Radiation Absorbed Dose from Technetium-99m DTPA

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The whole-body retention of intravenously administered [^{99m}Tc]DTPA was measured by urine analysis and whole-body counting in eight normal subjects. On average, the elimination of [^{99m}Tc]DTPA was faster in these subjects than in 11 patients under study for hypertension whose whole-body retention data were used in MIRD Dose Estimate Report No. 12 (*1*). The average residence time for [^{99m}Tc]DTPA in total body, less bladder contents, was only 65% of the MIRD value. However, despite this difference, the dosimetry is similar in both cases largely owing to the influence of radioactivity in bladder contents. Approximately 2–3% of the administered radioactivity was retained in the body for a time that was long relative to the physical half-life of ^{99m}Tc, and probably reflects a small amount of protein binding of the DTPA preparation.

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The radiation absorbed dose from technetium-99m diethylenetriaminepentaacetic acid ([^{99m}Tc]DTPA) was the subject of the MIRD Dose Estimate Report No. 12 (*1*). In that report, whole-body retention was based on observations on 11 patients under study for hypertension (*2*), while quantitative renal uptake measurements were made on six subjects with normal renal function. In our studies on a number of normal subjects we have observed that the elimination of intravenously administered [^{99m}Tc]DTPA from the body was consistently faster than was predicted by the average data given in MIRD 12. In view of the overriding importance, for dosimetry purposes, of the whole-body retention equation, since it establishes the total activity residence time, we report the results of whole-body retention measurements in eight normal subjects since they provide useful additional information for dosimetry of [^{99m}Tc]DTPA when used in conjunction with the data presented in MIRD 12. Using our whole-body retention information, together with the normal renal uptake data given in MIRD 12, dose estimates are presented for [^{99m}Tc]DTPA administered intravenously in normal subjects, with special reference to the influence of radioactivity in bladder contents.

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METHODS

Eight normal subjects were injected intravenously with [^{99m}Tc]DTPA and whole-body retention was measured by cumulative urine collection and whole-body counting up to 30 hr after administation.

Four normal males (29–49 yr) were given ~100 μCi (3.7 MBq) of [^{99m}Tc]DTPA obtained from either Amersham International* (two subjects) or Byk-Mallinckrodt† (two subjects) as part of a study to compare these two preparations. Further investigations in three of these subjects using the alternative preparation showed very similar retention data and consequently the different source of the DTPA preparation was not relevant for the purposes of this report. Both preparations were made using $CaNa_3$ DTPA (20–25 mg) and $SnCl_2$ (0.21 mg) and the Amersham preparation also contained a stabilizing agent, sodium para-amino benzoate (2.0 mg). The kits were reconstituted as recommended by the manufacturers. Thin layer chromatography was carried out on samples of the preparations using Kieselgel 60 (Merck) eluted with 95% acetone/water. Both preparations had similar amounts of free [^{99m}Tc]pertechnetate (~3.5%) 30 min after reconstitution.

The remaining four normal subjects (two males: 33 and 36 yr, and two females: 26 and 48 yr) were given ~5 mCi (185 MBq) [^{99m}Tc]DTPA intravenously for renal scintigraphy. In these cases the preparation was obtained from Amersham International (Amerscan Pentetate II).*

Individual urine collections were obtained up to 7 or 8 hr after administration of the radiopharmaceutical and the cumulative urine activity was used to establish the first part of the whole-body retention curve. This was necessary because the administered activity was too high to permit early whole-body counting. The amount of radioactivity in each urine

collection was determined either by measuring the total urine volume and counting duplicate 1 ml aliquots in an automatic gamma counter (LKB-Wallac 1280) (first group of four subjects), or by counting the complete individual urines in a bulk sample counter (*3*) after they had been made up to constant volume (second group of four subjects). Whole-body counting was carried out subsequently on all eight subjects but the time of the first count depended on the different amounts of activity administered in relation to the sensitivity of the counter. Thus, the first group of four subjects were whole-body counted ~7 hr after injection of [^{99m}Tc]DTPA immediately after the last urine collection was made, and this first whole-body measurement was normalized to the retention estimated from cumulative urinary radioactivity. At this time the average retention in these four subjects was 11% (range 7.4–17.1). Further whole-body measurements were made at ~24 and 30 hr postinjection. For the second group of four subjects, the first whole-body count was made at ~21 hr after injection and retention was estimated by calibrating with an anthropomorphic polyethylene phantom, uniformly filled with ^{99m}Tc. Subjects in this group were counted on one or two further occasions up to 30 hr. All whole-body counting was performed after bladder voiding and thus the whole-body retention curves exclude the contribution from radioactivity in bladder contents. Each whole-body biologic retention curve was fitted by a two-component exponential equation together with a small component assumed to have an infinite biologic half-life. These equations were used to estimate, for each subject, the total-body effective residence time of [^{99m}Tc]DTPA from which an average residence time was calculated as described in MIRD 12 (footnotes to Table 2). For reasons stated above, this value represents the residence time for total-body less bladder contents.

For dose calculations, it has been assumed, as in MIRD 12, that the source organs are kidneys, bladder contents, and the remainder of the body. In the latter, the remaining body activity is assumed to be distributed uniformly and its residence time is estimated by subtracting kidney residence time from that of the total body less bladder contents. For this purpose we have used the MIRD 12 value for the mean kidney residence time since this was measured quantitatively in subjects with normal renal function. While it would have been possible to estimate the actual residence times of bladder contents for each subject from his individual urinary excretion pattern, a more general approach was adopted, as in MIRD 12, by using the formula of Cloutier et al. (*4*) in conjunction with the whole-body retention equations to estimate residence times of bladder contents for a fixed voiding interval. The effects of considering four different values for this voiding sequence are shown later. In accordance with MIRD 12, a bladder model based on a constant bladder content of 200 ml (*5*) has been used, although a model which incorporates the changing bladder volume, the rate of urine flow, and the initial bladder content (*6*) may be more appropriate.

Estimates of doses to 23 target organs were made following the MIRD schema (*7*) using residence times calculated as outlined above and 'S' values (rad/μCi hr) obtained from the Oak Ridge National Laboratory. The 'S' value for the 'remaining body' as source organ was estimated using the formula of Coffey & Watson (*8*). For purposes of dose comparison, the MIRD 12 values of residence time in kidneys, bladder contents, and remaining body were used similarly to estimate doses to the same 23 target organs.

An effective dose equivalent (*9*) has been calculated as the weighted sum of the dose equivalent to the appropriate tissues at risk using risk weighting factors as defined in ICRP 26 (*10*). The actual target organ doses used for this calculation in the present study are indicated later (Table 2). The gonad dose was taken to be the mean of the values for ovaries and testes but, if required, specific effective dose equivalents for males or females can be readily estimated from the data provided. The concept of the effective dose equivalent, although introduced for the protection of radiation workers, has proved valuable in providing a single dose figure facilitating comparison of doses from different radiopharmaceuticals (*11*).

RESULTS AND DISCUSSION

The results of whole-body counting beyond 24 hr showed the presence of a small long-term retention component in all eight subjects. The average biologic elimination rate for this component was not significantly different from zero over the limited period available for study. Consequently, for each subject the final component was taken as the value measured at ~24 hr and, for purposes of dosimetry, its effective half-life was assumed to be equal to the half-life of ^{99m}Tc. The average value of this component was 2.5 ± 0.6 (s.d.) % of administered activity. Estimation of small long-term, whole-body retention components from cumulative urine activity alone is notoriously inaccurate. In our experience, retentions based on urine collections made for 24 hr have occasionally differed substantially from whole-body counting estimates of retention made at the same time, and the discrepancies invariably suggested loss of urinary activity. Data were rejected if these values differed by more than 5% of the administered activity. In our retention equations, the rapid components of elimination, which are less influenced by small losses of urinary radioactivity, have been determined from cumulative urine collections while the long-term retention has been more reliably estimated by whole-body counting. This final component is probably due to protein binding of [^{99m}Tc]DTPA (*12*). From the individual retention formulae, the equation representing the average biologic retention for total body less bladder contents is described by:

$$R_t = 0.312 \exp(-1.64t) + 0.663 \exp(-0.302t) + 0.025,$$

where R_t is the fractional retention after t hr, and the coefficients and exponents are the averages of the individual values estimated for the eight subjects. The above equation suggests that for a pure preparation of [^{99m}Tc]DTPA that does not result in a long-term, whole-body retention component, the average whole-body biologic retention equation in normals can be conveniently

described, for dosimetry purposes, by a single exponential having a half-time of 100 min; a value which we have used previously for dosimetry of GFR substances (*13,14*).

The mean residence time for total body less bladder contents in our eight subjects (Table 1) was 2.09 ± 0.30 (s.d.) hr, which is only 65% of the MIRD 12 value of 3.20 hr. Since we have used the MIRD value of 0.092 hr for the residence time in kidneys, our estimate for residence time in the remaining body is also lower than that given in MIRD 12. Residence times for activity in bladder contents are shown in Table 1 for five different voiding periods, 0, 1, 2.4, 3.5, and 4.8 hr. Where comparable, these values are higher than MIRD 12 values on account of the more rapid excretion of [^{99m}Tc]DTPA in our subjects. The use of the effective dose equivalent (μSv/MBq) has been adopted to provide a single dose value to compare the results of the present study with values estimated from data given in MIRD 12. For both studies, the organs whose dose estimates were used to calculate the effective dose equivalents are as listed in Table 2, chosen on the basis of dose estimates to 23 different target organs according to the criteria of ICRP 26 (*10*). The relative dose estimates given for the hypothetical situation when the bladder voiding period is zero (Table 1) reflect the higher MIRD 12 residence time in total body. However, for increasing bladder voiding periods, the effective dose equivalent in normal subjects increases more rapidly, with the result that for long voiding periods (e.g., 4.8 hr) it may be higher than that predicted for the patients in the MIRD 12 study, and the effective dose equivalents are equal for a voiding period of about 2.4 hr.

Thus, in the urinary excretion of [^{99m}Tc]DTPA, radioactivity in bladder contents plays an important part in determining radiation dose. Apart from its obvious influence on the dose to the bladder wall (Table 2) it also has a marked influence on the dose to nearby organs, in particular the gonads. For brevity, Table 2 includes only those target organs used for estimation of the effective dose equivalent. The dose values in Tables 1 and 2 indicate the substantial dose reduction that can be achieved by rapid bladder voiding following intravenous administration of [^{99m}Tc]DTPA. However, the values for bladder wall dose are highly dependent on the bladder model used for dosimetry, and when the changing bladder volume, the rate of urine flow and the initial bladder content are taken into account, these values may be higher and the dose-sparing effects of

TABLE 2
Absorbed Dose in Various Organs (μGy/MBq) for Different Bladder Voiding Periods Following i.v. Administration of [^{99m}Tc]DTPA to Normal Subjects

Organ	Bladder voiding period (hr)			
	1	2.4	3.5	4.8
Ovaries	2.13	3.41	4.42	5.57
Testes	1.41	2.22	2.87	3.60
Breast	0.89	0.90	0.90	0.90
Red marrow	1.89	2.28	2.59	2.93
Lungs	1.07	1.07	1.08	1.08
Thyroid	0.81	0.81	0.81	0.81
Bone surfaces	1.50	1.66	1.79	1.94
Bladder wall*	18.7	46.0	67.6	92.1
Kidneys	5.28	5.33	5.36	5.40
Small intestinal wall	1.76	2.28	2.70	3.17
Upper large intestinal wall	1.61	1.99	2.30	2.64
Lower large intestinal wall	2.06	3.35	4.38	5.54

* Based on the MIRD bladder model (constant 200 ml contents).

TABLE 1
Residence Times (hr) in Source Organs and Effective Dose Equivalent (μSV/MBq) for Different Bladder Voiding Periods Following i.v. Administration of [^{99m}Tc]DTPA to Man

Source organ	Residence time (hr)		Effective dose equivalent (μSv/MBq)	
	Present study	MIRD 12	Present study	MIRD 12*
Total body (excluding bladder contents)	2.087	3.20		
Kidneys	(0.092)†	0.092		
Remainder of body	1.995	2.84		
Bladder contents				
0 hr void	—	—	1.46	1.93
1 hr void	0.416	—	2.77	—
2.4 hr void	1.054	0.842	4.85	4.63
3.5 hr void	1.561	—	6.51	—
4.8 hr void	2.135	1.720	8.38	7.49

* Estimated from data presented in MIRD 12.
† Assumed same as MIRD 12 value.

shorter voiding periods may be much less for the bladder wall (*6,14*) than is predicted by the simple MIRD bladder model used here.

In conclusion, the dosimetry of [^{99m}Tc]DTPA in normal subjects is very similar to that in patients under study for hypertension due to the influence of bladder radioactivity and the short half-life of ^{99m}Tc. Despite the apparently longer whole-body retention of [^{99m}Tc] DTPA in patients under study for hypertension as reported in MIRD 12, the glomerular filtration rates, calculated from plasma radioactivity concentrations, were reasonably normal (*2*). In all probability our retention data for normal subjects represent the lower end of the range of a wide spectrum of values observed in patients and are presented as supplementary information which may be useful to other workers when taken in conjunction with the data of MIRD 12.

NOTES

* Amersham International, Buckinghamshire, UK.
† Byk-Mallinckrodt GMBH, Engelskirchen, FRG.

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