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To: Committee on the Use of Radioisotopes

From: S. I. Cohn, Ph.D. and J.A. Lenard, M.D.

Subject: Request for permission to administer trace levels of Cs-137, Zn-65 and Sr-85 in a clinical experiment. H-61

The Biological Turnover of Cs-137, Zn-65 and Sr-85

As a result of the world-wide increase in environmental radioactivity from nuclear weapons testing, the levels of internally-deposited radioisotopes have been rising in human beings. It is of great importance that data be obtained on (1) the absolute levels of the important fission products present in the population, (2) the biological turnover for these radioelements, and (3) the rate of equilibrium between the level in an individual and the amount in the environment.

A specific population that has shown a great increase in internal levels is that of the Marshallese people on Rongelap. In this population the body burdens of Cs-137 are one hundredfold greater, and the Sr-90 levels tenfold greater than present North American levels.

The whole-body gamma counter at BNL offers a unique tool for investigating some of these problems. It is proposed as an initial study that the metabolic turnover of three isotopes (Cs-137, Zn-65 and Sr-85) be studied in patients at Brookhaven. It is planned to extend this study in further work, particularly to very short-lived isotopes to be obtained from the BNL medical reactor.

However, before the whole-body counter can be used to determine absolute amounts of activity, the system must be carefully calibrated with known amounts of activity fixed in a characteristic way in the human body. The use of radioactive standards in pressedwood phantoms has not proved reliable as a substitute for actual human geometry and absorption. A new phantom of carefully constructed

likeness to a human being with compartments filled with tissue-equivalent fluid and appropriate replicas of the major organs into which isotopes can be introduced ~~is being~~ has been acquired, and may prove to be helpful in this study.)

The spectra of individual fission products taken individually and in combination are required for analysis of the complex spectra obtained from population studies. At present these data are needed for analysis of the measurements made on the Marshall Islanders, but they will also form the basis on which various population studies under consideration will have to be interpreted.

The second step following absolute determination of the levels of these radioisotopes is the assessment of the biological turnover. In the past, biological turnover data have been extrapolated from animal studies, but it is apparent that animal data are not always applicable to human beings. For example, the NBS Handbook indicates a biological half-life for Cs-137 of 17 days, based on animal studies. Studies with human beings, although limited, have already indicated that the biological turnover is probably over 100 days. Further, turnover rates are based on data obtained from single applications of the isotope, based on the assumption that a single application of an isotope is equivalent, in terms of human metabolic and turnover rates, to the application of the same total amount administered in fractionated doses over a period of time. In other words, the problem of chronic ingestion is represented as being identical with that of the administration of a single large dose. We propose to administer the isotope in both single doses and fractionated doses, to determine the effect of the multiple mode of application on the metabolic turnover rate. This approach should provide us with some information on the complex problem of chronic ingestion.

In order to study the rate of equilibration of the body burden with the dietary environment, the administration of small oral daily doses of these isotopes will be necessary. Such rates of equilibration, with the exception of Strontium, are not well-known. Determination of this rate of uptake is of considerable practical interest at this time. From these studies it will also be possible to determine the rate of gastro-intestinal absorption (circulatory uptake) of these isotopes.

Specific Proposals

1. Each of three patients will receive one of the following isotopes: Cs-137, Zn-65 and Sr-85, 1.5 μc, I.V. A calibrated spectrum will be obtained by the whole-body counting technique and will then be compared with that obtained from a phantom in which a like amount of radioactive material has been placed.

2. The biological turnover of radionuclides in these three patients will be followed by measuring body retention over a six-month period with frequent counting, and also by determination of urinary excretion rates.

3. Cs-137 and Zn-65 will be administered separately to two patients in daily oral doses of 0.1 μc and 0.33 μc, respectively, for at least 30 days. Sr-85 will be administered orally to one patient at a level of 0.5 μc per day for 30 days. The circulatory uptake of the isotopes will be measured by use of a columnated shielded counter placed over the forearm. The whole-body counting procedures will be followed for the period of administration, and for six months following cessation, to determine the time of attainment of equilibrium and the turnover and excretion rates. These data will be compared with those obtained following administration of the single dose of the isotope.

4. Each patient will have preliminary and follow-up blood work (WBC, differential, and platelet counts). The radioisotopes will be prepared in normal saline solution and sterilized before administration. In addition, aliquots will be administered to rabbits prior to human injection to make certain that there are no pyrogenic or other untoward effects.

Patients

The use of terminal cases would be less satisfactory for this study than the use of the patients proposed below, since a number of interfering physiological derangements can be expected in such cases, and further because of the impracticality of carrying out repeated whole-body counts in such patients. Dr. Irving L. Schwartz is beginning a study of metabolic disorders in patients, using a double tagging system with C-14 and tritium, and has offered the use of his patients in this study. It has been determined that there would be no interference in carrying out the two studies simultaneously, and the type of patients to be studied would be satisfactory for our purposes. *

*See addendum #4 attached.

Appendix

Dose Calculation

I.V. Administration of 1.5 μc to a 70-kg man

Cs^{137} $D_\beta = 73.8\ C\bar{E}_\beta\ T$ rads*

$= (73.8)(\frac{1.5}{70000})(0.23)(140)$ (C = μc/g
($\bar{E}_\beta$ = aver. β energy (0.23 - Hine and Brownell, pp 899)
(T = t 1/2 (days)

$= 50.9$ mr

$D_\gamma = .0346\,\Gamma\,CT\,\bar{g}$ rads** (Γ = Dose rate r/mc-hr at 1 cm (Hine and Brownell)
($\bar{g}$ = geometric factor (70-kg man)
((Hine and Brownell, pp 858)

$= (.0346)(3.2)(\frac{1.5}{70000})(140)(125)$

$= 41.6$ mr

Zn^{65} $D_\beta = 73.8\ C\bar{E}_\beta\ T$ rads

$= (73.8)(\frac{1.5}{70000})(.01)(200)$

$= 3.2$ mr

$D_\gamma = .0346\,\Gamma\,CT\,\bar{g}$

$= (.0346)(2.7)(\frac{1.5}{70000})(200)(125)$

$= 50$ mr

Sr^{85} $D_\gamma = .0346\,\Gamma\,CT\,\bar{g}$

$= (.0346)(3)(\frac{1.5}{70000})(65)(125)$ Assump: Sr distributed in whole body
If Sr assumed to be skeleton γ dose is approximately the same.

$= 18.1$ mr

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*See Hine and Brownell - Radiation Dosimetry - pp 832.
** " " " " - " " - pp 861.

for derivation of both these formulas.

Oral Administration of following isotopes for 30 days - Assumption: 100% retention of absorbed activity.

Cs^{137} Body burden = daily dose x time x fw

= μc x days x per cent

= (0.1)(30)(1.0) = 3.0 μc

fw = fraction of isotope absorbed into blood fro G.I. tract.

Therefore, dose is twice that calculated for I.V. administration of 1.5 μc (see above calculation).

D_β = 50.9 x 2 = 101.8 mr

D_γ = 41.6 x 2 = 83.2 mr

Zn^{65} Body burden = μc x days x fw

= (0.33)(30)(0.10) = 1 μc

Dose is $\frac{1.0}{1.5}$ or $\frac{2}{3}$ of above dose or calculated for 1.5 μc I.V.

$D_\beta = (\frac{2}{3})(3.2) = 2.1$ mr

$D^\gamma = (\frac{2}{3})(50) = 33.3$ mr

Sr^{85} Body burden = μc x days x fw

= (0.5)(30)(0.25)

= 3.75

$D_\gamma = (15.1)(\frac{3.75}{1.5}) = 45.3$ mr

Table 1. Dose to patients.

Patient	Isotope	Administration			Integrated Dose to Patient	
		Concentration (μc)	Frequency	Mode	Beta (mr)	Gamma (mr)
1	Sr-85	1.5	1	I.V.	-	18.1
2	Cs-137	1.5	1	I.V.	51	43.6
3	Zn-65	1.5	1	I.V.	3.2	30.
4	Sr-85	0.5	Daily - 30 days	Oral	-	48.3
5	Cs-137	0.1	" - " "	Oral	102	83.2
6	Zn-65	0.33	" - " "	Oral	2.1	33.

Table 2. Properties of isotopes employed.

Isotope	Radiol. t 1/2	Total Body Biol. t 1/2	Aver. β Energy $\bar{E}_\beta$	Gamma Energy E_γ	Γ r/mc-hr at 1 cm	fw Fraction Reaching Blood from G.I. Tract (Handbook 52)	MPC (μc) for Lifetime Concent. (Handbook 69)
Cs-137 β,γ	30 y	140 d	0.23	0.662	3.2	0.25	30
Zn-65 β^+,γ,e	245 d	200 d	.01	1.12	2.7	0.50	60
Sr-85 γ	65 d	190 d	-	0.51	3.0	0.10	60

Request approved:

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