.A. Nayak, Shri R.K. Bhattacharya, Shri M.L. Bedi and Shri A.N. Sahni displayed commendable ingenuity and skill in these assignments.

2.8 Experimental Medicine

The Experimental Medicine Division, originally guided by Dr. Kanti Rai and later, by Dr. B.N. Chaudhuri, has given excellent support to the clinical research programme by undertaking animal experimentation studies using radiotracers for obtaining a deeper understanding of metabolic processes in normal and disease states, as well as the interactions of the different physiological systems. A major effort has gone towards metabolic studies in thyroid and other endocrinological disorders and the role of trace elements in health and disease. Attention has also been directed towards physiological alterations under various types of stress (a problem of interest to the armed forces) including heat, cold and hypoxia. Animal experiments have also been of great value in assessing and validating any new diagnostic protocol as well as in the development of newer radiopharmaceuticals.

2.9 Radiobiology

It is interesting to recall that as early as 1962 Mazumdar noted transient EEG changes (lasting up to an hour) soon after administration of 2-4 mCi of ^{131}I to thyrotoxic patients[3]. The first such observation seems to have been made in 1959 by Soviet scientists. Somehow Mazumdar did not follow up the study of the effects of radiation on the central nervous system, a subject which acquired great importance in later years.

Studies in radiobiology were initiated by Major B.R. Kochhar in 1962. Among the problems studied were the histopathology of radiation dermatitis and radiation burns in animals, and methods of their management by indigenously available plant extracts. The effects of radiation on drugs as well as the effects of drugs on irradiated animals were also investigated.

2.10 Radiation Chemistry and Biochemistry

Dr. B.C. Ray Sarkar, with his rich experience in DRDO provided invaluable support as Deputy Director to Col. Mazumdar. He also initiated work in analytical chemistry and with Dr. U.P.S. Chauhan developed some elegant semimicro-analytical methods in clinical biochemistry. In addition he was in charge of a special cell that was dealing with certain problems referred by the Scientific Adviser to the Defence Minister. Dr. P.K. Ramachandran and Shri K.G.K. Sastry were associated with Dr. Ray Sarkar in this assignment. (This cell was transferred to DRDE, Gwalior in 1973).

Dr. K.P. Chakraborty (whose untimely demise has been a great blow to all colleagues) and Shri D.N. Zutshi developed radiation chemistry.

2.11 Radiation Entomology

Shri T. Koshy, a bachelor dedicated to his work and with extensive field experience in entomology (especially in relation to problems of the armed forces), joined INMAS in 1966. With limited manpower and budget he initiated an imaginative programme, 'Defence applications of radiation entomology in control of insects and vectors of diseases', which in a short period produced interesting and useful results.

Considerable success was achieved in a pilot project on control of the mosquito *Culex fatigans* by radiation-induced sterile male technique, which was tried out in a village near Delhi. Other contributions include methods of laboratory rearing of cockroaches, development of chemosterilisants and attractants in the control of cockroaches, development of newer repellants against leeches, cockroaches and disease carrying insects.

2.12 Respiratory Physiology

Col. Mazumdar had the breadth of vision to give freedom occasionally to promising lines of research even when they were not directly related to the mainstream of INMAS work. One example was the research in respiratory physiology carried out by Dr. K.P. Agarwal, first at INMAS and later at the INMAS Cell located at the VP Chest Institute, Delhi. Elegant methodologies were developed for the study of the nature of autonomic disturbances in bronchial asthma (which Dr. Agarwal himself suffered from) in animals and men, using electrophysiological and biochemical techniques, including the development of a whole body plethysmograph. Interesting results have been obtained on the changes in airway reactivity induced by asthma and methods of ameliorating the severity of the symptoms.

2.13 Electron Microscopy

INMAS was the first DRDO laboratory to acquire in 1962 an electron microscope which was intended for biomedical research. The Electron Microscope Division, which was under the charge of Dr. Kanwar Bahadur, continued to be located at the Defence Science Laboratory, even after INMAS moved to its new premises. The Division also provided consultancy service to sister DRDO laboratories in the fields of thin films, solid state, corrosion and related studies. The Division was transferred to the Defence Science Laboratory (now Defence Science Centre) in 1973.

3. TRAINING AND CONSULTANCY ACTIVITIES

Col. Mazumdar was the Senior Adviser (and later Consultant when he was promoted as Brigadier in July 1976) in nuclear medicine to the Armed Forces Medical Services and planned a series of nuclear medicine centres in the Command Hospitals of the three Services. This also involved organising suitable short-term courses at INMAS for medical specialists and technicians from the Armed Forces. INMAS has been conducting on a regular basis a 6-week course in nuclear medicine for AMC officers (since 1965), a 12-week course in radioisotopic techniques (since 1966) and a 16-week course in radiopharmaceuticals (since 1978) for AMC technicians.

Col. Mazumdar was actively involved in organising educational and training programmes for the officers of the Armed Forces on technical aspects of nuclear weapons and methods of protection. As Dr. S. Bhagavantam (the then Scientific Adviser) put it in his Foreword to a publication on INMAS brought out at the time of the inauguration of the Institute building in 1964, 'Finally, even though our country is committed to a policy of rejecting nuclear weapons, proper scientific understanding of biomedical problems that arise from radioactive fallout as a result of weapon tests

is the appropriate responsibility of the physician and the scientist. Radiation effects thus become a major subject of study in military medicine'.

4. THE POST-MAZUMDAR PERIOD AT INMAS

A brief account is given of the progress of INMAS under subsequent Directors after the retirement of Brig. Mazumdar on 29 August 1977.

4.1 Col. B.R. Kochhar

Col. Kochhar took over as Director on 17 September 1977. He encouraged research in radiobiology and radioprotectors. Old Delhi experienced unprecedented floods in 1978 and the area around INMAS building was under five feet of water. In spite of heroic rescue efforts by some of the staff, several costly and delicate instruments and equipment got damaged. Col. Kochhar retired on 29 Feburary 1980.

4.2 Col. N. Lakshmipathi, VSM

Col. Lakshmipathi took over as Director on 22 May 1980. During his period INMAS witnessed a massive expansion. His achievements were in the following fields: (i) expansion of the Thyroid Clinic to a Thyroid Research Centre, (ii) establishment of an integrated non-invasive Organ Imaging Centre, (iii) expansion of research programmes in radiation biology with special reference to radioprotectors, and (iv) establishment of a TLD-based Personnel Monitoring Centre for radiation workers in Defence. He also gave his support to the establishment of a Regional Radiopharmaceutical Dispensing Centre of BARC at INMAS, to cater to the needs of hospitals in and around Delhi. He retired as Major General on 30 November 1986.

4.2.1 Thyroid Research

An epidemiological survey initiated by Col. Lakshmipathi of 26,000 school children in Delhi showed a high incidence of goitre, particularly in post-pubertal girls from the lower socioeconomic group. His recommendation for the supply of prophylactic iodized salt supplementation for the Delhi population was accepted by the Ministry of Health and steps were taken to start supply from 1985. Studies are in progress at INMAS to evaluate long-term changes in thyroid pathophysiology after introduction of iodized salt.

The management of the solitary thyroid nodule is a complex problem since it is difficult to distinguish between benign and malignant areas. The diagnostic protocol developed at INMAS using non-invasive techniques (hormonal assay, ^{131}I uptake, ultrasound, dynamic radionuclide thyroid angiography with computer quantification, and fine needle aspiration cytology) has helped in drastically reducing unnecessary surgery of benign nodules.

The goitrogenic potency of some vegetables has been demonstrated both by chemical analysis for goitrogens and by studies on animals fed with the suspected item (like ladies finger with a high thiocyanate content).

4.2.2 Non-Invasive Organ Imaging

Although (probably) the first rectilinear scanner in the country was installed at INMAS in 1961-62, INMAS was rather late in acquiring a gamma camera which became available only in 1982. (The Radiation Medicine Centre of BARC had the distinction of acquiring the first gamma camera in the country). In the course of about 6 years, Col. Lakshmipathi succeeded in setting up almost all the imaging modalities under one roof. These included rectilinear scanner (black and white, colour, and photoscanning), gamma camera, SPECT, CT, ultrasonography, 2-D echo cardiography with colour Doppler, thermography, x-ray, xero- and ultrasonomammography, and magnetic resonance imaging (the first to be installed in southeast Asia). There are only a limited number of centres in the world which have such a full spectrum of imaging modalities. The only major system that is lacking is PET with a medical cyclotron.

The availability of the above facilities has enabled the establishment of an Early Breast Cancer Detection Centre at INMAS around 1985.

4.2.3 Radiopharmaceuticals

Among the new ^{99m}Tc-labelled pharmaceuticals developed over the years, the following may be mentioned: leukocytes (for localisation of abscesses), platelets (thrombi), *Cu*-GHA (spleen), *Cu*-mannitol (dynamic renal function), trimethyl and diethyl monoiodo-IDA (hepatobiliary), and *V*-DMSA (soft tissue tumour and bone metastases). 'Mix and use kits' have been developed for a number of ^{99m}Tc pharmaceuticals which have the advantage of better quality control and instant preparation.

The present thrust is towards immunoscintigraphy by production of tumour specific monoclonal antibodies, and development of HMPAO and its analogues for cerebral studies.

4.2.4 Immunoassays

Considerable progress has been made in the indigenous development of antisera for certain biological constituents of interest, and development of RIA and ELISA kits.

4.2.5 TLD-Based Personnel Monitoring Centre for Radiation Workers in Defence

A TLD-based Personnel Monitoring Centre was established in 1983 for the benefit of the radiation workers in Defence (military hospitals, DRDO establishments) under Dr. M.P. Jain. This is the only organisation outside the Department of Atomic Energy that has been recognised by the Division of Radiological Protection, BARC. At present around 1200 workers in Defence are served by this Centre.

Scientists have also carried out detailed radiation protection surveys of radiodiagnostic units in the field units under the DGAFMS, as well as assessed the radiation safety situation in the luminous paint industry in the Defence sector (which is the largest user in the country).

4.2.6 Radioprotectors

Research on radioprotectors has become one of the major thrust areas of INMAS. Evaluation of eligible radioprotectors is done on a variety of animal species ranging from mice to monkeys. Among the findings is that a suitable combination of radioprotective drugs like 5HT + AET or 5HT + MPG holds promise.

4.3 Dr. Viney Jain

Dr. Viney Jain took charge as Director on July 1987 and continued as Director till 14 Feburary 1990. He had earlier carried out outstanding work in biophysics at the All India Institute of Medical Sciences, New Delhi and at the National Institute of Mental Health and Neurosciences, Bangalore. His thrust was to strengthen the basic research component further at INMAS. As a continuation of his earlier research interests, he has initiated the following major programmes:

(a) Understanding of the basic mechanisms of regulation and control of DNA repair processes;
(b) Chemical radioprotectors. (A special aspect of this work is the use of 2-deoxyglucose as an adjunct to radiotherapy. 2-DG appears to act as a selective radiosensitizer for hypoxic tumour cells while affording protection to normal cells); and
(c) Development of photodynamic therapy of cancer.

4.4 Major General M.L. Sapra, AVSM, VSM

Maj. Gen. Sapra took over as Director on 15 February 1990. He is a specialist in medicine with wide academic, professional and administrative experience. His present plans are to expand and broadbase the scope of the Thyroid Research Centre into an Endocrinology Research Centre.

5. PROFILE OF INMAS GROWTH

In 1962 the total staff strength of INMAS was around 60. There were two significant increases in the strength—to 200 in 1969 and 350 in 1975—after which it has remained nearly steady at the latter figure. From an annual budget of Rs 20 lakhs in 1962, it has steadily increased, with a sudden spurt after 1985 (consequent on the acquisition of advanced organ imaging systems) and is now around Rs 250 lakhs. A total of around 230 projects have been initiated during the period 1962-88. Till 1982 most of the projects had a budget of less than Rs one lakh each. During 1983-88, ten projects had a budget in the range Rs 20-100 lakhs each and three had a budget exceeding Rs 100 lakhs each.

During the period 1962-87, INMAS scientists have published around 265 papers, one-third of them in foreign journals. The discipline-wise breakup is as follows: clinical nuclear medicine—18 per cent; experimental medicine—20 per cent; radiobiology—16 per cent; health physics and instrumentation—29 per cent; radiopharmaceuticals—6 per cent; and other subjects—11 per cent.

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APPENDIX

Directors of INMAS (after Brig. S.K. Mazumdar)

Col. B.R. Kochhar
(Sept 1977–Feb 1980)

Maj. Gen. N. Lakshmipathi
(May 1980–Nov 1986)

Dr. Viney Jain
(July 1987–Feb 1990)

Maj. Gen. M.L. Sapra, AVSM, VSM
(Feb 1990–)