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NUCLEAR MEDICINE PRACTICE AND RADIATION DOSES TO PATIENTS IN INDIA : PART III. CALCULATION OF RADIATION DOSES TO INDIAN PATIENTS.

The important parameters involved in the calculation of internal radiation dose to a patient undergoing nuclear medicine diagnostic investigations, are (i) the total quantity of administered radionuclide; (ii) physical characteristics of the radionuclide, like its half-life, type of emitted radiation, their energy and yield per disintegration; (iii) biokinetics of the radionuclide in the patient's body, *ie* its transportation, retention and finally excretion; (iv) weight and size of the body organs; and (v) the values of tissue weighting factor of irradiated tissues and organs that take into account the difference in their radiosensitivity to radiation detriment.

Good and reliable data usually exist on the total quantity of the administered radionuclide as well as on the physical characteristics of the radiation emitted. To provide information on other parameters, a major step was taken by the International Commission on Radiological Protection (ICRP) in evolving a Reference Man with well defined characteristics[1]. The Reference Man is basically a Caucasian and a west European or North American in habitat and customs. He is defined as being between 20-30 years of age weighing 70 kg and 170 cm in height. He lives in a climate with an average temperature ranging between 20-30°C. The ICRP also formulated metabolic, physiological and anatomical parameters for infants and children of various age groups[2]. The modified methodology[3], applied for effective dose estimation, was a step forward in improving the internal radiation dosimetry; however, the doses calculated were appropriate for the ICRP Reference Man with its basic characteristics. The distinctive parameters formulated for The ICRP Reference Man, would obviously, not be directly applicable to other populations. Efforts were made in various countries to formulate their own Reference Man specifications. Japanese workers have generated data for a Japanese Reference Man[4] and have also proposed anatomical and physical data for an Asian Reference Man[5].

Data on physical, physiological, anatomical and metabolic characteristics for healthy Indians are limited. Gharpure and Jhala[6-8] reported on the weights of various organs and their relationship with body weight. Vijaya Raghavan *et al*[9] and ICMR[10] provided valuable data on the development of Indian children. Preliminary values for an average 'Indian Man' came from extensive studies carried out at the Bhabha Atomic Research Centre[11-15] The main source of data on the body weight and height has been the reports on extensive nation-wide surveys carried out both for rural and urban populations in India by the National Nutrition Monitoring Bureau (NNMB)[16-18]. Recently, the physical, anatomical and physiological characteristics of Indian population were described by Jain *et al*[19] and Dang *et al*[20] by studying over 12,000 autopsies of accidental death victims in various parts of the country. The main criteria for selection of cases were

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that the subjects were physiologically and nutritionally normal and did not show any pathological changes. These studies provided the required data for evolving the Indian Reference Man. The effective doses of the radiopharmaceuticals studied have been calculated taking into consideration the anatomical and physical difference between the average Indian adult and the ICRP Reference Man.

Further, due to variations in dietary habits, water intake, climatic conditions and ethnic considerations, it was felt that the biological behaviour of many of the radiopharmaceuticals studied might be different in the Indian population as compared to the ICRP Reference Man. However, no reliable data especially with regard to quantitative measurement, are available. This may be due to the fact that clinicians are often only interested in the initial distribution and metabolism of a test substance, whereas for dosimetric calculations long-term retention data are of prime importance. Recently, long-term retention studies demonstrated that the biological half-lives of ^{3}H, ^{131}I and ^{137}Cs (which are present in a nuclear power reactor environment) were 5, 55 and 66 days respectively in Indian adults[21] in comparison to 10, 120 and 110 days respectively, reported for the ICRP Reference Man. A method has been evolved to estimate the effective doses in Indian adults due to these radionuclides taking into consideration their different metabolic behaviour.

Analysing the cancer morbidity and mortality data of Jussawala *et al*[22-24], Mehta and Sarangapani[25] demonstrated that the relative contribution of various organs in the Indian population to the total radiation health detriment might be significantly different from those assumed by the International Commission on Radiological Protection. They also suggested a set of new tissue weighting factor values for the Indian Population. The effect of this suggested change in tissue weighting factor values on effective doses of some selected and widely used radiopharmaceuticals has also been examined.

Estimation of Effective Doses of Some Radiopharmaceuticals

The total body weight and some organ weights of an average Indian adult are compared with that of ICRP Reference Man in Table I. The weights of these nine organs were used to estimate the absorbed dose coefficients for Indian adults for the radiopharmaceuticals studied. Using the methodology of Yamaguchi[26] for the principal gamma energies, dose transformation factors (DTF) were computed for these organs. For other organs, if the weight of the organ was less than or equal to 20g, DTF was taken as 1 and for others, DTF was computed considering the organ masses to be proportional to body mass. The absorbed dose coefficients to the various organs due to the radiopharmaceutical[2], were then multiplied by the respective DTF values to give the absorbed dose coefficients for the organs of Indian adults. Employing the tissue weighting factor values as given by the ICRP[27] and using the modified methodology of dose estimation[3], effective dose to Indian patients were calculated.[28-31]

Table I. Comparison of Indian adult male organs weight and total body weight[20] with ICRP Reference Man[1].

Organ	Weights (g)	
	Indian	ICRP Reference Man
Brain	1236±127	1400
Heart	234±52	330
Kidneys	224±48	310
Liver	1135±251	1800
Lungs	841±154	1000
Spleen	137±67	180
Pancreas	96±34	100
Testes	35±5	35
Thyroid	19±7	20
Total Body	51500±8500	70000

Superscript nos. refer to the sl. nos. in the reference list.

The data on long-term retention of different radiopharmaceuticals in the Indian population, is extremely limited. Using data from a recent study on the biological half- lives of ingested ^{3}H, ^{131}I and ^{137}Cs in Indian adults[21], the effective half-lives of these radionuclides were calculated in Indian adults as well as in the ICRP Reference Man and the corresponding modifying factor was calculated. When the ICRP value of the effective dose[32] due to one of the radionuclide is multiplied by its modifying factor, the effective dose in an Indian adult is obtained for that radionuclide.[33]

In all the effective dose estimations, the tissue weighting factor values as given in 1990 ICRP recommendations[27], were used. These values were arrived at keeping in view the contribution of various organs to the total radiation health detriment averaged over the populations

of China, Japan, Puerto Rico, UK and USA. In the light of the observations of Mehta and Sarangapani[25] and the suggested values of tissue weighting factor for the Indian population, the effective doses of some selected and widely used radiopharmaceuticals were recalculated and compared with the values obtained earlier.

Comparison of the effective dose coefficients for Indian adults with the ICRP values (ICRP 1992)[34] due to radiopharmaceuticals used in India is shown in Table II. In all instances, the values of the dose coefficients were higher in the Indian adult by about 12% (5-18%). This indicates that for the same amount of administered activity, due to smaller weight and body stature, an Indian adult receives a higher effective dose and is at higher risk for radiation health detriment.

Table III depicts the effective dose from ingestion of ^{3}H, ^{131}I and ^{137}Cs in an average Indian considering the anatomical difference between ICRP Reference Man and average Indian, and both the anatomical and physiological differences. There was no difference between ICRP values and Indian values for ^{3}H as the radionuclide is a pure beta emitter and has uniform whole body distribution. In case of ^{131}I and of ^{137}Cs, the values for an Indian adult were higher by 3 and 15% respectively. If anatomical as well as biological turnover in the ICRP Reference Man and in an average Indian are considered, the effective doses were always lower. Thus the smaller body weight and stature cause higher radiation dose but the faster turnover of these radionuclides in an Indian adult has the effect of lowering the radiation dose.

Table II. Comparison between effective dose coefficient values calculated for Indian adults and ICRP values (ICRP 1992)[34] due to radiopharmaceuticals used in India.

Radiopharmaceuticals	Effective values (mSv/MBq) ICRP 1992 (A)	Effective values (mSv/MBq) for Indian adults (B)	Difference between two values (%) $\frac{(A-B)}{A} \times 100$
^{99m}Tc pertechnetate (no blocking agent)	1.4 E-02	1.5 E-02	7
^{99m}Tc DTPA	5.2 E-03	6.02 E-03	15
^{99m}Tc Gluconate Glucoheptonate	5.4 E-03	6.05 E-03	12
^{99m}Tc HMPAO	9.3 E-03	9.83 E-03	7
^{99m}Tc HSA	6.1 E-03	6.71 E-03[47]	10
^{99m}Tc large colloid (Sulphur colloid)	9.2 E-03	10.32 E-03	12
^{99m}Tc DMSA	8.7 E-03	9.98 E-03	15
^{99m}Tc Phosphates	5.8 E-03	6.6 E-03	13
^{99m}Tc Erythrocytes	6.6 E-03	7.4 E-03	12
^{99m}Tc MAA	1.1 E-02	1.3 E-02	18
^{67}Ga Citrate	1.1 E-01	1.29 E-01	17
^{131}I Hippuran	5.3 E-02	6.17 E-02	16
^{201}Tl Chloride	2.3 E-01	2.6 E-01	13
^{131}I Sodium iodide (5% uptake)	6.1 E-02 (0% uptake)	3.7 E-02	-
^{131}I Sodium iodide (45% uptake)	2.4 E+01 (35%uptake)	3.2 E+01	-
^{99m}Tc labelled citrate complex	7.1 E-03	7.8 E-03	9
^{99m}Tc MA G_3 (normal kidney function)	7.3 E-03	7.7 E-03	5
^{99m}Tc denatured RBC	2.9 E-02	3.4 E-02	16
^{99m}Tc aerosol (DTPA)	6.1 E-03	7.0 E-03	14
^{99m}Tc MIBI	8.5 E-03	9.1 E-03	7
^{99m}Tc IDA	1.5 E-02	1.63 E-02	9
^{51}Cr EDTA	2.1 E-03	2.4 E-03	14
$^{51}CrTc$ Platelets	1.8 E-01	2.01 E-01	12
^{75}Sc methionine	2.5 E+00	2.9 E-00	16

Superscript no. refers to the sl.no. in the reference list.

Table III. Comparison of effective dose from ingestion of ^{3}H, ^{131}I and ^{137}Cs in an average Indian[33] and ICRP Reference Man[22].

Radio-nuclide	Effective dose Sv/Bq		
	ICRP	Indian; Anatomical consideration only	Indian; Anatomical and physiological consideration
^{3}H	1.8 E-11	1.8 E-11 (0%)	9.00 E-12 (-50%)
^{131}I	2.17 E-08	2.24 E-08 (+3.2%)	2.10 E-08 (-3.2%)
^{137}Cs	1.34 E-08	1.54 E-08 (+14.9%)	9.27 E-09 (-30.8%)

Superscript nos. refer to the sl nos. in the reference list.

The effect of suggested tissue weighting factor for the Indian population on effective dose coefficients due to some radiopharmaceuticals are shown in Table IV. With anatomical considerations only as shown earlier, the effective dose was always higher in the Indian adult, in comparison to the ICRP Reference Man, however, when the new suggested tissue weighting factor values were used for effective dose estimation, the doses were lower by about 15% from Indian values for these radionuclides. As no data are available on biological turnover of these radiodiagnostic agents in the Indian population, the study could not be extended further.

Table IV. Comparison of effective dose coefficients calculated with Indian values of W_T[25] and ICRP values[34] due to some radiopharmaceuticals (effective dose in mSv/MBq).

Radio-pharmaceuticals	ICRP	Indian values with anatomical conisderations	Values with Indian values for W_T
^{99m}Tc Pertechnetate (no blocking agent)	1.4 E-02	1.48 E-02	1.32 E-02
^{99m}Tc DTPA	5.2 E-03	6.02 E-03	5.57 E-03
^{99m}Tc Phosphate Phosphonate	5.8 E-03	6.6 E-03	6.11 E-03
^{99m}Tc RBC	6.6 E-03	7.4 E-03	6.48 E-03
^{99m}Tc HSA	6.1 E-03	6.71 E-03	6.0 E-03
^{67}Ga Citrate	1.1 E-01	1.29 E-01	10.37 E-02
^{201}Tl Chloride	2.3 E-01	2.6 E-01	14.99 E-02

Superscript nos. refer to the sl.nos. in the reference list.

W_T: Tissue weighting factor

Conclusions

For realistic internal radiation dosimetry, population specific data on organ weights, biological half-lives of various radiodiagnostic agents and organ/tissue weighting factor values for the irradiated organs or tissues, are needed.. Smaller stature and organs weights of Indians result in higher effective dose per unit intake of radioactivity in comparison to the ICRP Reference Man. However, the relatively shorter biological half-lives or faster turnover of the three radionuclides *ie* ^{3}H, ^{131}I and of ^{137}Cs (for which the data are available), has the effect of lowering the effective dose. When both the factors are considered together they tend to cancel the effect of each other. Further, the study of Mehta and Sarangapani[25] stated that Indians are at lower risk of radiation health detriment in comparison to ICRP Reference Man for the similar exposure situations. It is therefore important to consider all the factors that contribute to effective dose estimates so that the values may be meaningful and realistic.

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This write-up (in 3 parts) contributed by Dr. M.M. Gupta was based on the work carried out by him as an ICMR Emeritus Medical Scientist at the Institute of Nuclear Medicine and Allied Sciences, Delhi.

ABSTRACTS

Some Research Projects Completed Recently

Tumour cell kinetics in gestational trophoblastic disease as a predictive index of tumour aggressiveness.

The expression of markers of cell proliferation in gestational trophoblastic disease, was evaluated immunohistochemically. Efforts were also made to correlate the status of markers of cell proliferation with the clinical profile, particularly the regression pattern of the tumours, the level of βhCG and histologic nature of the tissue.

The markers included proliferating cell nuclear antigen (PCNA), nuclear organizer region associated proteins

(AgNORs), cell kinetic marker (Ki67) and epidermal growth factor receptor (EGFR). The study material comprised histologically graded trophoblastic tumours obtained from 122 patients of gestational trophoblastic disease and 50 normal placentae of comparable gestational age collected after medical termination of pregnancy and term delivery. Both normal and pathological placentae belonged to gestational ages between 6-36 weeks, with the mean gestational age of normal placentae being 17.75±11.21 weeks and that of the pathological placentae being 15.96±6.11 weeks.

The PCNA, Ki67 and EGFR expressed more strongly by the molar placentae in comparison to normal placentae of similar gestational age. EGFR and PCNA were expressed strongly by the molar placentae of all gestational ages unlike normal placentae where the expression was restricted to the first and second trimesters.

The PCNA staining pattern could differentiate spontaneously regressing tumours from slowly regressing tumours and Ki67 staining pattern could identify those tumours which require chemotherapy for regression. It is thus clear that the staining indices of PCNA in combination with ki67 would serve as a better marker in the assessment of the prognosis of trophoblastic tumours.

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Gene regulation and expression of brush border enzymes and transport proteins in animals induced for malabsorption.

This study aimed at investigating the underlying mechanism of malabsorption in male Wistar strain albino rats (80-100g) exposed to chronic alcohol ingestion and giardiasis. The results indicated that *Giardia lamblia* infection in rats induced malabsorption of glucose and decreased the activities of the brush border disaccharidases and alkaline phosphatases which was primarily due to down regulation of the expression of the alkaline phosphatase, sucrase and lactase in rat intestine. There was also a decrease in the progression of epithelial cells across the villus axis in response to giardia infection. Chronic ethanol feeding also induced solute malabsorption, which was presumably due to morphological alterations in the intestine. *G.lamblia* induced identical changes in mRNA levels of the brush border enzymes and also sodium dependent D-glucose levels in both control and ethanol fed rat intestine.

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Publication:

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ICMR NEWS

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

Meetings of the Scientific Advisory Committees:

Centre for Advanced Research for Bone Marrow Transplantation for Thalassaemia, Vellore	August 24, 1998
National Institute of Nutrition, Hyderabad	August 28, 1998
Food and Drug Toxicology Research Centre, Hyderabad and National Centre for Laboratory Animal Science, Hyderabad	August 29, 1998
Institute of Immunohaematology, Mumbai	September 9, 1998
Tuberculosis Research Centre, Chennai	September 10-11, 1998
Vector Control Research, Centre Pondicherry	September 14-15, 1998
Centre for Research in Medical Entomology, Madurai	September 16-17, 1998

Meetings of Sub-Groups/Sub-Committees/Task Forces (TFS):

TF on Epidemiology of Glaucoma	August 18, 1998 (at New Delhi)

Sub-Committee of the ICMR-DBT Collaborative Project on Haemoglobinopathies	August 18, 1998 (at New Delhi)
TF on Epidemiology, Culture, Immunology and Molecular Biology of *Rhinosporidium seeberi*	August 19, 1998 (at New Delhi)
TF on Hepatitis	August 26-27, 1998 (at New Delhi)
TF on Eradication of Poliomyelitis	September 7, 1998 (at New Delhi)
Sub-Group of the Centre for Advanced Research on Health Consequences of Earthquake Disaster with Special Reference to Mental Health	September 7-9, 1998 (at Pune)

Participation of ICMR Scientists in Scientific Events:

Dr. Lalit Kant, Sr. Deputy Director-General, ICMR Hqs; Dr. S.K. Bhattacharya, Director, National Institute of Cholera and Enteric Diseases (NICED), Calcutta; and Dr. S.M. Mehendale, Dy. Director, National AIDS Research Institute, Pune, participated in the workshop on Epidemiology and Policy for Control of HIV/AIDS in Asia at Bangkok (August 24-September 4, 1998).

Dr. A.K. Jain, Sr. Research Officer, Institute of Pathology, New Delhi, participated in the XIV International Congress of Electron Microscopy at Mexico (August 31 - September 4, 1998).

Dr. G.B. Nair, Dy. Director, NICED, Calcutta, participated in the World Congress of Gastroenterology at Vienna (September 6-11, 1998).

Dr. S. Poopathi, Sr. Research Officer, Centre for Research in Medical Entomology, Madurai, participated in the IV International Congress of Dipteriology at Oxford (September 6-11, 1998).

Dr. U. Sengupta, Director and Dr. S.R. Qamra, Asstt. Director, Central JALMA Institute for Leprosy, Agra; Dr. M.D. Gupte, Director, Institute for Research in Medical Statistics, Chennai; Sh. R.S. Vallishayee, Dy. Director (Sr. Grade), CJIL Field Unit, Avadi, Chennai; and Dr. Aleyamma Thomas, Dy. Director, Tuberculosis Research Centre, Chennai, participated in the XV International Leprosy Congress at Beijing (September 7-12, 1998).

Hindi Day Celebrations:

As part of the Hindi Day Celebrations by the ICMR Headquarters, a popular lecture (in Hindi) on "Paralytic Stroke and its Prevention" was delivered on September 15, 1998 by Dr. D.C. Jain, Head, Department of Neurology, Safdarjung Hospital, New Delhi.

ICMR AIDED SYMPOSIA/SEMINARS/WORKSHOPS/COURSES/CONFERENCES

Symposium/Seminar/Workshop/ Course/Conference	Date & Place	Contact Address
XIV International Conference on Alzheimer's Disease	September 24-27, 1998; (at Mangalore)	Dr. K. Jacob Roy, Organising Secretary, ADI 98, P.O.Box NO.53, Kunnamkulam-680503.
Symposium on Alzheimer's Disease and Neurocognitive Disorders	October 3-4, 1998; (at Delhi)	Col. D.S. Goel, Senior Advisor (Psychiatry), Base Hospital, Delhi Cantt-110010.
International Symposium on Temporomandibular Joint Disorders and Chronic Orofacial Pain	October 30-31, 1998; (at Mangalore)	Prof. P.K. Dayal, Organising Secretary of the Symposium, KMC College of Dental Surgery, Mangalore-575001.
Symposium on Current Trends in Autoimmune Diseases Immunology	October 30-31, 1998; (at Lucknow)	Prof. S. Naik, Department of Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow-226014.
XXXI Annual Conference of the Indian Pharmacological Society	December 17-20, 1998; (at Lucknow)	Dr. V.N. Puri, Organisng Secretary of the Conference, Division of Pharmacology, Central Drug Research Institute, Lucknow-226001.

COUNCIL'S TRAINING PROGRAMMES FOR 1998-99

Leprosy

At the Central JALMA Institute for Leprosy, Agra:

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

Reproductive Biology

At the Institute for Research in Reproduction, Mumbai:

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

Endocrinology

At the National Institute of Nutrition, Hyderabad:

- Annual Certificate Course on Endocrinological Techniques and their Applications (August 1-September 15, 1998).

Nutrition

At the National Institute of Nutrition, Hyderabad:

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

Occupational Health

At the National Institute of Occupational Health, Ahmedabad:

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

Medical Entomology

At the Vector Control Research Centre, Pondicherry:

- Postgraduate Diploma Course in Medical Entomology (from August 10, 1998).

Biomedical Statistics

At the Institute for Research in Medical Statistics, Chennai:

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

Haematology

At the Institute of Immunohaematology, Mumbai:

- Training Course in Transfusion Medicine for Blood Bank Medical Officers (August 11-October 9, 1998).
- Training Course in Blood Group Serology and Blood Bank Methodology for Blood Bank Technicians (August 11-September 10, 1998).
- Training Course in Advanced Haematology and Immunohaematology (September 21-October 9, 1998).

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