Biokinetic Behavior of Technetium-99m-DMSA in Children

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After intravenous administration of ^{99m}Tc-DMSA, biokinetic data were collected from studies on 24 children aged from 5 wk to 14.8 yr (15 normal and 9 with renal pathology). **Methods:** Patients were imaged with a gamma camera up to 30 hr postinjection and the absolute activities in the kidneys, liver, spleen, bladder, knees and whole body were estimated using an attenuation-corrected conjugate counting technique. Renal uptake and elimination rates and urinary excretion of radioactivity were also measured. **Results:** In children with normal renal function, maximal kidney uptake was 42.4% ± 5.4% and was taken up with a half-time of 1.0 ± 0.2 hr. Renal excretion amounted to 18.0% ± 4.4% at 24 hr and was lowest in children aged less than 1 yr. In children with abnormal renal function, apart from the expected reduction in renal uptake there was evidence of wider variations in uptake rate and increased urinary excretion. Mean uptakes in liver and spleen were approximately 5% and 2%, respectively, in all patients and uptake in knees, assumed to reside in the metaphyseal growth complexes, was 1.4%. **Conclusion:** In children with normal renal function, there was little evidence of age-dependent biokinetic factors other than reduced urinary excretion and lower uptake in knees in children aged less than 1 yr. The results therefore suggest that a single biokinetic model may suffice for radiation dosimetry purposes in normal children irrespective of age.

Key Words: technetium-99m-DMSA; pediatrics; biokinetics; age-dependency; renal function

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Technetium-99m-dimercaptosuccinic acid (^{99m}Tc-DMSA) is used in routine pediatric nuclear medicine for the diagnosis of kidney disorders (*1, 2*). Although the biokinetics of this radiopharmaceutical are well documented in the adult (*1, 3*), there is little quantitative information in children. The biokinetic behavior of certain radiopharmaceuticals in children and infants is known to differ from that in adults (*4, 5*). The aim of this study therefore, was to obtain biokinetic data from children of differing ages and degrees of renal dysfunction after the administration of ^{99m}Tc-DMSA in order to look for evidence of age-dependency and to examine the effects of renal pathology.

MATERIALS AND METHODS

Subjects

Twenty-four children (15 boys, 9 girls) aged from 5 wk to 14.8 yr (mean 5.6 yr) were selected from patients undergoing routine diagnostic ^{99m}Tc-DMSA imaging for investigation of renal impairment at the nuclear medicine department of Great Ormond Street Hospital for Children NHS Trust (Table 1). Serum creatinine measurements were made on all children within a few days prior to the DMSA studies. On the basis of the latter values and clinical evidence, the subjects were divided into two groups: normal renal function (15 children) and abnormal renal function (9 children).

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Normal Group. Fifteen children underwent ^{99m}Tc-DMSA imaging for clinical indications and had normal serum creatinine levels and no clinical evidence of renal insufficiency. Abdominal ultrasound examination was normal. One patient had a single kidney with compensatory hypertrophy and was included in this group.

Abnormal Group. Seven children with sustained elevation of serum creatinine levels were considered to be in chronic renal failure (CRF). Of these, three had renal dysplasia, one of which had sustained systemic hypertension (Patient 23). The four other children in CRF were hypertensive and on multiple drug therapies, two with Stage 4 neuroblastoma (Patients 6 and 15), one with dermatomyositis (Patient 7) and one with renovascular disease (Patient 17). There was no distinguishing feature in any of these seven children in clinical or biochemical terms to separate them into different subgroups. Two additional children had normal serum creatinine levels, one of which (Patient 8) had acute renal failure secondary to a urinary tract infection in an obstructed renal pelvis associated with marked proteinuria despite a normal ultrasound of the contralateral kidney. The obstruction had been drained for 48 hr before the scan and the patient had been on antibiotics for 7 days. The other child (Patient 14) was suffering from steroid-resistant nephrotic syndrome, had marked proteinuria and a ^{51}Cr-EDTA glomerular filtration rate (GFR) of 41 ml/min/1.73m^2.

Consent was obtained from parents or older children to perform extra imaging and make urine collections for the biokinetic study. Approval for these additional investigations was obtained from the hospital's ethical committee.

Radiopharmaceutical Administration

Technetium-99m-DMSA was prepared according to the manufacturer's recommendations and chromatographically checked for free pertechnetate, which was always less than 0.1%. The activity for injection was calculated using a body surface area scaling factor (*6*) on the adult dose activity of 100 MBq. The activity in the dose syringe was measured in a radionuclide assay calibrator.

Gamma Camera Measurements

Imaging of dose syringes and patients was performed on a gamma camera fitted with a low-energy, high-sensitivity collimator. Prior to injection, measurements were performed to obtain the midplane count-rate of the injected activity (see Appendix) for subsequent calculation of percentage organ uptake in patients. The dose syringe was imaged in an acrylic block on the patient couch placed directly over the gamma camera. The acrylic block was used to ensure that dead-time losses were negligible. A correction was made for the attenuation through the block in order to obtain the dose syringe count-rate on the patient couch. The dose syringe alone was then placed sequentially on the supine patient over the kidneys, bladder and one knee and imaged through the patient (transmitted count-rate). It was assumed that measurements over the left and right kidneys were also appropriate for the spleen and liver, respectively. After the injection, the residual activity in the syringe and infusion set was measured by imaging on the patient couch.

TABLE 1
Pharmacokinetics of Technetium-99m-DMSA in Children

Patient no.	Age	Sex	Clinical details	Creatinine (upper limit) μmole.l^{-1}	Left kidney Uptake (%)	Left kidney λ_u	Left kidney λ_e	Right kidney Uptake (%)	Right kidney λ_u	Right kidney λ_e	Global uptake (%)	Liver uptake (%)	Spleen uptake (%)	Knees uptake (%)	% Excreted in urine 6 hr	% Excreted in urine 24 hr
11	14.8 yr	F	Normal	61 (102)	24.2	0.64	0	25.2	0.61	0	49.4	4.5	2.7	1.4	10.8	16.5
18	13.0 yr	F	Normal	56 (102)	18.8	0.72	0.001	18.6	0.99	0	37.4	5.8	3.2	1.3	No data	No data
2	12.8 yr	M	Normal	70 (120)	27.0	0.75	0.018	22.4	0.85	0.005	49.4	2.4	0.8	4.1	9.3	20.5
10	11.0 yr	M	Normal	62 (81)	22.9	0.46	0.005	24.2	0.49	0.001	47.1	5.4	4.0	3.1	13.4	22.0
21	10.2 yr	M	Normal	40 (81)	17.0	0.83	0.012	20.2	0.74	0.012	37.2	6.1	2.6	1.0	No data	No data
16	8.2 yr	F	Normal	38 (74)	18.6	0.68	0.007	22.1	0.92	0.005	40.7	2.1	1.8	1.9	18.7	23.1
1	6.1 yr	F	Normal	31 (70)	No kidney			44.0	0.76	0.011	44.0	5.7	0.9	1.6	7.5	16.6
22	4.1 yr	F	Normal	38 (65)	20.7	0.72	0.017	21.9	0.68	0.016	42.6	4.3	1.6	0.9	13.7	20.4
12	1.3 yr	M	Normal	28 (51)	19.5	0.56	0.017	18.6	0.77	0.011	38.1	3.3	0.8	1.1	13.8	25.0
9	11.5 mo	F	Normal	32 (51)	23.5	0.77	0.008	25.9	0.77	0.011	49.4	5.1	2.6	0.6	9.0	15.8
13	8 mo	M	Normal	25 (53)	15.8	0.47	0.018	16.5	0.62	0.018	32.3	1.2	1.0	0.9	13.0	21.0
24	6 mo	M	Normal	29 (53)	22.4	0.57	0.005	26.0	0.55	0.006	48.4	7.4	1.8	0.7	3.0	11.0
4	5 mo	F	Normal	39 (53)	19.4	0.92	0.006	19.6	0.55	0.010	39.0	7.3	1.3	0.4	9.3	14.3
5	4 mo	M	Normal	20 (61)	23.0	0.64	0.016	19.1	0.70	0.012	42.1	6.3	1.6	0.7	6.2	11.4
3	7 wk	M	Normal	29 (61)	19.5	0.73	0.009	19.9	0.76	0.004	39.4	1.7	1.5	1.3	7.8	15.8
23	5.2 yr	M	CRF (D)	70 (65)	No kidney			28.1	0.54	0	28.1	5.0	1.8	2.2	19.6	30.0
19	3.5 mo	F	CRF (D)	67 (61)	6.7	1.07	0.011	9.0	0.60	0.017	15.7	7.2	3.1	1.2	14.9	30.5
20	5 wk	M	CRF (D)	77 (61)	1.7	0.84	0.009	4.5	0.64	0.028	6.2	5.2	2.3	1.4	17.0	36.0
17	12.5 yr	M	CRF (O)	188 (81)	5.7	0.17	0.006	7.0	0.18	0.002	12.7	6.3	1.6	0.6	3.1	6.7
7	5.1 yr	M	CRF (O)	49 (65)	13.1	0.63	0.004	12.1	0.57	0.007	25.2	2.6	0.5	1.2	14.0	24.3
6	2.8 yr	M	CRF (O)	68 (56)	No kidney			5.1	0.61	0.021	5.1	4.0	1.5	1.7	34.0	47.9
15	2.3 yr	M	CRF (O)	55 (51)	No kidney			9.1	0.45	0.025	9.1	6.7	0.8	1.4	22.0	No data
14	11.2 yr	M	Nephrotic syndrome	54 (81)	11.3	0.48	0.008	8.0	0.73	0.006	19.3	4.4	2.8	1.3	32.1	43.0
8	7.0 yr	F	ARF	67 (70)	2.9	0.61	0	18.0	0.68	0.007	20.9	2.6	3.2	1.7	6.0	15.0

CRF (D) = chronic renal failure (dysplasia); CRF (O) = chronic renal failure (other); ARF = acute renal failure; Global = both kidneys combined; λ_u = renal uptake rate (hr^{-1}); λ_e = renal elimination rate (hr^{-1}).

Following injection of the ^{99m}Tc-DMSA, 60-sec anterior and posterior images of the patient were made at 30 min 1, 2, 4, 6, 24 and 30 hr. Views included kidneys, bladder, liver, spleen and knees. In addition, the injection site was imaged and estimates of extravasation of the injectate were always less than 3% of the full syringe activity (0–2.8%).

Whole-Body Counting

Immediately after each set of organ images had been obtained, whole-body retention measurements were made using the gamma camera with the collimator removed. The face of the camera was aligned vertically and the patient stood or was held at a distance sufficient to avoid significant dead-time losses and reduce geometry effects. This distance remained constant throughout each patient study. Both anterior and posterior measurements were made on each occasion.

Excreted Radioactivity

Urine was collected every hour for the first 6 hr and then at natural voids up to 30 hr. Urine bottles and diapers were imaged on the patient couch and self-absorption corrections were made for diapers and different volumes of urine, from previously made calibrations.

Data Processing

All acquisition data were stored on computer, including counts and measurement times. For all images of organs, excreted activity and dose syringe, count-rates were determined by choosing suitable rectangular regions of interest (ROIs), and a region surrounding each ROI was used for background correction. All count-rates were corrected for radioactive decay. The liver and spleen ROIs were drawn to include the right kidney and left kidney, respectively, and corrections were made for background and kidney activity. The geometric mean of conjugate pairs of anterior and posterior ROI counts was used to obtain the midplane count-rate of each organ at the various measurement times. The percentage uptake in each organ was calculated from the latter values and the midplane count-rate of the injected dose which was obtained for each organ. No correction for organ thickness (*7*) was made, as this is relatively small for pediatric subjects. In all the measurements with the gamma camera placed above the couch, count-rates were multiplied by the factor 0.94, to compensate for the effect of couch attenuation, which is inherent in posterior measurements.

The first whole-body geometric mean count-rate, made before any excretion had occurred, was taken to be the 100% whole-body retention value. All subsequent whole-body measurements were related to this value and, after correction for radioactive decay, whole-body and organ retention data were expressed in terms of percentage of administered activity. The pharmacokinetic behavior of intravenously administered ^{99m}Tc-DMSA in whole-body, liver and spleen was described by instantaneous uptake followed by a clearance phase. On the other hand, the kidneys demonstrated a distinct initial uptake phase to a maximum value followed by a clearance phase. The clearance phase was described by a two-compartment model in the case of the whole-body and by a single-compartment model for kidneys, liver and spleen. A computer program was written to give a least-squares single-exponential fit passing through the maximum value, to the initial uptake phase of the time-activity curves and a PLOT program, supplied by the Oak Ridge Institute of Science and Education (ORISE), was used to give a least-squares single- or bi-exponential fit to clearance phases using an iterative procedure.

Statistical Analysis

Summary statistics of measured data are presented as mean ± 1 s.d. and differences between mean values for different subject groups were tested for significance using Student's t-test. Where appropriate, differences between observed data for left and right kidneys were tested using the paired sample t-test. Correlation coefficients between various datasets were calculated and tested for significance by t-test.

RESULTS AND DISCUSSION

Recovery of Administered Activity at 24 Hours

Measurements up to 30 hr were achieved in 14 patients, with 24-hr measurements in 23 patients. Of the latter, urine collections were incomplete in 6 and whole-body counting was unsatisfactory in 3. In the remaining 14 patients, the mean 24-hr recovery of administered activity (cumulative urinary excretion plus whole-body retention) was 97.3% ± 4.4%. In four patients, an early urine sample was lost and the lost activity was estimated from whole-body retention data. When these four patients were included in the above group, the mean 24-hr recovery was 97.6 ± 4.0% (n = 18).

Maximal Renal Uptake of Technetium-99m-DMSA

Normal Renal Function. In 15 normal patients aged from 7 wk to 14.8 yr the maximal global renal uptake of ^{99m}Tc-DMSA was 42.4% ± 5.4% of administered activity (Table 1). This value is in good agreement with the results of Arnold et al. (*1*) who found a mean value of 44% in 6 normal volunteers (presumably adults) and those of Elliott et al. (*3*) who observed in an unspecified group of subjects that the plateau for global renal uptake was 45%–50%. Previous studies in children reported a similar value (*5*). One of the patients in the present study had a unilateral functioning kidney which showed compensated uptake of 44.0%, close to the mean for patients with normal bilateral function. In the other 14 patients, there was no significant difference between maximal uptake values for the individual kidneys (paired difference 0.56% ± 2.5%; $p > 0.4$).

There were nine children over 1 yr of age and six under 1 yr of age. Average maximal global renal uptakes were 42.9% ± 4.9% and 41.8% ± 6.4%, respectively, and there was no significant difference between the means of these two groups ($p > 0.7$). Similarly, there was no significant age-dependency in individual kidney uptake ($p > 0.7$). This result was not entirely unexpected, as the mean age of the children under 1 yr was 6 mo, at which age the maturation of the tubules almost should be complete and therefore there would be no age-dependency of renal uptake. This is supported with evidence from human studies that the maturation of the kidney tubules (as measured by ^{99m}Tc-MAG3 clearance) is near completion at 6 mo of age (98.6% of the adult value) (*8*). Similar results have been found in ^{99m}Tc-DMSA studies on suckling pigs, where global kidney uptake approached expected normal values after the neonatal period (age 4–7 wk) (*9*). These findings suggest that the global uptake of ^{99m}Tc-DMSA is similar in the sample population that we have investigated. However, it is not possible to draw conclusions from the present study about renal uptake in neonates and infants less than 3 mo of age owing to insufficient patients within this age range.

Abnormal Renal Function. Nine patients with renal pathology (three dysplasia with CRF; four CRF for other reasons; one nephrotic syndrome; one acute renal failure) were investigated. Taking all abnormal patients together, the mean global kidney uptake was 15.8% ± 8.2%, including the results of three patients with single kidneys, the uptake values of which were 5.2%, 9.1% and 28.1% of administered activity. The mean global uptake in this group is significantly different from that of the normal group ($p < 0.001$). The mean global renal uptakes of the three children with dysplasia and the four with other pathology, all in CRF, were 16.7% ± 11.0% and 13.0% ± 8.7%, respectively, and not significantly different ($p > 0.6$). Furthermore, these means were not significantly different from the uptake value for single studies in a nephrotic patient (19.3%) and an acute renal failure patient (20.9%). However, larger studies would be needed to establish whether significant differences in kidney uptake exist between different types of renal pathology.

Rates of Renal Uptake of Technetium-99m-DMSA

The kidney biological retention data were described as the sum of exponential uptake and elimination components (Table 1). The rate constants of these two components (λ_u and λ_e) have been used to compare renal kinetics in the different patient groups.

Normal Renal Function. In 15 children with normal renal function, the mean values of λ_u for left and right kidneys were 0.67 ± 0.13 hr^{-1} (n = 14) and 0.72 ± 0.14 hr^{-1} (n = 15), respectively, and a paired t-test showed no significant difference (0.04 ± 0.16 hr^{-1}; $p > 0.3$; n = 14). Consequently, the left and right kidney uptakes were considered as a single group, giving a mean λ_u value of 0.70 ± 0.14 hr^{-1} (n = 29). The mean uptake half-time in normals was 1.0 ± 0.2 hr which agrees well with the results of Arnold et al. (*1*) and Elliott et al. (*3*), and the time-to-maximum uptake was 6.8 ± 0.5 hr. When this group was subdivided by age (less than or greater than 1 yr), the mean λ_u values of 0.67 ± 0.13 hr^{-1} (n = 12) and 0.72 ± 0.14 hr^{-1} (n = 17), respectively, were not significantly different ($p > 0.3$). There was no evidence of age-dependency of renal uptake rate in our group of normal children.

Abnormal Renal Function. In nine children with abnormal renal function, only gamma camera images from 1 hr were used to calculate the renal uptake rates, since at 30 min the combination of low uptake and high background resulted in unreliable estimates of uptake. Taking all abnormal patients as a single group, the mean uptake rates of left and right kidneys were 0.63 ± 0.31 hr^{-1} (n = 6) and 0.56 ± 0.16 hr^{-1} (n = 9), respectively, and were not significantly different on paired t-test (0.07 ± 0.25 hr^{-1}; $p > 0.5$; n = 6). The mean value of combined left and right kidney uptake rates was 0.59 ± 0.22 hr^{-1} (n = 15). This value was significantly different from that of the normal group ($p = 0.05$). There was, however, a much wider range of λ_u values in the abnormal group (0.17 to 1.07 hr^{-1}) compared with that of the normal group (0.46 to 0.99 hr^{-1}). One patient in CRF (Patient 17) had significantly lower rates of kidney uptake (0.17 hr^{-1}) than those of the rest of the abnormals. Excluding this patient leads to a mean value for λ_u in the other abnormal patients of 0.65 ± 0.16 hr^{-1} which is not significantly different from that of the normal group.

Rates of Renal Elimination of Technetium-99m-DMSA

The mean kidney biological elimination rate (λ_e) in the normal group was 0.009 ± 0.006 hr^{-1} (n = 29) and in the abnormal group was 0.0108 ± 0.0086 hr^{-1} (n = 14), and there was no significant difference between them ($p > 0.4$) (Table 1). In the former, there was no significant difference ($p > 0.3$) between λ_e values from children older or younger than one year.

Urinary Excretion

The renal clearance of ^{99m}Tc-DMSA is demonstrated by the observed 6-hr and 24-hr cumulative urine activity (Table 1).

Normal Renal Function (n = 15). In two children (Patients 18 and 21), urine samples were lost and are excluded from the analysis. In the other 13 patients, these values were 10.4% ± 4.1% at 6 hr and 18.0% ± 4.4% at 24 hr. The 24-hr urinary excretion value for patients younger than 1 yr (14.9% ± 3.7%; n = 6), was significantly lower ($p = 0.008$) than patients older than 1 yr (20.6% ± 3.2%; n = 7). In children less than 1 yr of age, the normal global renal uptake of DMSA, together with the low urinary excretion, results in a higher proportion of the injected DMSA distributed throughout the body, seen on clinical images as a high background. This observation has been interpreted by some clinicians to represent poor uptake by the kidneys. The present study, however, shows normal renal uptake of DMSA. A possible explanation for the low urine excretion may relate to the maturation of the kidney where the rate of tubular maturation is greater than GFR and therefore in children less than 1 yr of age the low GFR will result in a lower amount of DMSA in the glomerular filtrate and so a lower proportion of DMSA in the urine.

Abnormal Renal Function. Failure to collect overnight urine invalidated the estimate of 24-hr urine excretion in one patient (Patient 15). Another patient in CRF (Patient 17), exhibited a different biokinetic pattern from all the other patients in which the kidney uptake, kidney uptake rate and urinary excretion were all low (see below). Excluding Patient 17, and the 24-hr urine data of Patient 15, the mean cumulative activity in urine of the other abnormal patients was 20.0% ± 9.4% (n = 8) at 6 hr and 32.4% ± 11.1% (n = 7) at 24 hr and these values were significantly higher ($p < 0.0025$) than values for the normal group. One patient with steroid resistant nephrotic syndrome (Patient 14) does show a very high urinary loss of DMSA coupled with low renal uptake. The pathology affects the glomerulus and results in glomerular proteinuria and may account for the high urinary loss. Varying degrees of tubular damage are seen in this condition.

There is increased urinary excretion of DMSA in children in CRF yet the kidney uptake is reduced. Urinary excretion is believed to result from the non-protein bound DMSA in the normal patients. In pathology it is associated either with glomerular proteinuria or with renal tubular pathology. In CRF (including dysplasia), there is pathology in both the glomerulus and tubule, resulting in low kidney uptake and high urinary excretion, but the total 24-hr activity in the kidneys and urine is on average 11.5% less in abnormal patients than it is in normal patients. This suggests that there is some distribution of the DMSA into the extracellular compartment. The dose of DMSA injected is very small yet the tubular maximum may be exceeded in these poorly functioning kidneys. The theory suggested is that the damaged tubule takes up as much DMSA as possible, but this is a relatively small amount, resulting in a low extraction fraction. In addition, either the tubular cell can not retain the DMSA or there is glomerular proteinuria and so a high proportion passes into the urine. This results in the high extravascular activity with low renal, and high urinary activity. Patient 17 is unique in this series, having the most severe CRF due to progressive renovascular disease over a 2-yr period. The renovascular disease was shown on arteriography to involve only the small intrarenal vessels diffusely throughout both kidneys. This raises the possibility that all the nephrons were suffering from progressive subacute ischaemia with a consequent low renal extraction fraction of DMSA. The low urine excretion suggests that the small proportion of DMSA taken up by the tubules was retained within the tubules and the low GFR prevented free DMSA escaping into the glomerular filtrate. The low GFR seen in a child with sepsis and in acute renal failure (Patient 8) may also explain why despite the low global renal uptake of DMSA there is nevertheless low 24-hr urinary excretion.

When normal and abnormal patients were considered as a single group, there was a significant negative correlation between global kidney uptake and both the 6-hr ($r = -0.53$; $p < 0.02$; n = 22) and 24-hr ($r = -0.59$; $p < 0.005$; n = 21) cumulative urinary excretion. This result shows that when renal uptake is reduced, some of the excess ^{99m}Tc-DMSA is cleared to urine.

Uptake in Liver and Spleen

Normal Renal Function. The mean uptake of ^{99m}Tc-DMSA in liver and spleen in 15 children with normal renal function was 4.6% ± 2.0% and 1.9% ± 1.0%, respectively (Table 1). Comparison of these data with those found by other workers is difficult because of the lack of quantitative data in the literature. Elliott et al. (*3*) for example, report that uptake into the liver and spleen constitutes some 5% of administered activity. In 6 normal children younger than 1 yr, the values of 4.8% ± 2.8% for liver uptake and 1.6% ± 0.6% for spleen uptake were not significantly different ($p > 0.6$ and > 0.4, respectively) from those of the 9 children older than 1 yr, i.e., 4.4% ± 1.5% and 2.0% ± 1.2%. Considering all normal patients as a single group, correlations were tested between liver or spleen uptake and age, global kidney uptake and urinary excretion. Significant correlation was found only between liver uptake and 24-hr urine activity ($r = -0.66$; $p < 0.02$).

Abnormal Renal Function. The mean values of liver uptake (4.9% ± 1.7%) and spleen uptake (2.0% ± 1.0%) were not significantly different from normal values ($p > 0.6$) (Table 1). Liver uptake in patients in CRF with dysplasia (n = 3) was not significantly different ($p > 0.5$) from that in patients in CRF with other pathology (n = 4) but the spleen uptake in dysplasia patients (2.4% ± 0.7%) was significantly greater ($p < 0.05$) than that in CRF patients with other pathology (1.2% ± 0.6%). No significant correlations were found between liver or spleen uptake and age, global kidney uptake and urinary excretion ($p > 0.2$ in all cases).

Liver and spleen uptakes were also examined for evidence of correlation with the residual amount of ^{99m}Tc-DMSA not accounted for in kidneys, liver, spleen, knees and urine at 24 hr. There was no significant correlation between liver uptake and residual activity either in the normal group or in all the patients considered together ($p > 0.6$). A negative correlation ($r = -0.64$; $p < 0.02$; n = 13) between spleen uptake and residual activity was found in normals but not in the total group of subjects ($p > 0.3$). Thus, although the amount of residual ^{99m}Tc-DMSA activity varied widely (24–73%), there was no evidence of this affecting the uptake in liver and spleen. This result suggests a saturation effect on DMSA uptake in liver and spleen.

Uptake in Knees

Combined uptake in knees of 15 children with normal renal function was 1.40% ± 0.99% with a range from 0.4% to 4.1% of administered activity (Table 1). The mean uptake in 6 children younger than one year (0.77% ± 0.31%) was significantly lower ($p < 0.025$) than that in 9 children older than 1 yr (1.82% ± 1.08%). In nine abnormal children, the mean uptake in knees (1.40% ± 0.44%) was not significantly different from that of the normal group.

CONCLUSION

There is considerable current effort on an international scale to investigate the existence of age-dependent parameters which

have a bearing on radiation dose and its effects (*10*). The study of radiopharmaceutical dosimetry forms a part of this overall strategy. It is essential for this purpose to have a comprehensive and reliable database of biodistribution and biokinetic information. The present work was carried out to examine evidence for age-dependent as well as pathological effects in children over a wide age range who were administered ^{99m}Tc-DMSA for diagnostic purposes.

Our main findings in this study are that children with normal renal function had a mean kidney uptake of 42% (maximum); a kidney uptake half-time of 1 hr and elimination half-time of 77 hr; and a mean urinary output at 24 hr of 18%. However, children younger than 1 yr showed a significantly lower 24-hr urinary output than children older than 1 yr. In contrast, children in renal failure had a reduced mean kidney uptake; elimination half-times similar to children with normal kidneys; and a higher mean 24-hr urinary excretion than that in normal children. One patient in CRF, due to ischaemia from progressive renovascular disease, exhibited a different biokinetic pattern in which kidney uptake, kidney uptake rate and urinary excretion were all low.

The results of our study have demonstrated that there is little evidence of age-dependency apart from reduced urinary excretion and knee uptake in children with normal renal function and younger than 1 yr. The reduced urinary excretion in younger children will have implications for the radiation dosimetry of total body and bladder. However, the differences are relatively small and in general, the biokinetics in normal children can be approximated by those observed in normal adults. This result lends support to the use of adult biokinetic data to predict pediatric radiation dose estimates for this radiopharmaceutical, as in previous reports (*11*). As expected, in pathological cases of renal disease the major observed difference compared with normal biokinetics is a reduction in global kidney uptake. It remains to be seen how the changes seen in renal pathology tend to alter the overall pattern of radiation dosimetry of ^{99m}Tc-DMSA.

APPENDIX

Midplane Count-Rate

To obtain the midplane count-rate of the injected activity, the dose syringe was counted on the patient couch with the camera underneath and then through the patient at the level of the kidneys, bladder and knee (the transmitted count-rate). The geometric mean of the count-rate of these conjugate pairs, was taken to be equivalent to the count-rate of the dose syringe at midplane depth.

This procedure eliminates the problem of estimating the depth of the organs and making assumptions about the effective attenuation coefficient. It also compensates for variations in effective thickness of the body, e.g., spine, lungs. In practice however, there is always a small residue of activity left in the dose syringe and infusion set. The conjugate method requires the count-rate of the activity in the dose syringe that is actually injected. Clearly this is not possible to measure, but the theory described below shows how this can be achieved.

Midplane count-rate of injected activity:

$$M(\text{counts} \cdot \text{min}^{-1}) = (A - r)\exp(-\mu t/2) \qquad \text{Eq. 1}$$

where μ (cm^{-1}) = the effective attenuation coefficient; t (cm) = the thickness of the body measured over the organ; A (counts $\cdot$ min^{-1}) = count-rate of the dose syringe as measured on the camera; and r (counts $\cdot$ min^{-1}) = count-rate of the residue in the dose syringe as measured on the camera after the injection. The transmitted count-rate of the dose syringe,

$$T(\text{counts} \cdot \text{min}^{-1}) = A\exp(-\mu t).$$

Substituting for $\exp(-\mu t)$ in Equation 1 above gives:

$$M = (A - r)(T/A)^{1/2}.$$

Therefore, the calculation of midplane count-rate of the injected activity does not require knowledge of the values of the effective attenuation coefficient and patient thickness. The estimated midplane count-rate is given by the count-rate of the injected activity times $(T/A)^{1/2}$ and if there is no residue, this reduces to the geometric mean of the count-rates of the dose syringe measured on the camera and through the patient, i.e $(AT)^{1/2}$.

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